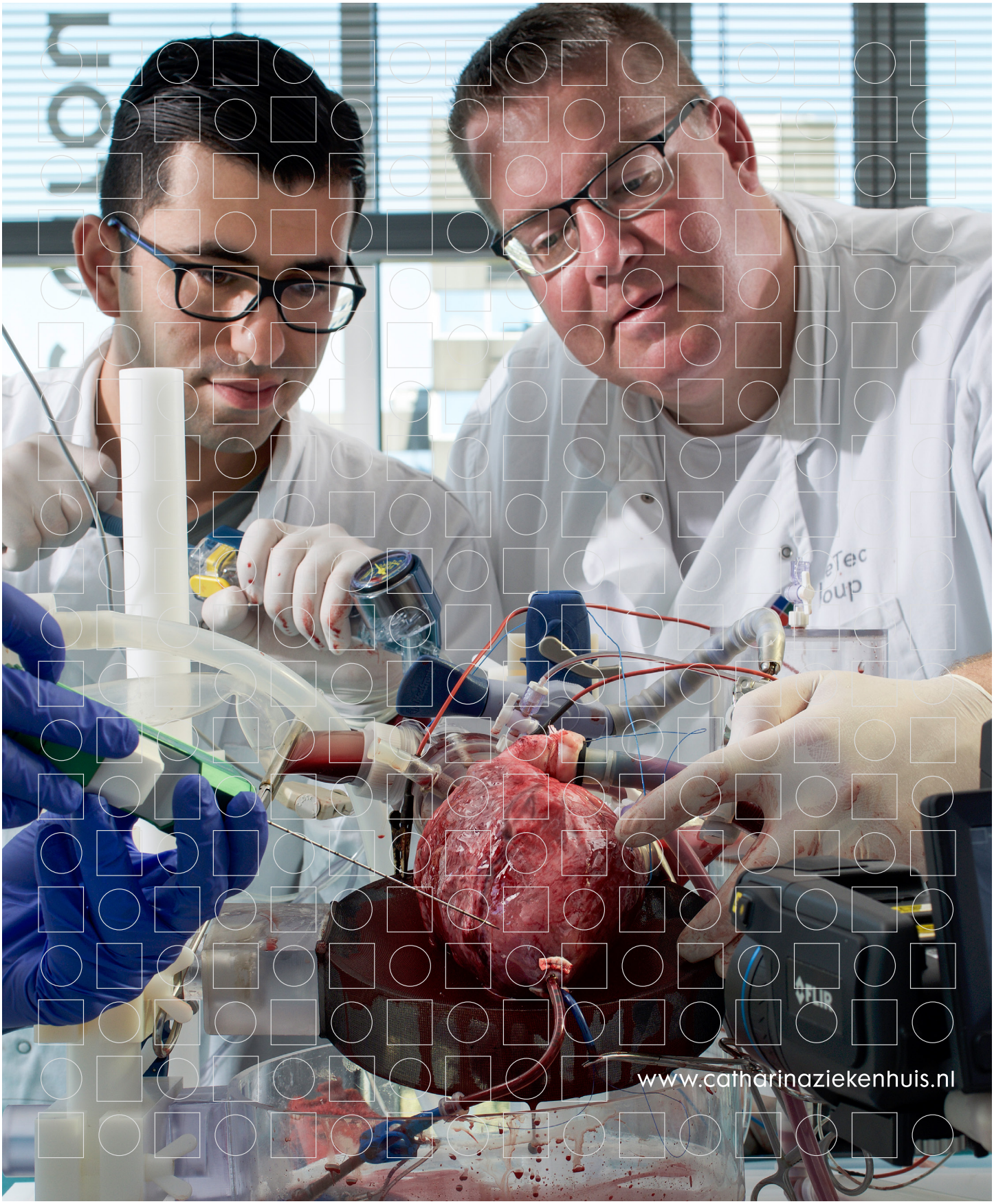
Wetenschappelijk jaaroverzicht

catharina
een santeon ziekenhuis

2018



Wetenschappelijk Jaaroverzicht 2018

Onder redactie van:
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Een uitgave van het Catharina Ziekenhuis
Eindhoven, 2019

Inhoudsopgave

Medical science has proven time and again that when the resources are provided, great progress in the treatment, cure, and prevention of disease can occur.

Michael J.Fox (1961)
Acteur

Algemeen Klinisch Laboratorium

A value proposition for trough level-based anti-TNFa drug dosing

Scharnhorst V, Schmitz EM, van de Kerkhof D, Derijks LJ, Broeren MA

Clin Chim Acta. 2018 Dec 3;489:89-95

Treatment of inflammatory bowel diseases and rheumatic disorders with anti-tumor necrosis factor alpha (TNFa) drugs is expensive, while a significant proportion of patients does not show adequate clinical response. Therapeutic drug monitoring (TDM) enables patient-specific anti-TNFa therapy. The role of laboratory tests in clinical care has recently been described in a value proposition framework. It describes care processes, stakeholders, costs, risks, benefits and patient outcomes based on the use of a laboratory test in a clinical care pathway. We have applied this concept to the use of TDM for anti-TNFa drugs, describing evidence that supports the intervention and its cost effectiveness, steps that need to be adjusted in the care pathway, possible treatment algorithms and measures to assess adoption of this framework into clinical practice. For effective TDM, an assay for measurement of drug levels together with appropriate target ranges and an anti-drug-antibody assay have to be implemented. Also, instead of only reporting the drug concentration, laboratorians, pharmacists and clinicians should deliver added value by introducing a TDM-based treatment algorithm into clinical practice. Thus, to maximize effectiveness of TDM of anti-TNFa therapy in routine care, adjustment of current care pathways and cooperation of many stakeholders are needed.

Impactfactor 2.926

Age of platelet concentrates and time to the next transfusion

Caram-Deelder C, van der Bom JG, Putter H, Leyte A, **Kerkhof DV**, Evers D, Beckers EA, Weerkamp F, Hudig F, Zwaginga JJ, Rondeel JMM, de Vooght KMK, Péquériaux NCV, Visser O, Wallis JP, Middelburg RA

Transfusion. 2018 Jan 58(1):121-131. Epub 2017 Oct 31

BACKGROUND:

Storage time of platelet (PLT) concentrates has been negatively associated with clinical efficacy outcomes. The aim of this study was to quantify the association between storage time of PLT concentrates and interval to the next PLT transfusion for different types of PLT components, stored for up to 7 days and transfused to transfusion-dependent hematooncology patients with thrombocytopenia.

STUDY DESIGN AND METHODS:

From a cohort of patients from 10 major Dutch hospitals, patients were selected whose transfusion patterns were compatible with PLT transfusion dependency due to hematooncologic disease. Mean time to the next transfusion and mean differences in time to the next transfusion for different storage time categories (i.e., fresh, <4 days; intermediate, 4-5 days; and old, >5 days) were estimated, per component type, using multilevel mixed-effects linear models.

RESULTS:

Among a cohort of 29,761 patients who received 140,896 PLT transfusions we selected 4441 hematooncology patients who had received 12,724 PLT transfusions during periods of PLT transfusion dependency. Transfusion of fresh, compared to old, buffy coat-derived PLTs in plasma was associated with a delay to the next transfusion of 6.2 hours (95% confidence interval [CI], 4.5-8.0 hr). For buffy coat-derived PLTs in PAS-B and -C this difference was 7.7 hours (95% CI, 2.2-13.3 hr) and 3.9 hours (95% CI, -2.1 to 9.9 hr) while for apheresis PLTs in plasma it was only 1.8 hours (95% CI, -3.5 to 7.1 hr).

CONCLUSION:

Our results indicate that the time to the next transfusion shortens with increasing age of transfused buffy coat-derived PLT concentrates. This association was not observed for apheresis PLTs.

Impactfactor 3.423

Cholestatic liver injury as a side-effect of dabigatran and the use of coagulation tests in dabigatran intoxication and after reversal by idarucizumab in bleeding and sepsis

Comuth WJ, Haase AM, Henriksen LØ, Malczynski J, **van de Kerkhof D**, Münster AB

Scand J Clin Lab Invest. 2018 Feb - Apr;78(1-2):1-5. Epub 2017 Nov 17

Idarucizumab, an antidote specific for dabigatran, became available recently. Dabigatran is not associated with increased risk of hepatotoxicity in comparison with warfarin, but it is seen as a rare side-effect. Cases of cholestatic liver injury due to dabigatran have not been reported previously. We present a case of severe gastro-intestinal bleeding with underlying dabigatran intoxication in a patient with renal failure and the effect of reversal of dabigatran using idaruzicumab on coagulation assays. International normalized ratio (INR) and activated partial thromboplastin time (APTT) results were elevated in a setting of sepsis, possibly due to liver failure. INR and APTT can be elevated if sepsis is complicated by disseminated intravascular coagulation (DIC) or liver failure, making it challenging to determine dabigatrans contribution to their prolongation. A rebound effect after administration of idarucizumab and slow elimination of dabigatran due to reduced kidney function could be detected using the Hemoclot® diluted thrombin time (dTT) in this situation, in contrast to with non-dilutional assays. Before admission, cholestatic liver injury started shortly after initiation of dabigatran etexilate therapy. As no other cause was found,

this liver injury was likely to be drug-induced. Bleeding cessated promptly after administration of idarucizumab in dabigatran intoxication.

In conclusion, the anticoagulant effect of dabigatran can be measured by Hemoclot® dTT in sepsis and cholestatic liver injury was seen as a possible rare side-effect of dabigatran treatment.

Impactfactor 1.498

Clinical performance of a new point-of-care cardiac troponin I test

Christ M, Geier F, Blaschke S, Giannitsis E, Khellaf M, Mair J, Pariente D, **Scharnhorst V**, Semjonow V, Hausfater P

Clin Chem Lab Med. 2018 Jul 26 56(8):1336-1344

BACKGROUND:

We evaluated the clinical performance of the Minicare cardiac troponin-I (cTnI), a new point-of-care (POC) cTnI test for the diagnosis of acute myocardial infarction (AMI) in a prospective, multicentre study (ISRCTN77371338).

METHODS:

Of 474 patients (=18 years) admitted to an emergency department (ED) or chest pain unit (CPU) with symptoms suggestive of acute coronary syndrome (ACS; =12 h from symptom onset), 465 were eligible. Minicare cTnI was tested immediately, 3 h and 6 h after presentation. AMI diagnoses were adjudicated independently based on current guidelines.

RESULTS:

The diagnostic performance of the Minicare cTnI test at 3 h was similar for whole blood and in plasma: sensitivity 0.92 vs. 0.90; specificity 0.91 vs. 0.90; positive predictive value (PPV) 0.68 vs. 0.66; negative predictive value (NPV) 0.98 vs. 0.98; positive likelihood ratio (LR+) 10.18 vs. 9.41; negative likelihood ratio (LR-) 0.09 vs. 0.11. The optimal diagnostic performance was obtained at 3 h using cut-offs cTnI >43 ng/L plus cTnI change from admission =18.5 ng/L: sensitivity 0.90, specificity 0.96, PPV 0.81, NPV 0.98, and LR+ 21.54. The area under the receiver operating characteristics (ROC) curve for cTnI whole blood baseline value and absolute change after 3 h curve was 0.93.

CONCLUSIONS:

These data support the clinical usefulness of Minicare cTnI within a 0 h/3 h-blood sampling protocol supported by current guidelines for the evaluation of suspected ACS.

Impactfactor 3.556

Comprehensive characteristics of the anticoagulant activity of dabigatran in relation to its plasma concentration

Comuth WJ, Henriksen LÃ, **van de Kerkhof D**, Husted SE, Kristensen SD, de Maat MPM, Munster AB

Thromb Res. 2018 Apr 164:32-39. Epub 2018 Feb 17

BACKGROUND:

Issues with laboratory measurement of dabigatran include: 1. Do coagulation assays reflect dabigatran plasma concentrations? 2. Do samples from patients treated with dabigatran have the same coagulability as dabigatran-spiked samples from healthy volunteers? 3. What is the long-term stability of dabigatran after storage at -80?°C? This study aims to evaluate these questions.

MATERIALS AND METHODS:

Ecarin chromogenic assay (ECA), a laboratory-developed diluted thrombin time (LD-dTT), prothrombin time (PT) and activated partial thromboplastin time (APTT) and ROTEM® were used to measure dabigatran anticoagulant activity and liquid chromatography-tandem mass spectrometry (LC-MS/MS) to measure dabigatran plasma concentrations. ROTEM® (EXTEM, INTEM, FIBTEM) was performed in whole blood and the other assays in platelet poor plasma (PPP), both in samples spiked with dabigatran (0, 25, 50, 100, 250, 500 and 1000?ng/mL) from healthy donors and in ex vivo samples from patients treated with dabigatran etexilate. Citrated PPP samples were frozen and stored at -80?°C, 1, 3, 6 and 12?months until analysis.

RESULTS:

EXTEM and FIBTEM clotting time (CT), ECA and LD-dTT correlate well with dabigatran plasma concentrations. With the exception of few ROTEM® parameters, there were no differences between spiked and patient samples. Samples were stable for at least 12?months at -80?°C.

CONCLUSIONS:

EXTEM and FIBTEM CT, ECA and LD-dTT are suitable for measuring the effect of dabigatran in treated patients. In general, results from spiked plasma samples are similar to those of patient samples. Storage of dabigatran plasma samples for up to 12?months does not influence measured levels.

Impactfactor 2.779

Improved testing for vitamin B(12) deficiency: correcting MMA for eGFR reduces the number of patients classified as vitamin B(12) deficient

van Loon SL, Wilbik AM, Kaymak U, van den Heuvel ER, **Scharnhorst V, Boer AK**

Ann Clin Biochem. 2018 Nov 55(6):685-692. Epub 2018 Jun 6

Background Methylmalonic acid (MMA) can detect functional vitamin B12 deficiencies as it accumulates early when intracellular deficits arise. However, impaired clearance of MMA from blood due to decreased glomerular filtration rate (eGFR) also results in elevated plasma MMA concentrations. Alternative to clinical trials, a data mining approach was chosen to quantify and compensate for the effect of decreased eGFR on MMA concentration. Methods Comprehensive data on patient's vitamin B12, eGFR and MMA concentrations were collected (n?=?2906). The relationship between vitamin B12, renal function (eGFR) and MMA was modelled using weighted multiple linear regression. The obtained model was used to estimate the influence of decreased eGFR on MMA. Clinical impact was examined by comparing the number of patients labelled vitamin B12 deficient with and without adjustment in MMA. Results Adjusting measured MMA concentrations for eGFR in the group of patients with low-normal vitamin B12 concentrations (90-300?pmol/L) showed that the use of unadjusted MMA concentrations overestimates vitamin B12 deficiency by 40%. Conclusions Through a data mining approach, the influence of eGFR on the relation between MMA and vitamin B12 can be quantified and used to correct the measured MMA concentration for decreased eGFR. Especially in the elderly, eGFR-based correction of MMA may prevent over-diagnosis of vitamin B12 deficiency and corresponding treatment.

Impactfactor 1.983

Optimizing charge state distribution is a prerequisite for accurate protein biomarker quantification with LC-MS/MS, as illustrated by hepcidin measurement

Schmitz EM, Leijten NM, van Dongen JL, Broeren MA, Milroy LG, Brunsveld L, **Scharnhorst V, van de Kerkhof D**

Clin Chem Lab Med. 2018 Aug 28;56(9):1490-1497

BACKGROUND:

Targeted quantification of protein biomarkers with liquid chromatography-tandem mass spectrometry (LC-MS/MS) has great potential, but is still in its infancy. Therefore, we elucidated the influence of charge state distribution and matrix effects on accurate quantification, illustrated by the peptide hormone hepcidin.

METHODS:

An LC-MS/MS assay for hepcidin, developed based on existing literature, was improved by using 5 mM ammonium formate buffer as mobile phase A and as an elution solution for solid phase extraction (SPE) to optimize the charge state distribution. After extensive analytical validation, focusing on interference and matrix effects, the clinical consequence of this method adjustment was studied by performing receiving operating characteristic (ROC)-curve analysis in patients with iron deficiency anemia (IDA, n=44), anemia of chronic disease (ACD, n=42) and non-anemic patients (n=93).

RESULTS:

By using a buffered solution during sample preparation and chromatography, the most abundant charge state was shifted from 4+ to 3+ and the charge state distribution was strongly stabilized. The matrix effects which occurred in the 4+ state were therefore avoided, eliminating bias in the low concentration range of hepcidin. Consequently, sensitivity, specificity and positive predictive value (PPV) for detection of IDA patients with the optimized assay (96%, 97%, 91%, respectively) were much better than for the original assay (73%, 70%, 44%, respectively).

CONCLUSIONS:

Fundamental improvements in LC-MS/MS assays greatly impact the accuracy of protein quantification. This is urgently required for improved diagnostic accuracy and clinical value, as illustrated by the validation of our hepcidin assay.

Impactfactor 3.556

Protocolled Redefinition of the Therapeutic Range for Unfractionated Heparin: Lost in Translation?

Coene KLM, van der Graaf F, **van de Kerkhof D**

Clin Appl Thromb Hemost. 2018 Jan 24(1):164-171. Epub 2016 Nov 16

BACKGROUND:

Protocolled treatment with unfractionated heparin (UFH) is a subject of ongoing debate. Even though international guidelines prescribe calibration of the activated partial thromboplastin time (aPTT) to 0.3 to 0.7 U/mL anti-Xa activity to establish an UFH therapeutic range, evidence for this approach remains scarce. In this study, we evaluated different strategies to delineate the UFH therapeutic range and analyzed the effects on patient therapeutic classification.

METHODS:

In 109 patient samples, the aPTT was measured with 2 different reagents, both of which used mechanical clot detection. The UFH therapeutic range was determined using 3 previously described methods: calibration of the aPTT to 0.3 to 0.7 U/mL anti-Xa activity, application of 1.5 to 2.5 times the control aPTT, or using 0.3 to 0.7 U/mL anti-Xa activity directly. We also applied the UFH therapeutic range of a second hospital to our patient population.

RESULTS: Application of the guideline-prescribed anti-Xa calibration method would result in patients receiving increased UFH dosage in comparison to our previous UFH nomogram. Between-method and between-laboratory variations in aPTT and anti-Xa activity assays are a likely cause of these discrepancies. Additionally, we show that individual patient characteristics, such as weight and UFH treatment duration, likely contribute to the discordance between different strategies to establish an UFH therapeutic range.

CONCLUSION:

No consensus is reached between different strategies to define the UFH therapeutic range, which could result in relevant differences in UFH doses applied in patients. Clinicians and laboratory specialists should critically evaluate UFH monitoring protocols and be aware of their shortcomings.

Impactfactor 1.852

Salivary cortisol in the diagnosis of adrenal insufficiency: cost efficient and patient friendly

Langelaan MLP, Kisters JMH, Oosterwerff MM, **Boer AK**

Endocr Connect. 2018 Apr 7(4):560-566. Epub 2018 Mar 12

Saliva as a diagnostic tool is patient friendly and offers analytical advantages. Hormonal analysis of saliva is not influenced by changes in concentrations of binding globulins as the free concentration of the hormones is measured. Analysis of salivary cortisol is common practice in the diagnostic work-up of hypercortisolism. We investigated the potential role of measuring salivary cortisol when adrenal insufficiency (AI) is suspected, to reduce the numbers of ACTH stimulation tests. Over a period of 6 years, patients undergoing an ACTH stimulation test (tetracosactide, 250?µg) in our hospital were included. Plasma cortisol (Elecsys, Cobas, Roche Diagnostics) and salivary cortisol and cortisone (LC-MS/MS) were determined at t?=?0, 30 and 60?min after stimulation. Based on peak plasma cortisol levels, AI was ruled out in 113 patients and was established in 16 patients. Patients without AI displayed maximal salivary cortisol concentrations of 12.6-123.4?nmol/L (95th percentile) after stimulation, as opposed to 0.5-15.2?nmol/L in AI patients. At t?=?0?min, a minimal salivary cortisol concentration of 1.0?nmol/L was observed in patients without AI, whereas AI patients had a maximum concentration of 5.9?nmol/L. Using these cut-off values, 34% of the initial patient group could be diagnosed without an ACTH stimulation test (28% >5.9?nmol/L, 6% <1.0?nmol/L). A novel diagnostic algorithm, including early morning salivary cortisol analysis can reduce the numbers of ACTH stimulation tests in patients suspected of AI. This patient-friendly method can thereby reduce total health care costs.

Impactfactor 3.041

Switching from infliximab innovator to biosimilar in patients with inflammatory bowel disease: a 12-month multicentre observational prospective cohort study

Schmitz EMH, Boekema PJ, Straathof JWA, van Renswouw DC, Brunsveld L, **Scharnhorst V**, van de Poll MEC, Broeren MAC, Derijks LJJ

Aliment Pharmacol Ther. 2018 Feb 47(3):356-363. Epub 2017 Dec 5

BACKGROUND:

Infliximab biosimilars have become available for treatment of inflammatory bowel disease (IBD). However, data showing long-term safety and effectiveness of biosimilars in IBD patients are limited.

AIM:

To study prospectively the switch from infliximab innovator to biosimilar in an IBD cohort with 12 months follow-up to evaluate safety and effectiveness.

METHODS:

Adult IBD patients from two hospitals treated with infliximab innovator (Remicade; Janssen Biotech, Horsham , Pennsylvania, USA) were switched to infliximab biosimilar (Inflectra; Hospira, Lake Forest, Illinois, USA) as part of routine care, but in a controlled setting. Blood samples were taken just before the first, second, fourth and seventh infusion of biosimilar. Infliximab trough levels, antibodies-to-infliximab (ATI), CRP and ESR were measured and disease activity scores were calculated.

RESULTS:

Our cohort consisted of 133 IBD patients (64% CD, 36% UC). Before switching we found widely varying infliximab levels (median 3.5 µg/mL). ATI were detected in eight patients (6%). Most patients were in remission or had mild disease (CD: 82% UC: 90%). After switching to biosimilar, 35 patients (26%) discontinued therapy within 12 months, mostly due to subjective higher disease activity (9%) and adverse events (AE, 9.8%). AE included general malaise/fatigue (n = 7), arthralgia (n = 2), skin problems (n = 2) and infusion reactions (n = 2). No differences in IFX levels, CRP, and disease activity scores were found between the four time points (P = .0917).

CONCLUSIONS:

We found no differences in drug levels and disease activity between infliximab innovator and biosimilar in our IBD cohort, indicating that biosimilars are safe and effective. The high proportions of discontinuers were mostly due to elective withdrawal or subjective disease worsening.

Impactfactor 7.357

Vaststellen van lactaatafkapwaarden voor foetale nood : retrospectieve data-analyse van MBO-gegevens

Nienke Geerts, Arjen-Kars Boer

Laboratoriumgeneeskunde 2018;1(5):26-33

Microbloedonderzoek (MBO) is een techniek voor foetale bewaking durante partu die in combinatie met cardiotocografie (CTG)-bewaking gebruikt wordt. Deze combinatie van methoden reduceert het aantal onnodige operatieve bevallingen in verband met foetale nood. Recent onderzoek toont aan dat de lactaatconcentratie

mogelijk de voorkeur heeft boven een pH-meting. In deze studie is de lactaatafkapwaarde voor onze patiëntenpopulatie als onderdeel van een volledige bloedgasanalyse op de ABL90 vastgesteld (Radiometer; testvolume 65 µl). Daarnaast zijn de voorspellende waarden van beide parameters vergeleken.

Impactfactor --

Anesthesiologie

Aligning Event Logs to Task-Time Matrix Clinical Pathways in BPMN for Variance Analysis

Yan H, Van Gorp P, Kaymak U, Lu X, Ji L, Chiau CC, **Korsten HHM**, Duan H

IEEE J Biomed Health Inform. 2018 Mar;22(2):311-317.Epub 2017 Sep 18

Clinical pathways (CPs) are popular healthcare management tools to standardize care and ensure quality. Analyzing CP compliance levels and variances is known to be useful for training and CP redesign purposes. Flexible semantics of the business process model and notation (BPMN) language has been shown to be useful for the modeling and analysis of complex protocols. However, in practical cases one may want to exploit that CPs often have the form of task-time matrices. This paper presents a new method parsing complex BPMN models and aligning traces to the models heuristically. A case study on variance analysis is undertaken, where a CP from the practice and two large sets of patients data from an electronic medical record (EMR) database are used. The results demonstrate that automated variance analysis between BPMN task-time models and real-life EMR data are feasible, whereas that was not the case for the existing analysis techniques. We also provide meaningful insights for further improvement.

Impactfactor: 3.850

Awareness and Management of Dysphagia in Dutch Intensive Care Units: A Nationwide Survey

van Snippenburg W, Kröner A, Flim M, Hofhuis J, **Buise M**, Hemler R, Spronk P

Dysphagia. 2018 Aug 1. [Epub ahead of print]

Dysphagia is a common problem in the intensive care unit (ICU), yet no national guidelines on dysphagia prevention, screening, and management exist. We performed a survey to learn which strategies are commonly being used in Dutch ICUs. A survey was developed based on current literature and experts' opinions. It comprised questions regarding hospital and ICU characteristics, perceived prevalence and importance of dysphagia, screening strategies, modalities used to prevent aspiration, and interventions used to improve swallowing function. It was sent to all 90 non-pediatric ICUs in The Netherlands. 67 of 90 addressed ICUs (74%) replied to our survey. A median relevance score of 4 (IQR 4-5) out of 5 was given to the topic of dysphagia. In 22% and 45% of ICUs, patients were always screened for dysphagia after extubation or tracheotomy, respectively. The water swallow test was always part of the work-up in 88% of ICUs. Fiberoptic endoscopic evaluation of swallowing was used occasionally in 60%of ICUs, versus videofluoroscopic swallowing study in 25%. In 49% of ICUs, no standardized active rehabilitation protocol for dysphagia existed. In the remaining 51%, swallowing exercises were always part of standard rehabilitation, occasionally supplemented by electrical stimulation or surface-EMG biofeedback training in 6 and 10%, respectively. Most Dutch ICUs do not regularly screen for dysphagia and almost half do not seem to have a diagnostic, treatment, or rehabilitation protocol, despite recognizing it as a significant and relatively frequent problem in the ICU with potentially serious patient consequences.

Impactfactor: 2.531

Cardiac structure and function before and after bariatric surgery: a clinical overview

Lascaris B, Pouwels S, Houthuizen P, Dekker LR, Nienhuijs SW, **Bouwman RA, Buise MP**

Clin Obes. 2018 Dec;8(6):434-443

Obesity, defined as a body mass index of =30 kg/m2 , is the most common chronic metabolic disease worldwide and its prevalence has been strongly increasing. Obesity has deleterious effects on cardiac function. The purpose of this review is to evaluate the effects of obesity and excessive weight loss due to bariatric surgery on cardiac function, structural changes and haemodynamic responses of both the left and right ventricle.

Impactfactor: --

Comparison of ultrasound guidance with palpation and direct visualisation for peripheral vein cannulation in adult patients: a systematic review and meta-analysis

van Loon FH, Buise MP, Claassen JJ, Dierick-van Daele AT, **Bouwman AR**

Br J Anaesth. 2018 Aug;121(2):358-366

BACKGROUND:

Peripheral vein cannulation is a routine and straightforward invasive procedure, although i.v. access can be difficult to obtain. To increase the success rate of inserting an i.v. catheter, many devices have been proposed, including ultrasonography. The objective of this study was to compare ultrasound guidance with the traditional approach of palpation and direct visualisation for peripehral vein cannulation. The primary outcome was successful peripheral i.v. cannulation.

METHODS:

Database search was performed on PubMed, Clinical Key, CINAHL, Cochrane Library of Clinical Trials, and Trip Database (from January 2000 to December 2017). Random-effect meta-analysis was performed to determine the pooled odds ratio for success in peripheral i.v. cannulation.

RESULTS:

After database review and eligibility screening, eight studies were included in the final analysis, with a total of 1660 patients. The success rate in the ultrasound group was 81% (n=855), and was 70% (n=805) in the control group, resulting in a pooled odds ratio for success upon ultrasound-guided peripheral i.v. cannulation of 2.49 (95%

confidence interval 1.37-4.52, P=0.003). Furthermore, the ultrasound-guided technique reduced the number of punctures and time needed to achieve i.v. access, and increased the level of patient satisfaction, although it did not result in a decreased number of complications.
CONCLUSIONS:
Ultrasound guidance increases the success rate of peripheral i.v. cannulation, especially in patients with known or predicted difficult i.v. access.

Impactfactor: 6.499

Emergency percutaneous transtracheal jet ventilation in a hypoxic cardiopulmonary resuscitation setting: a life-saving rescue technique

Dong PV, Ter Horst L, Krage R

BMJ Case Rep. 2018 Jan 26 2018. pii: bcr-2017-222283

(Un)anticipated difficult airway remains a challenge in anaesthesia. Percutaneous transtracheal jet ventilation has been shown to be an adequate technique for temporary oxygenation and ventilation and has been described as an acknowledged method in emergency settings of an unanticipated difficult airway. These emergency settings can be considered as low incidence high-risk situations. Both technical and non-technical skills should be trained regularly as education and simulation continues to play an important factor in patient safety. Furthermore, postoperative laryngeal oedema due to altered lymphatic drainage patterns must be considered as a possible mechanism of an upper airway obstruction in combination with a history of neck dissection and radiotherapy.

Impactfactor: --

In vitro pharmacokinetic phantom for two-compartment modeling in DCE-MRI

Wahyulaksana G, Saporito S, den Boer JA, **Herold IH**, Mischi M

Phys Med Biol. 2018 Oct 17;63(20):205012

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is an established minimally-invasive method for assessment of extravascular leakage, hemodynamics, and tissue viability. However, differences in acquisition protocols, variety of pharmacokinetic models, and uncertainty on physical sources of MR signal hamper the reliability and widespread use of DCE-MRI in clinical practice. Measurements performed in a controlled in vitro setup could be used as a basis for standardization of the acquisition procedure, as well as objective evaluation and comparison of pharmacokinetic models. In this paper, we present a novel flow phantom that mimics a two-compartmental (blood plasma and extravascular extracellular space/EES) vascular bed, enabling systemic validation of acquisition protocols. The phantom consisted of a hemodialysis filter with two compartments, separated by hollow fiber membranes. The aim of this phantom was to vary the extravasation rate by adjusting the flow in the two compartments. Contrast agent transport kinetics within the phantom was interpreted using two-compartmental pharmacokinetic models. Boluses of gadolinium-based contrast-agent were injected in a tube network connected to the hollow fiber phantom; time-intensity curves (TICs) were obtained from image series, acquired using a T1-weighted DCE-MRI sequence. Under the assumption of a linear dilution system, the TICs obtained from the input and output of the system were then analyzed by a system identification approach to estimate the trans-membrane extravasation rates in different flow conditions. To this end, model-based deconvolution was employed to determine (identify) the impulse response of the investigated dilution system. The flow rates in the EES compartment significantly and consistently influenced the estimated extravasation rates, in line with the expected trends based on simulation results. The proposed phantom can therefore be used to model a two-compartmental vascular bed and can be employed to test and optimize DCE-MRI acquisition sequences in order to determine a standardized acquisition procedure leading to consistent quantification results.

Impactfactor: 2.665

Laparoscopic Sterilization Under Local Anesthesia with Conscious Sedation Versus General Anesthesia : Systematic Review of the Literature

Huppelschoten AG, **Bijleveld K, Braams L**, Schoot BC, van Vliet HAAM

J Minim Invasive Gynecol. 2018 Mar - Apr;25(3):393-401

Authors' Reply. - J Minim Invasive Gynecol. 2018 May - Jun 25(4):740-741. Epub 2018 Jan 31

Female sterilization is the most popular and common contraceptive method worldwide. Because hysteroscopic sterilization techniques are used less often due to side effects, the number of laparoscopic sterilization is increasing. A systematic overview concerning the most optimal anesthetic technique for laparoscopic sterilization is lacking. We performed a systematic review to compare conscious sedation with general anesthesia for laparoscopic sterilization procedures with respect to clinical relevant outcome measures, such as operating times, perioperative parameters and complications, patient comfort, recovery, and patient satisfaction. We searched Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE for randomized controlled trials comparing general anesthesia with conscious sedation for laparoscopic sterilization. Two authors (AGH and HAAMvV) abstracted and entered data into RevMan. Methodologic quality of the included trials was critically appraised. For our main outcome measures mean differences (continuous variables) and risk ratios (dichotomous variables) with 95% confidence intervals using random-effect models were calculated. Four randomized controlled trials were included comparing general

anesthesia versus local anesthesia with conscious sedation for laparoscopic sterilization. The methodologic quality of the studies was moderate to good. Both techniques were comparable with regard to operating times, complications, and postoperative pain. However, local anesthesia with conscious sedation showed better results compared with general anesthesia with respect to recovery times, patient complaints of sore throat, and patient recovery and satisfaction. In conclusion, this systematic review about anesthetic techniques for laparoscopic sterilization showed that both general anesthesia and conscious sedation have no major anesthetic complications and may therefore be safe. Patients might benefit from conscious sedation in terms of recovery times, sore throat, and patient recovery and satisfaction, but only a few studies are included in the review and are relatively old. New research regarding this subject is needed to advise our patients most optimally in the future about the best anesthetic technique to be used when choosing for a laparoscopic sterilization procedure.

Impactfactor: 3.061

Pain upon inserting a peripheral intravenous catheter: Size does not matter

van Loon FH, Puijn LA, van Aarle WH, Dierick-van Daele AT, **Bouwman AR**

J Vasc Access. 2018 May;19(3):258-265

BACKGROUND:

Approximately 1.2 billion peripheral intravenous catheters are inserted across the world annually. It is known that intravenous cannulation may be a painful procedure, which affects cognitive abilities by increasing anxiety and discomfort.

AIM:

We hypothesized that inserting a smaller sized peripheral intravenous catheter has a lower level of pain sensation compared to a larger sized catheter.

METHODS:

This observational, cross-sectional study was conducted between May and October 2016, in which surgical patients, aged 18 years or older, were eligible to participate. Experienced anesthesiologists and nurse anesthetists routinely obtained peripheral intravenous access according to the standards of care. The primary outcome was pain (verbal numeric rating scale, 0-10) upon intravenous cannulation.

RESULTS:

A total of 1063 patients were included and they were divided into four groups: group 1, 22 gauge (N = 29); group 2, 20 gauge (N = 447); group 3, 18 gauge (N = 531); and group 4, sized over 18 gauge (N = 56). Inserting an 18-gauged peripheral intravenous catheter resulted in the lowest pain score (3.2 ± 2.0). As a result of the multivariate linear analysis, five factors were significantly associated with pain upon inserting a peripheral intravenous catheter (sex, American Society of Anesthesiology classification, a patients risk profile on the A-DIVA scale, site of cannulation on the extremity, and whether or not the attempt was successful); however, the size of the inserted peripheral intravenous catheter had no significant relation to the primary outcome.

CONCLUSION:

Inserting a smaller sized peripheral intravenous catheter did not result in a lower pain sensation. Moreover, to prevent pain upon inserting a peripheral intravenous catheter, an unsuccessful attempt must be avoided.

Impactfactor: 1.306

Perioperative lipid-enriched enteral nutrition versus standard care in patients undergoing elective colorectal surgery (SANICS II): a multicentre double-blind randomised controlled trial

Peters EG, Smeets BJJ, Nors J, Back CM, Funder JA, Sommer T, Laurberg S, Løve US, Leclercq WKG, Slooter GD, de Vries Reilingh TS, Wegdam JA, Nieuwenhuijzen GAP, Hiligsmann M, **Buise MP**, Buurman WA, de Jonge WJ, Rutten HJT, Luyer MDP

Lancet Gastroenterol Hepatol. 2018 Apr 3(4):242-251. Epub 2018 Feb 14

BACKGROUND:

Postoperative ileus and anastomotic leakage severely impair recovery after colorectal resection. We investigated the effect of perioperative lipid-enriched enteral nutrition versus standard care on the risk of postoperative ileus, anastomotic leakage, and other clinical outcomes.

METHODS:

We did an international, multicentre, double-blind, randomised, controlled trial of patients (=18 years) undergoing elective colorectal surgery with primary anastomosis at six clinical centres in the Netherlands and Denmark. Patients were randomly assigned (1:1), stratified by location (colonic and rectal) and type of surgery (laparoscopic and open), via online randomisation software, with block sizes of six, to receive either continuous lipid-enriched enteral tube feeding from 3 h before until 6 h after surgery (intervention) or no perioperative nutrition (control). Surgeons, patients, and researchers were masked to treatment allocation for the entire study period. The primary outcome was postoperative ileus. Secondary outcomes included anastomotic leakage, pneumonia, preoperative gastric volumes, time to functional recovery, length of hospital stay, the need for additional interventions, intensive care unit admission, postoperative inflammatory response, and surgical complications. Analyses were by intention to treat. This study is registered with ClinicalTrials.gov, number NCT02175979, and trialregister.nl, number NTR4670.

FINDINGS:

Between July 28, 2014, and February 20, 2017, 280 patients were randomly assigned, 15 of whom were excluded after random allocation because they fulfilled one or more exclusion criteria. 265 patients received perioperative nutrition (n=132) or standard care (n=133) and were included in the analyses. A postoperative ileus occurred in 37 (28%) patients in the intervention group versus 29 (22%) in the control group (risk ratio [RR] 1·09, 95% CI 0·95-1·25; p=0·24). Anastomotic leakage occurred in 12 (9%) patients in the intervention group versus 11 (8%) in the control group (RR 1·01, 95% CI 0·94-1·09; p=0·81). Pneumonia occurred in ten (8%) patients in the intervention group versus three (2%) in the control group (RR 1·06, 95% CI 1·00-1·12; p=0·051). All other secondary outcomes were similar between groups (all p>0·05).

INTERPRETATION:

Perioperative lipid-enriched enteral nutrition in patients undergoing elective colorectal surgery has no advantage over standard care in terms of postoperative complications.

Impactfactor: --

Pressure gradient vs. flow relationships to characterize the physiology of a severely stenotic aortic valve before and after transcatheter valve implantation

Johnson NP, Zelis JM, Tonino PAL, Houthuizen P, **Bouwman RA**, Brueren GRG, Johnson DT, Koolen JJ, **Korsten HHM**, Wijnbergen IF, Zimmermann FM, Kirkeeide RL, Pijls NHJ, Gould KL

Eur Heart J. 2018 Jul 21 39(28):2646-2655

Aims:

Echocardiography and tomographic imaging have documented dynamic changes in aortic stenosis (AS) geometry and severity during both the cardiac cycle and stress-induced increases in cardiac output. However, corresponding pressure gradient vs. flow relationships have not been described.

Methods and results:

We recruited 16 routine transcatheter aortic valve implantations (TAVI's) for graded dobutamine infusions both before and after implantation; 0.014? pressure wires in the aorta and left ventricle (LV) continuously measured the transvalvular pressure gradient (?P) while a pulmonary artery catheter regularly assessed cardiac output by thermodilution. Before TAVI, ?P did not display a consistent relationship with transvalvular flow (Q). Neither linear resistor (median R2 0.16) nor quadratic orifice (median R2?<?0.01) models at rest predicted stress observations; the severely stenotic valve behaved like a combination. The unitless ratio of aortic to left ventricular pressures during systolic ejection under stress conditions correlated best with post-TAVI flow improvement. After TAVI, a highly linear relationship (median R2 0.96) indicated a valid valve resistance.

Conclusion:

Pressure loss vs. flow curves offer a fundamental fluid dynamic synthesis for describing aortic valve pathophysiology. Severe AS does not consistently behave like an orifice (as suggested by Gorlin) or a resistor, whereas TAVI devices behave like a pure resistor. During peak dobutamine, the ratio of aortic to left ventricular pressures during systolic ejection provides a 'fractional flow reserve' of the aortic valve that closely approximates the complex, changing fluid dynamics. Because resting assessment cannot reliably predict stress haemodynamics, 'valvular fractional flow' warrants study to explain exertional symptoms in patients with only moderate AS at rest.

Impactfactor: *23.425*

RegressionExplorer: Interactive Exploration of Logistic Regression Models with Subgroup Analysis

Dingen D, Veer MV, Houthuizen P, Mestrom EHJ, **Korsten EHHM**, **Bouwman ARA**, Wijk JV

IEEE Trans Vis Comput Graph. 2018 Sep 13. [Epub ahead of print]

We present RegressionExplorer, a Visual Analytics tool for the interactive exploration of logistic regression models. Our application domain is Clinical Biostatistics, where models are derived from patient data with the aim to obtain clinically meaningful insights and consequences. Development and interpretation of a proper model requires domain expertise and insight into model characteristics. Because of time constraints, often a limited number of candidate models is evaluated. RegressionExplorer enables experts to quickly generate, evaluate, and compare many different models, taking the workflow for model development as starting point. Global patterns in parameter values of candidate models can be explored effectively. In addition, experts are enabled to compare candidate models across multiple subpopulations. The insights obtained can be used to formulate new hypotheses or to steer model development. The effectiveness of the tool is demonstrated for two uses cases: prediction of a cardiac conduction disorder in patients after receiving a heart valve implant and prediction of hypernatremia in critically ill patients.

Impactfactor: *3.078*

[Risk of heart failure diminished thanks to stomach reduction in obesity] - Hartfalen afgenomen door maagverkleining bij obesitas

Botter B, Koolen E, van Montfort G, Bracke F, **Bouwman A, Buise M**

Ned Tijdschr Geneeskd. 2018;162:D1972

BACKGROUND:

Obesity is a chronic disease and a risk factor for heart failure. In end-stage heart failure, heart transplantation may

be the only available treatment option, but obesity is a contraindication for this treatment because of its unfavourable prognosis. Bariatric surgery and its subsequent weight loss may affect the indication for transplantation in patients with heart failure and morbid obesity.
CASE DESCRIPTION:
A 46-year-old patient with morbid obesity and heart failure underwent gastric sleeve resection in preparation of a heart transplantation. Without it, he would not have been considered eligible for transplantation because of his obesity. The bariatric intervention was also intended to use weight loss as a way to reduce the symptoms of his heart failure and to make rehabilitation possible. One year after surgery, the condition of the patient had improved so much that heart transplantation was no longer necessary.
CONCLUSION:
Bariatric surgery is safe for morbidly obese patients with severe heart failure and may sometimes even avoid heart transplantation.

Impactfactor: --

Robust and semantic needle detection in 3D ultrasound using orthogonal-plane convolutional neural networks

Pourtaherian A, Ghazvinian Zanjani F, Zinger S, Mihajlovic N, Ng GC, **Korsten HHM**, de With PHN

Int J Comput Assist Radiol Surg. 2018 Sep 13(9):1321-1333. Epub 2018 May 31

PURPOSE:
During needle interventions, successful automated detection of the needle immediately after insertion is necessary to allow the physician identify and correct any misalignment of the needle and the target at early stages, which reduces needle passes and improves health outcomes.
METHODS:
We present a novel approach to localize partially inserted needles in 3D ultrasound volume with high precision using convolutional neural networks. We propose two methods based on patch classification and semantic segmentation of the needle from orthogonal 2D cross-sections extracted from the volume. For patch classification, each voxel is classified from locally extracted raw data of three orthogonal planes centered on it. We propose a bootstrap resampling approach to enhance the training in our highly imbalanced data. For semantic segmentation, parts of a needle are detected in cross-sections perpendicular to the lateral and elevational axes. We propose to exploit the structural information in the data with a novel thick-slice processing approach for efficient modeling of the context.
RESULTS:
Our introduced methods successfully detect 17 and 22 G needles with a single trained network, showing a robust generalized approach. Extensive ex-vivo evaluations on datasets of chicken breast and porcine leg show 80 and 84% F1-scores, respectively. Furthermore, very short needles are detected with tip localization errors of less than 0.7 mm for lengths of only 5 and 10 mm at 0.2 and 0.36 mm voxel sizes, respectively.
CONCLUSION:
Our method is able to accurately detect even very short needles, ensuring that the needle and its tip are maximally visible in the visualized plane during the entire intervention, thereby eliminating the need for advanced bi-manual coordination of the needle and transducer.

Impactfactor --

Safety of moderate-to-deep sedation performed by sedation practitioners: A national prospective observational study

Koers L, Eberl S, Cappon A, **Bouwman A**, Schlack W, Hermanides J, Preckel B

Eur J Anaesthesiol. 2018 Sep;35(9):659-666

BACKGROUND:
In the Netherlands, a significant proportion of moderate-to-deep sedation is performed by sedation practitioners under the indirect supervision of an anaesthesiologist but there are limited safety data available.
OBJECTIVE:
To estimate the rate of sedation-related adverse events and patient relevant outcomes (PRO).
DESIGN:
This was a prospective national observational study. Data were collected with a modified adverse event reporting tool from the International Sedation Task Force of the World Society of Intravenous Anaesthesia.
SETTING:
A total of 24 hospitals in the Netherlands where moderate-to-deep sedation was performed by sedation practitioners from the 1 February 2015 to 1 March 2016.
PATIENTS:
Consecutive adults undergoing moderate-to-deep sedation for gastrointestinal, pulmonary and cardiac procedures.
INTERVENTION:
Observation: Analysis included descriptive statistics and a multivariate logistic regression model for an association between adverse events and PRO.
MAIN OUTCOME MEASURES:

The primary outcome was the rate of unfavourable PRO (admission to ICU, permanent neurological deficit, pulmonary aspiration or death). Secondary outcome was the rate of moderate-to-good PRO (unplanned hospital admission or escalation of care). Composite outcome was the sum of all primary and secondary outcomes.
RESULTS:
A total of 11?869 patients with a median age of 64 years [interquartile range 51 to 72] were included. ASA physical score distribution was: first, 19.1%; second, 57.6%; third, 21.6%; fourth, 1.2%. Minimal adverse events occurred in 1517 (12.8%), minor adverse events in 113 (1.0%) and major adverse events in 80 instances (0.7%).
PRIMARY OUTCOME:
Five (0.04%) unfavourable PRO were observed; four patients needing admission to the intensive care unit; and one died. Secondary outcome: 12 (0.1%) moderate-to-good PRO were observed. Moderate and major adverse events were associated with the composite outcome [3.7 (95% confidence interval 1.1 to 11.9) and 40.6 (95% confidence interval 11.0 to 150.4)], but not minimal or minor adverse events.
CONCLUSION:
Moderate-to-deep sedation performed by trained sedation practitioners has a very low rate of unfavourable outcome.

Impactfactor: 3.958

Shift Towards Older Bariatric Patients

Versteegden DPA, **Buise MP**, Nienhuijs SW

Obes Surg. 2018 Feb 28(2):555-556

Geen abstract beschikbaar

Impactfactor: 3.895

Study protocol of the randomised placebo-controlled GLOBE trial: GLP-1 for bridging of hyperglycaemia during cardiac surgery

Hulst AH, Visscher MJ, Godfried MB, Thiel B, Gerritse BM, Scohy TV, **Bouwman RA, Willemsen MGA**, Hollmann MW, DeVries JH, Preckel B, Hermanides J

BMJ Open. 2018 Jun 4;8(6):e022189

INTRODUCTION:
Perioperative hyperglycaemia is common during cardiac surgery and associated with postoperative complications. Although intensive insulin therapy for glycaemic control can reduce complications, it carries the risk of hypoglycaemia. GLP-1 therapy has the potential to lower glucose without causing hypoglycaemia. We hypothesise that preoperative liraglutide (a synthetic GLP-1 analogue) will reduce the number of patients requiring insulin to achieve glucose values<8?mmol l-1 in the intraoperative period.
METHODS AND ANALYSIS:
We designed a multi-centre randomised parallel placebo-controlled trial and aim to include 274 patients undergoing cardiac surgery, aged 18-80 years, with or without diabetes mellitus. Patients will receive 0.6?mg liraglutide or placebo on the evening before, and 1.2?mg liraglutide or placebo just prior to surgery. Blood glucose is measured hourly and controlled with an insulin bolus algorithm, with a glycaemic target between 4-8?mmol l-1. The primary outcome is the percentage of patients requiring insulin intraoperatively.
ETHICS AND DISSEMINATION:
This study protocol has been approved by the medical ethics committee of the Academic Medical Centre (AMC) in Amsterdam and by the Dutch competent authority. The study is investigator-initiated and the AMC, as sponsor, will remain owner of all data and have all publication rights. Results will be submitted for publication in a peer-reviewed international medical journal.

Impactfactor: 2.413

The Hemodynamic Effects of Different Pacing Modalities After Cardiopulmonary Bypass in Patients With Reduced Left Ventricular Function

Gielgens RCW, Herold IHF, van Straten AHM, van Gelder BM, Bracke FA, **Korsten HHM**, Soliman Hamad MA, **Bouwman RA**

J Cardiothorac Vasc Anesth. 2018 Feb 32(1):259-266. . Epub 2017 Jul 8

OBJECTIVES:
Patients with decreased left ventricular function undergoing cardiac surgery have a greater chance of difficult weaning from cardiopulmonary bypass and a poorer clinical outcome. Directly after weaning, interventricular dyssynchrony, paradoxical septal motion, and even temporary bundle-branch block might be observed. In this study, the authors measured arterial dP/dtmax, mean arterial pressure (MAP), and cardiac index using transpulmonary thermodilution, pulse contour analysis, and femoral artery catheter and compared the effects between right ventricular (A-RV) and biventricular (A-BiV) pacing on these parameters.
DESIGN:
Prospective study.

SETTING:
Single-center study.
PARTICIPANTS:
The study comprised 17 patients with a normal or prolonged QRS duration and a left ventricular ejection fraction =35% who underwent coronary artery bypass grafting with or without valve replacement.
INTERVENTIONS:
Temporary pacing wires were placed on the right atrium and both ventricles. Different pacing modalities were used in a standardized order.
MEASUREMENTS AND MAIN RESULTS:
A-BiV pacing compared with A-RV pacing demonstrated higher arterial dP/dtmax values (846 ± 646 mmHg/s v 800 ± 587 mmHg/s, p = 0.023) and higher MAP values (77 ± 19 mmHg v 71 ± 18 mmHg, p = 0.036).
CONCLUSION:
In patients with preoperative decreased left ventricular function undergoing coronary artery bypass grafting, A-BiV pacing improve the arterial dP/dtmax and MAP in patients with both normal and prolonged QRS duration compared with standard A-RV pacing. In addition, arterial dP/dtmax and MAP can be used to evaluate the effect of intraoperative pacing. In contrast to previous studies using more invasive techniques, transpulmonary thermodilution is easy to apply in the perioperative clinical setting.

Impactfactor: 1.574

The RAQET Study: the Effect of Eating a Popsicle Directly After Bariatric Surgery on the Quality of Patient Recovery; a Randomised Controlled Trial

Pouwels S, Stepaniak PS, **Buise MP, Bouwman RA**, Nienhuijs SW

Indian J Surg. 2018 Jun;80(3):245-251.

Quality of recovery could be influenced positively if there is less postoperative sore throat (POST). Eating a popsicle might attenuate this sore throat. Especially for bariatric surgery, early recovery is important. Adding popsicles to the postoperative protocol could be beneficial. Our hypothesis is that offering a popsicle in the recovery room to patients after bariatric surgery will decrease POST and will increase quality of postoperative recovery. Patients undergoing elective bariatric surgery, between the 23 February 2015 and 3 April, were randomised to either the popsicle group or control group. Primary endpoint was the incidence of POST and secondly if a reduction in POST influences quality of recovery at the first day postoperative measured with the Bariatric Quality Of Recovery (BQoR) questionnaire. One hundred and thirty-three patients were assessed for eligibility. For the final analysis, 44 patients in the intervention and 65 in the control group were available. Eating a popsicle after bariatric surgery had no significant effect on the incidence of POST. Significant effects (in favour of the popsicle group) were seen in muscle pain score (p = 0.047) and sore mouth score (p = 0.012). Popsicle intragroup analysis revealed that eating the whole popsicle (compared to partially eating the popsicle) has positive effects on nausea (p = 0.059), feeling cold (p = 0.008), and mean total comfort score (p = 0.011). Of the patients who became nauseous and/or had to vomit because of the popsicle, n = 4 had more severe pain (p = 0.04) and the mean pain score was higher (p = 0.09). The present study demonstrates that offering a popsicle early during recovery after bariatric surgery is feasible without adverse effects, although eating popsicle did not reduce postoperative sore throat. There are possible beneficial effects, such as reduced muscle pains and less sore mouth, that may enhance the quality of recovery. More research is necessary to further substantiate the effect of eating popsicles on the quality of recovery in this patient population.

Impactfactor: 0.509

The safety and efficiency of a fast-track protocol for sleeve gastrectomy: a team approach

Vreeswijk SJ, van Rutte PW, Nienhuijs SW, **Bouwman RA**, Smulders JF, **Buise MP**

Minerva Anestesiol. 2018 Aug;84(8):898-906

BACKGROUND:
Increasing numbers of morbid obese patients has led to increased numbers of bariatric procedures. Fast-track protocols are being developed to enhance the available resources, while maintaining a safe procedure. Reported results on safety merely apply to a mixed bariatric population. The objective was to evaluate safety and efficiency of the fast-track principles in patients undergoing sleeve gastrectomy.
METHODS:
Retrospective observational study including patients undergoing primary sleeve gastrectomy at the Obesity Centre of the Catharina Hospital Eindhoven, the Netherlands. Conventional perioperative care (CC) (2008-2011) versus a fast-track protocol (FT) (2011-2013), using short-acting anesthetic agents, a multi-modal pain protocol to reduce opioids, and early mobilization. The main parameters for safety were intraoperative, early and late postoperative complications. Procedure time and hospital stay were used to evaluate efficiency.
RESULTS:
This study included 805 patients, 494 patients were subjected to the conventional care and 318 patients to fast-track protocol. A reduction of median operation time from 60 (CC) to 40 minutes (FT) (P<0.001) and a reduction in median length of hospital stay from three to two days (P=0.001), with a significant reduction in early postoperative

complications (9.9% [CC] vs. 5% [FT], P=0.016) was achieved. The amount of late complications was comparable for both groups (5.1% [CC] vs. 4.4% [FT] [P=0.738]).

CONCLUSIONS:

Implementation of a fast-track protocol for sleeve gastrectomy is safe and efficient. It effectively reduces operation time and length of hospital stay, while improving postoperative outcome. This pleads for standard implementation of the fast-track protocol in sleeve gastrectomy.

Impactfactor: 1.784

The surgical safety checklist and patient outcomes after surgery: a prospective observational cohort study, systematic review and meta-analysis

Abbott TEF, Ahmad T, Phull MK, Fowler AJ, Hewson R, Biccard BM, Chew MS, Gillies M, Pearse RM; International Surgical Outcomes Study (ISOS) group: **Bouwman RA**

Br J Anaesth. 2018 Jan;120(1):146-155

BACKGROUND:

The surgical safety checklist is widely used to improve the quality of perioperative care. However, clinicians continue to debate the clinical effectiveness of this tool.

METHODS:

Prospective analysis of data from the International Surgical Outcomes Study (ISOS), an international observational study of elective in-patient surgery, accompanied by a systematic review and meta-analysis of published literature. The exposure was surgical safety checklist use. The primary outcome was in-hospital mortality and the secondary outcome was postoperative complications. In the ISOS cohort, a multivariable multi-level generalized linear model was used to test associations. To further contextualise these findings, we included the results from the ISOS cohort in a meta-analysis. Results are reported as odds ratios (OR) with 95% confidence intervals.

RESULTS:

We included 44 814 patients from 497 hospitals in 27 countries in the ISOS analysis. There were 40 245 (89.8%) patients exposed to the checklist, whilst 7508 (16.8%) sustained =1 postoperative complications and 207 (0.5%) died before hospital discharge. Checklist exposure was associated with reduced mortality [odds ratio (OR) 0.49 (0.32-0.77); P<0.01], but no difference in complication rates [OR 1.02 (0.88-1.19); P=0.75]. In a systematic review, we screened 3732 records and identified 11 eligible studies of 453 292 patients including the ISOS cohort. Checklist exposure was associated with both reduced postoperative mortality [OR 0.75 (0.62-0.92); P<0.01; I2=87%] and reduced complication rates [OR 0.73 (0.61-0.88); P<0.01; I2=89%).

CONCLUSIONS:

Patients exposed to a surgical safety checklist experience better postoperative outcomes, but this could simply reflect wider quality of care in hospitals where checklist use is routine.

Impactfactor: 6.499

Apotheek

A Proof of Principle Study of the Terminal Sterilization of Prefilled Syringes Using A Water Cascade Process
Anne J.A. Drost-Wijnne, Ralph A.C. Van Wezel, Maarten J. Deenen, Joost P.C.M. Van Doornmalen Gomez Hoyos and **René J.E. Grouls**
Pharm Technol Hosp Pharm 2018; 3(4): 191–198

Background: A new development in drug compounding is the production of ready-to-administer sterilized prefilled syringes. A challenge with these syringes is the method of terminal sterilization. There is no information available whether water cascade sterilization is a suitable method. We investigated the effect of this sterilization method on cyclic olefin (co)polymer (CCP/COC) syringes. Methods: For two brands ten prefilled syringes were sterilized using water cascade sterilization. The closure integrity, stopper movement, weight, diameter and physical appearance were determined before and after sterilization. As sterility test, additional syringes were filled with tryptic soy broth (TSB) and sterilized. After fourteen days microbiological growth was determined. Results: Closure integrity testing showed no dye penetration inside the syringe. Together with the results for weight this showed that closure integrity is guaranteed. No significant stopper movement, deviation in diameter or visual anomalies were observed. No microbiological growth in TSB was visible. Conclusion: The results of this proof of principle study show that the physical and microbiological stability of the cyclic olefin (co)polymer syringes is guaranteed during sterilization using a water cascade sterilizer. These results do not rule out the necessity for further stability.

Impactfactor: --

Betere overleving na een Staphylococcus aureus-bacteriëmie bij betrokkenheid van het antibioticateam en bundelaanpak?
M. van den Hurk, J. Fonville, H.S.M. Ammerlaan, C. Miedema, **S. Sanders**, I Overdevest
TVI : tijdschrift voor infectieziekten, 2018;13(1):3-10

Staphylococcus aureus is een van de meest voorkomende verwekkers van een bacteriëmie. Een Staphylococcus aureus-bacteriëmie (SAB) heeft een hoge mortaliteit, mede door een vaak gecompliceerd beloop met strooihaarden. Uit literatuuronderzoek blijkt dat een bundelaanpak en de betrokkenheid van een multidisciplinair antibioticateam de uitkomst van SAB significant verbeteren. We hebben retrospectief beoordeeld wat de invloed is van ons antibioticateam op de aanpak van SAB en op de mortaliteit en het recidiefrisico voor de patiënt. Tevens werd onderzocht welke onderdelen in het behandeltraject de meeste invloed hadden op de prognose van de patiënt.

Impactfactor --

Effectiveness and safety of reduced-dose fluoropyrimidine therapy in patients carrying the DPYD*2A variant: A matched pair analysis.
Henricks LM, van Merendonk LN, Meulendijks D, **Deenen MJ**, Beijnen JH, de Boer A, Cats A, Schellens JHM.
Int J Cancer. 2018 Nov 28. [Epub ahead of print]

Carriers of the genetic DPYD*2A variant, resulting in dihydropyrimidine dehydrogenase deficiency, are at significantly increased risk of developing severe fluoropyrimidine-associated toxicity. Upfront DPYD*2A genotype-based dose reductions improve patient safety, but uncertainty exists whether this has a negative impact on treatment effectiveness. Therefore, our study investigated effectiveness and safety of DPYD*2A genotype-guided dosing. A cohort of 40 prospectively identified heterozygous DPYD*2A carriers, treated with a ~50% reduced fluoropyrimidine dose, was identified. For effectiveness analysis, a matched pair-analysis was performed in which for each DPYD*2A carrier a matched DPYD*2A wild-type patient was identified. Overall survival and progression-free survival were compared between the matched groups. The frequency of severe (grade = 3) treatment-related toxicity was compared to 1] a cohort of 1606 wild-type patients treated with full dose and 2] a cohort of historical controls derived from literature, i.e. 86 DPYD*2A variant carriers who received a full fluoropyrimidine dose. For 37 out of 40 DPYD*2A carriers, a matched control could be identified. Compared to matched controls, reduced doses did not negatively affect overall survival (median 27 months versus 24 months, p = 0.47) nor progression-free survival (median 14 months versus 10 months, p = 0.54). Risk of severe fluoropyrimidine-related toxicity in DPYD*2A carriers treated with reduced dose was 18%, comparable to wild-type patients (23%, p = 0.57) and significantly lower than the risk of 77% in DPYD*2A carriers treated with full dose (p < 0.001). Our study is the first to show that DPYD*2A genotype-guided dosing appears to have no negative effect on effectiveness of fluoropyrimidine-based chemotherapy, while resulting in significantly improved patient safety.

Impactfactor: 7.360

The Effect of Obesity on Anti-Xa Concentrations in Bariatric Patients
Schijns W, **Deenen MJ**, Aarts EO, Homan J, Janssen IM, Berends FJ, Kaasjager KA
Obes Surg. 2018 Jul;28(7):1997-2005

BACKGROUND:
Morbidly obese patients are at increased risk to develop venous thromboembolism (VTE), especially after bariatric surgery. Adequate postoperative thrombosis prophylaxis is of utmost importance. It is assumed that morbidly obese

patients need higher doses of low molecular weight heparin (LMWH) compared to normal-weight patients; however, current guidelines based on relative efficacy in obese populations are lacking.
OBJECTIVES:
First, we will evaluate the relationship between body weight descriptors and anti-Xa activity prospectively. Second, we will determine the dose-linearity of LMWH in morbidly obese patients.
SETTING:
This study was performed in a general hospital specialized in bariatric surgery.
METHODS:
Patients were scheduled for a Roux-en-Y gastric bypass with a total bodyweight (TBW) of =?140 kg. Patients (n?=?50, 64% female) received a daily postoperative dose of 5700 IU of nadroparin for 4 weeks. Anti-Xa activity was determined 4 h after the last nadroparin administration. To determine the dose linearity, anti-Xa was determined following a preoperative dose of 2850 IU nadroparin in another 50 patients (52%).
RESULTS:
TBW of the complete group was 148.5?±?12.6 kg. Mean anti-Xa activity following 5700 IU nadroparin was 0.19?±?0.07 IU/mL. Of all patients, 32% had anti-Xa levels below the prophylactic range. Anti-Xa activity inversely correlated with TBW (correlation coefficient -?0.410) and lean body weight (LBW; correlation coefficient -?0.447); 67% of patients with a LBW =?80 kg had insufficient anti-Xa activity concentrations. No VTE events occurred.
CONCLUSIONS:
In morbidly obese patients, a postoperative dose of 5700 IU of nadroparin resulted in subprophylactic exposure in a significant proportion of patients. Especially in patients with LBW =?80 kg, a higher dose may potentially be required to reach adequate prophylactic anti-Xa levels.

Impactfactor: 3.895

The impact of liver resection on the dihydrouracil:uracil plasma ratio in patients with colorectal liver metastases

Jacobs BA, Snoeren N, Samim M, Rosing H, de Vries N, **Deenen MJ**, Beijnen JH, Schellens JHM, Koopman M, van Hillegersberg R

Eur J Clin Pharmacol. 2018 Jun;74(6):737-744

PURPOSE:
The dihydrouracil (DHU):uracil (U) plasma ratio is a promising marker for identification of dihydropyrimidine dehydrogenase (DPD)-deficient patients. The objective of this study was to determine the effect of liver resection on the DHU:U plasma ratio in patients with colorectal liver metastases (CRLM).
METHODS:
An observational study was performed in which DHU:U plasma ratios in patients with CRLM were analyzed prior to and 1 day after liver resection. In addition, the DHU:U plasma ratio was quantified in six additional patients 4-8 weeks after liver resection to explore long-term effects on the DHU:U plasma ratio. Quantification of U and DHU plasma levels was performed using a validated ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) assay.
RESULTS:
The median (range) DHU:U plasma ratio in 15 patients prior to liver resection was 10.7 (2.6-14.4) and was significantly reduced to 5.5 (<?quantification limit (LLOQ-10.5) 1 day after resection (p?=?0.0026). This reduction was caused by a decrease in DHU plasma levels from 112.0 (79.8-153) ng/mL to 41.2 (<?LLOQ-160) ng/mL 1 day after resection (p?=?0.0004). Recovery of the DHU:U plasma ratio occurred 4-8 weeks after liver resection, which was shown by a median (range) DHU:U plasma ratio in six patients of 9.1 (6.9-14.5).
CONCLUSION:
Liver resection leads to very low DHU:U plasma ratios 1 day after liver resection, which is possibly caused by a reduction in DPD activity. Quantification of the DHU:U plasma ratios directly after liver resection could lead to false-positive identification of DPD deficiency and is therefore not advised.

Impactfactor: 2.679

The relation between the load, duration and steam penetration capacity of a surface steam sterilization process; a case study

van Doornmalen Gomez Hoyos JPCM, **van Wezel RAC**, Kopinga K

PDA J Pharm Sci Technol. 2018 Nov 27. pii: pdajpst.2017.008490. [Epub ahead of print]

BACKGROUND:
In practice it is claimed that the characteristics of a load influence a surface steam sterilization process. [Rev#2 Com#1] 'Limited and mainly qualitative' information on this topic has been found in the literature.
AIM:
To find if a load influences the duration and the related characteristics of a surface steam sterilization process.
METHOD:
In a case study 30 days of every load monitoring with an objective, quantifying steam penetration test has been performed. This resulted in 98 production processes with load monitoring. The acquired data was analyzed.

FINDINGS:

A relation is found between the weight of a load and the duration of a surface steam sterilization process.

CONCLUSIONS:

It is demonstrated in this case study that the heavier a sterilizer load the longer the process will take. Additionally, it is concluded that when the duration of a process is longer, diffusion will have more effect and steam penetration increases.

Impactfactor: --

Cardiologie

A Novel Angiographic Quantification of Â Aortic Regurgitation After TAVR Provides an Accurate Estimation of Regurgitation Fraction Derived From Cardiac Magnetic Resonance Imaging

Abdel-Wahab M, Abdelghani M, Miyazaki Y, Holy EW, Merten C, Zachow D, **Tonino P**, Rutten MCM, van de Vosse FN, Morel MA, Onuma Y, Serruys PW, Richardt G, Soliman OI

JACC Cardiovasc Interv. 2018 Feb 12 11(3):287-297. Epub 2018 Jan 17

OBJECTIVES:

This study sought to compare a new quantitative angiographic technique to cardiac magnetic resonance-derived regurgitation fraction (CMR-RF) for the quantification of prosthetic valve regurgitation (PVR) after transcatheter aortic valve replacement (TAVR).

BACKGROUND:

PVR after TAVR is challenging to quantify, especially during the procedure.

METHODS:

Post-replacement aortograms in 135 TAVR recipients were analyzed offline by videodensitometry to measure the ratio of the time-resolved contrast density in the left ventricular outflow tract to that in the aortic root (videodensitometric aortic regurgitation [VD-AR]). CMR was performed within an interval of =30 days (11 ± 6 days) after the procedure.

RESULTS:

The average CMR-RF was 6.7 ± 7.0% whereas the average VD-AR was 7.0 ± 7.0%. The correlation between VD-AR and CMR-RF was substantial (r = 0.78, p < 0.001). On receiver-operating characteristic curves, a VD-AR =10% corresponded to >mild PVR as defined by CMR-RF (area under the curve: 0.94; p < 0.001; sensitivity 100%, specificity 83%), whereas a VD-AR =25% corresponded to moderate-to-severe PVR (area under the curve: 0.99; p = 0.004; sensitivity 100%, specificity 98%). Intraobserver reproducibility was excellent for both techniques (for CMR-RF, intraclass correlation coefficient: 0.91, p < 0.001; for VD-AR intraclass correlation coefficient: 0.93, p < 0.001). The difference on rerating was -0.04 ± 7.9% for CMR-RF and -0.40 ± 6.8% for VD-AR.

CONCLUSIONS:

The angiographic VD-AR provides a surrogate assessment of PVR severity after TAVR that correlates well with the CMR-RF.

Impactfactor 9.881

Adapting detection sensitivity based on evidence of irregular sinus arrhythmia to improve atrial fibrillation detection in insertable cardiac monitors

Pürerfellner H, Sanders P, Sarkar S, Reisfeld E, Reiland J, Koehler J, Pokushalov E, Urban L, **Dekker LRC**

Europace. 2018 Nov 1;20(FI_3):f321-f328

Aims:

Intermittent change in p-wave discernibility during periods of ectopy and sinus arrhythmia is a cause of inappropriate atrial fibrillation (AF) detection in insertable cardiac monitors (ICM). To address this, we developed and validated an enhanced AF detection algorithm.

Methods and results:

Atrial fibrillation detection in Reveal LINQ ICM uses patterns of incoherence in RR intervals and absence of P-wave evidence over a 2-min period. The enhanced algorithm includes P-wave evidence during RR irregularity as evidence of sinus arrhythmia or ectopy to adaptively optimize sensitivity for AF detection. The algorithm was developed and validated using Holter data from the XPECT and LINQ Usability studies which collected surface electrocardiogram (ECG) and continuous ICM ECG over a 24-48?h period. The algorithm detections were compared with Holter annotations, performed by multiple reviewers, to compute episode and duration detection performance. The validation dataset comprised of 3187?h of valid Holter and LINQ recordings from 138 patients, with true AF in 37 patients yielding 108 true AF episodes =2-min and 449?h of AF. The enhanced algorithm reduced inappropriately detected episodes by 49% and duration by 66% with <1% loss in true episodes or duration. The algorithm correctly identified 98.9% of total AF duration and 99.8% of total sinus or non-AF rhythm duration. The algorithm detected 97.2% (99.7% per-patient average) of all AF episodes =2-min, and 84.9% (95.3% per-patient average) of detected episodes involved AF.

Conclusion:

An enhancement that adapts sensitivity for AF detection reduced inappropriately detected episodes and duration with minimal reduction in sensitivity.

Impactfactor 5.231

Angiographic and clinical outcomes of antegrade versus retrograde techniques for chronic total occlusion revascularizations: Insights from the PRISON IV trial

Zivelonghi C, van Andel M, Venturi G, Amoroso G, **Teeuwen K**, Tijssen JGP, Tavella D, Ribichini F, Ten Berg JM, Resning BJ, Henriques JPS, Suttorp MJ, Agostoni P, Van der Schaaf RJ

Catheter Cardiovasc Interv. 2018 Oct 2. [Epub ahead of print]

OBJECTIVES:
Available data indicate mixed outcomes after using retrograde techniques for chronic total occlusion(CTO) recanalization, with generally higher need for repeat revascularization. Aim of this study is to analyze the angiographic and clinical outcome of patients treated with retrograde techniques in the PRISON-IV trial.
METHODS AND RESULTS:
This is a post-hoc sub-analysis from the randomized PRISON-IV trial. Briefly, 330 patients with a successfully recanalized CTO lesion were randomized 1:1 to receive either hybrid-SES or EES. The hybrid-SES failed to reach the non-inferiority primary endpoint of in-segment late lumen loss at 9-month angiography follow-up. In the present analysis, we divided the population according to the first technical approach, namely antegrade (n?=?285) or retrograde approach (n?=?45). Demographic characteristics were similar between the two groups, while angiographic features disclosed higher CTO lesion complexity in the group treated with retrograde techniques (J-CTO score: 1.8?±?1.1 vs 2.6?±?1.1, respectively, P?<?0.001), with longer occlusions (17.6?±?10?mm vs 28.8?±?18.7?mm, P?<?0.001) and longer stented segment (48.9?±?24.4?mm vs 73.1?±?33.2?mm, P?<?0.001). Quantitative coronary analysis disclosed similar results at follow-up angiography, with a non-significantly higher in-stent late-lumen loss in the retrograde group (0.08?±?0.52?mm vs 0.18?±?0.56?mm, P?=?0.32). Clinical follow-up at 12-months showed similar outcome, with a non-significantly higher target-lesions revascularization rate in the retrograde group (6% vs 11.1% respectively, P?=?0.2). Significant improvements in angina functional class were observed in both groups.
CONCLUSIONS:
The present analysis supports the benefits of retrograde techniques in CTO revascularization, with non-significant differences in angiographic and clinical outcomes at late follow-up.

Impactfactor 2.602

Angiography Versus Hemodynamics to Predict the Natural History of Coronary Stenoses: Fractional Flow Reserve Versus Angiography in Multivessel Evaluation 2 Substudy

Ciccarelli G, Barbato E, Toth G, Gahl B, Xaplanteris P, Fournier S, Milkas A, Bartunek J, Vanderheyden M, **Pijls N**, Tonino P, Fearon WF, Jüni P, De Bruyne B
Circulation. 2018 Apr 3;137(14):1475-1485

Erratum in
Correction to: Angiography Versus Hemodynamics to Predict the Natural History of Coronary Stenoses: Fractional Flow Reserve Versus Angiography in Multivessel Evaluation 2 Substudy. [Circulation. 2018]
Abstract
BACKGROUND:
Among patients with documented stable coronary artery disease and in whom no revascularization was performed, we compared the respective values of angiographic diameter stenosis (DS) and fractional flow reserve (FFR) in predicting natural history.
METHODS:
The present analysis included the 607 patients from the FAME 2 trial (Fractional Flow Reserve Versus Angiography in Multivessel Evaluation 2) in whom no revascularization was performed. FFR varied from 0.20 to 1.00 (average 0.74±0.16), and DS (by quantitative coronary analysis) varied from 8% to 98% (average 53±15). The primary end point, defined as vessel-oriented clinical end point (VOCE) at 2 years, was a composite of prospectively adjudicated cardiac death, vessel-related myocardial infarction, vessel-related urgent, and not urgent revascularization. The stenoses were divided into 4 groups according to FFR and %DS values: positive concordance (FFR=0.80; DS=50%), negative concordance (FFR>0.80; DS<50%), positive mismatch (FFR=0.80; DS<50%), and negative mismatch (FFR>0.80; DS=50%).
RESULTS:
The rate of VOCE was highest in the positive concordance group (log rank: X2=80.96; P=0.001) and lowest in the negative concordance group. The rate of VOCE was higher in the positive mismatch group than in the negative mismatch group (hazard ratio, 0.38; 95% confidence interval, 0.21-0.67; P=0.001). There was no significant difference in VOCE between the positive concordance and positive mismatch groups (FFR=0.80; hazard ratio, 0.77; 95% confidence interval, 0.57-1.09; P=0.149) and no significant difference in rate of VOCE between the negative mismatch and negative concordance groups (FFR>0.80; hazard ratio, 1.89; 95% confidence interval, 0.96-3.74; P=0.067).
CONCLUSIONS: In patients with stable coronary disease, physiology (FFR) is a more important determinant of the natural history of coronary stenoses than anatomy (DS).

Impactfactor 18.880

Atrial Fibrillation Detection Using a Novel Cardiac Ambulatory Monitor Based on Photo-Plethysmography at the Wrist

Bonomi AG, Schipper F, Eerikäinen LM, Margarito J, van Dinther R, Muesch G, de Morree HM, Aarts RM, Babaeizadeh S, McManus DD, **Dekker LR**
J Am Heart Assoc. 2018 Aug 7;7(15):e009351

Background Long-term continuous cardiac monitoring would aid in the early diagnosis and management of atrial fibrillation (AF). This study examined the accuracy of a novel approach for AF detection using photo-plethysmography signals measured from a wrist-based wearable device.
Methods and Results ECG and contemporaneous pulse data were collected from 2 cohorts of AF patients: AF patients (n=20) undergoing electrical cardioversion (ECV) and AF patients (n=40) that were prescribed for 24 hours ECG Holter in outpatient settings (HOL). Photo-plethysmography and acceleration data were collected at the wrist and processed to determine the inter-pulse interval and discard inter-pulse intervals in presence of motion artifacts. A Markov model was deployed to assess the probability of AF given irregular pattern in inter-pulse interval sequences. The AF detection algorithm was evaluated against clinical rhythm annotations of AF based on ECG interpretation. Photo-plethysmography recordings from apparently healthy volunteers (n=120) were used to establish the false positive AF detection rate of the algorithm. A total of 42 and 855 hours (AF: 21 and 323 hours) of photo-plethysmography data were recorded in the ECV and HOL cohorts, respectively. AF was detected with >96% accuracy (ECV, sensitivity=97%; HOL , sensitivity=93%; both with specificity=100%). Because of motion artifacts, the algorithm did not provide AF classification for 44±16% of the monitoring period in the HOL group. In healthy controls, the algorithm demonstrated a <0.2% false positive AF detection rate. Conclusions A novel AF detection algorithm using pulse data from a wrist-wearable device can accurately discriminate rhythm irregularities caused by AF from normal rhythm.

Impactfactor *4.450*

Avoiding Surgical Skill Decay: A Systematic Review on the Spacing of Training Sessions

Cecilio-Fernandes D, Cnossen F, Jaarsma DA, **Tio RA**

J Surg Educ. 2018 Mar - Apr;75(2):471-480

OBJECTIVE:
Spreading training sessions over time instead of training in just 1 session leads to an improvement of long-term retention for factual knowledge. However, it is not clear whether this would also apply to surgical skills. Thus, we performed a systematic review to find out whether spacing training sessions would also improve long-term retention of surgical skills.
DESIGN:
We searched the Medline, PsycINFO, Embase, Eric, and Web of Science online databases. We only included articles that were randomized trials with a sample of medical trainees acquiring surgical motor skills in which the spacing effect was reported. The quality and bias of the articles were assessed using the Cochrane Collaboration's risk of bias assessment tool.
RESULTS:
With respect to the spacing effect, 1955 articles were retrieved. After removing duplicates and articles that did not meet the inclusion criteria, 11 articles remained. The overall quality of the experiments was "moderate." Trainees in the spaced condition scored higher in a retention test than students in the massed condition.
CONCLUSIONS:
Our systematic review showed evidence that spacing training sessions improves long-term surgical skills retention when compared to massed practice. However, the optimal gap between the re-study sessions is unclear.

Impactfactor *2.302*

Bioresorbable polymer drug-eluting stents - Authors' reply

Kandzari DE, Mauri L, **Koolen JJ**, Doros G, Waksman R

Lancet. 2018 Mar 10 391(10124):936-937

Geen abstract beschikbaar.

Impactfactor *53.254*

Cardiac Outcomes After Treatment for Depression in Patients With Acute Coronary Syndrome

Zimmermann FM, El Farissi M, Tonino PA

JAMA. 2018 Nov 27;320(20):2151-2152

Comment in:
Cardiac Outcomes After Treatment for Depression in Patients With Acute Coronary Syndrome-Reply. [JAMA. 2018]
Comment on:
Effect of Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac Outcomes in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. [JAMA. 2018]

Impactfactor *47.661*

Cardiac structure and function before and after bariatric surgery: a clinical overview

Lascaris B, Pouwels S, **Houthuizen P, Dekker LR,** Nienhuijs SW**,** Bouwman RA, Buise MP

Clin Obes. 2018 Dec;8(6):434-443

Obesity, defined as a body mass index of =30 kg/m2 , is the most common chronic metabolic disease worldwide and its prevalence has been strongly increasing. Obesity has deleterious effects on cardiac function. The purpose of this review is to evaluate the effects of obesity and excessive weight loss due to bariatric surgery on cardiac function, structural changes and haemodynamic responses of both the left and right ventricle.

Impactfactor --

Catheter ablation of symptomatic idiopathic ventricular arrhythmias : AÂ five-year single-centre experience

Oomen AWGJ, Dekker LRC, Meijer A

Neth Heart J. 2018 Apr 26(4):210-216

AIMS:
This study was designed to gain insight into the patient characteristics, results and possible complications of ablation procedures for symptomatic idiopathic premature ventricular complexes (PVC) and idiopathic ventricular tachycardia (VT).
METHODS:
Data were collected from all patients who underwent radiofrequency catheter ablation for symptomatic PVCs and idiopathic VT in the Catharina Hospital between 1 January 2011 and 31 December 2015. The procedural endpoint was elimination or non-inducibility of the clinical arrhythmia. Successful sustained ablation was defined as the persistent elimination of at least 80% of the PVCs or the absence of VTs at follow-up. In case of suspected PVC-induced cardiomyopathy, the systolic left ventricular function was reassessed 3 months post procedure.
RESULTS:
Our cohort consisted of 131 patients who underwent one or more ablation procedures; 99 because of symptomatic premature ventricular complexes, 32 because of idiopathic VT. In total 147 procedures were performed. The procedural ablation success rate was 89%. Successful sustained ablation rate was 82%. Eighteen (13.2%) patients had suspected PVC-induced cardiomyopathy. In 15 of them (83%), successful sustained ablation was achieved and the left ventricular ejection fraction improved from a mean of 39% (±8.8) to 55.4% (±8.1). Most arrhythmias originated from the right ventricular outflow tract (60%) or aortic cusps (13%). Complications included three tamponades.
CONCLUSION:
Catheter ablation therapy for idiopathic ventricular arrhythmias is very effective with a sustained success rate of 82%. In patients with PVC-induced cardiomyopathy, it leads to improvement of systolic left ventricular function. However, risk for complications is not negligible, even in experienced hands.

Impactfactor *1.476*

Catheter-Based Measurements of Absolute Coronary Blood Flow and Microvascular Resistance: Feasibility, Safety, and Reproducibility in Humans

Xaplanteris P, Fournier S, Keulards DC, Adjedj J, Ciccarelli G, Milkas A, Pellicano M**, Van't Veer M**, Barbato E**, Pijls NH**, De Bruyne B

Circ Cardiovasc Interv. 2018 Mar;11(3):e006194

BACKGROUND:
The principle of continuous thermodilution can be used to calculate absolute coronary blood flow and microvascular resistance (R). The aim of the study is to explore the safety, feasibility, and reproducibility of coronary blood flow and R measurements as measured by continuous thermodilution in humans.
METHODS AND RESULTS:
Absolute coronary flow and R can be calculated by thermodilution by infusing saline at room temperature through a dedicated monorail catheter. The temperature of saline as it enters the vessel, the temperature of blood and saline mixed in the distal part of the vessel, and the distal coronary pressure were measured by a pressure/temperature sensor-tipped guidewire. The feasibility and safety of the method were tested in 135 patients who were referred for coronary angiography. No significant adverse events were observed; in 11 (8.1%) patients, bradycardia and concomitant atrioventricular block appeared transiently and were reversed immediately on interruption of the infusion. The reproducibility of measurements was tested in a subgroup of 80 patients (129 arteries). Duplicate measurements had a strong correlation both for coronary blood flow (?=0.841, P<0.001; intraclass correlation coefficient=0.89, P<0.001) and R (?=0.780, P<0.001; intraclass correlation coefficient=0.89, P<0.001). In Bland-Altman plots, there was no significant bias or asymmetry.
CONCLUSIONS:
Absolute coronary blood flow (in L/min) and R (in mm Hg/L/min or Wood units) can be safely and reproducibly measured with continuous thermodilution. This approach constitutes a new opportunity for the study of the coronary microcirculation.

Impactfactor *6.504*

Clinical Outcomes and Cost-Effectiveness of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Stable Coronary Artery Disease: Three-Year Follow-Up of the FAME 2 Trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation)

Fearon WF, Nishi T, De Bruyne B, Boothroyd DB, Barbato E, **Tonino P**, Juni P, **Pijls NHJ**, Hlatky MA FAME 2 Trial Investigators

Circulation. 2018 Jan 30 137(5):480-487. Epub 2017 Nov 2

BACKGROUND:
Previous studies found that percutaneous coronary intervention (PCI) does not improve outcome compared with medical therapy (MT) in patients with stable coronary artery disease, but PCI was guided by angiography alone. FAME 2 trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) compared PCI guided by fractional flow reserve with best MT in patients with stable coronary artery disease to assess clinical outcomes and cost-effectiveness.
METHODS:
A total of 888 patients with stable single-vessel or multivessel coronary artery disease with reduced fractional flow reserve were randomly assigned to PCI plus MT (n=447) or MT alone (n=441). Major adverse cardiac events included death, myocardial infarction, and urgent revascularization. Costs were calculated on the basis of resource use and Medicare reimbursement rates. Changes in quality-adjusted life-years were assessed with utilities determined by the European Quality of Life-5 Dimensions health survey at baseline and over follow-up.
RESULTS:
Major adverse cardiac events at 3 years were significantly lower in the PCI group compared with the MT group (10.1% versus 22.0%; P<0.001), primarily as a result of a lower rate of urgent revascularization (4.3% versus 17.2%; P<0.001). Death and myocardial infarction were numerically lower in the PCI group (8.3% versus 10.4%; P=0.28). Angina was significantly less severe in the PCI group at all follow-up points to 3 years. Mean initial costs were higher in the PCI group ($9944 versus $4440; P<0.001) but by 3 years were similar between the 2 groups ($16?792 versus $16?737; P=0.94). The incremental cost-effectiveness ratio for PCI compared with MT was $17?300 per quality-adjusted life-year at 2 years and $1600 per quality-adjusted life-year at 3 years. The above findings were robust in sensitivity analyses.
CONCLUSIONS:
PCI of lesions with reduced fractional flow reserve improves long-term outcome and is economically attractive compared with MT alone in patients with stable coronary artery disease.

Impactfactor 18.880

Comparison between electrocardiogram- and photoplethysmogram-derived features for atrial fibrillation detection in free-living conditions

Eerikäinen LM, Bonomi AG, Schipper F, **Dekker LR**, Vullings R, de Morree HM, Aarts RM

Physiol Meas. 2018 Aug 8;39(8):084001

OBJECTIVE: Atrial fibrillation (AF) is the most commonly experienced arrhythmia and it increases the risk of stroke and heart failure. The challenge in detecting the presence of AF is the occasional and asymptomatic manifestation of the condition. Long-term monitoring can increase the sensitivity of detecting intermittent AF episodes, however it is either cumbersome or invasive and costly with electrocardiography (ECG). Photoplethysmography (PPG) is an unobtrusive measuring modality enabling heart rate monitoring, and promising results have been presented in detecting AF. However, there is still limited knowledge about the applicability of the PPG solutions in free-living conditions. The aim of this study was to compare the inter-beat interval derived features for AF detection between ECG and wrist-worn PPG in daily life.
APPROACH: The data consisted of 24?h ECG, PPG, and accelerometer measurements from 27 patients (eight AF, 19 non-AF). In total, seven features (Shannon entropy, root mean square of successive differences (RMSSD), normalized RMSSD, pNN40, pNN70, sample entropy, and coefficient of sample entropy (CosEn)) were compared. Body movement was measured with the accelerometer and used with three different thresholds to exclude PPG segments affected by movement.
MAIN RESULTS: CosEn resulted as the best performing feature from ECG with Cohens kappa 0.95. When the strictest movement threshold was applied, the same performance was obtained with PPG (kappa??=??0.96). In addition, pNN40 and pNN70 reached similar results with the same threshold (kappa??=??0.95 and 0.94), but were more robust with respect to movement artefacts. The coverage of PPG was 24.0%-57.6% depending on the movement threshold compared to 92.1% of ECG.
SIGNIFICANCE: The inter-beat interval features derived from PPG are equivalent to the ones from ECG for AF detection. Movement artefacts substantially worsen PPG-based AF monitoring in free-living conditions, therefore monitoring coverage needs to be carefully selected. Wrist-worn PPG still provides a promising technology for long-term AF monitoring.

Impactfactor 2.006

Comparison of ICD shock rates in Japanese and non-Japanese patients in the PainFree SST study

Kurita T, Ando K, Ueda M, Shizuta S, Okamura H, Matsumoto N, Gerritse B, Fagan DH, Schloss EJ, **Meijer A**, Auricchio A, Sterns LD, Okumura K PainFree SST investigators

Pacing Clin Electrophysiol. 2018 Sep 41(9):1185-1191. Epub 2018 Aug 13

BACKGROUND:
The PainFree Smart Shock Technology (SST) study showed a low implantable cardioverter-defibrillator (ICD) inappropriate shock rate. However, the majority of patients were from Western countries with patient characteristics different from those in Japan. ICD shock rates using the novel SST algorithms in Japanese patients are still unknown.
METHODS:
All 2,770 patients in the PainFree SST study (Japan [JPN]: N = 181, other geographies [OJPN]: N = 2,589) were included in this analysis.
RESULTS:
Japanese patients had higher average left ventricular ejection fraction (P < 0.0001), higher prevalence of secondary prevention indications (P < 0.0001), nonischemic cardiomyopathy (P < 0.0001), and permanent atrial fibrillation (P < 0.0001). The appropriate shock rate at 12 months was not different between JPN and OJPN: 6.4% and 6.3%, respectively (P = 0.95). The inappropriate shock rate at 12 months was significantly higher in Japanese patients (2.9% vs 1.7%, P = 0.017). However, after propensity score matching to adjust for the difference in baseline characteristics, the difference in inappropriate shock rate was not statistically significant (P = 0.51).
CONCLUSIONS:
There was no difference in the appropriate shock rate between Japan and other geographies. The inappropriate shock rate in Japan was low, although it was slightly higher compared to other geographies due to baseline characteristics, including a higher prevalence of permanent AF. There was not a statistically significant difference after adjusting for baseline characteristics.

Impactfactor *1.441*

Comparison of level of cognitive process between case-based items and non-case-based items of the interuniversity progress test of medicine in the Netherlands

Cecilio-Fernandes D, Kerdijk W, Bremers AJ, Aalders W, **Tio RA**

J Educ Eval Health Prof. 2018 15:28. Epub 2018 Dec 12

PURPOSE:
It is assumed that case-based questions require higher order cognitive processing, whereas questions that are not case-based require lower order cognitive processing. In this study, we investigated to what extent case-based questions and questions that are not case-based, relate to Bloom's taxonomy.
METHODS:
In this article, 4800 questions of the Progress Test were classified whether it was a case-based question and the level of Bloom's taxonomy. Lower-order questions require students to remember or/and basically understand the knowledge. Higher-order questions require students to apply, analyze, or/and evaluate. A phi-coefficient was calculated to investigate the relations between the presence of case-based questions and the required level of cognitive processing.
RESULTS:
Our results demonstrated that case-based questions were measuring higher levels of cognitive processing in 98.1% of the questions. Of the non-case-based questions, 33.7% required a higher level of cognitive processing. The phi-coefficient demonstrated a significant moderate correlation between the presence of a patient case in a question and its required level of cognitive processing (phi-coefficient = 0.55, p<0.001).
CONCLUSION:
Medical teachers should be aware of the association between item formats (case-based versus non-case-based) and the cognitive processes they elicit in order to meet a certain balance in a test, taking the learning objectives as well as the test difficulty into account.

Impactfactor --

Defibrillator shocks and their effect on objective and subjective patient outcomes: Results of the PainFree SST clinical trial

Sears SF, Rosman L, Sasaki S, Kondo Y, Sterns LD, Schloss EJ, Kurita T, **Meijer A**, Raijmakers J, Gerritse B, Auricchio A

Heart Rhythm. 2018 May 15(5):734-740. Epub 2017 Dec 24

BACKGROUND:
The effect of implantable cardioverter-defibrillator (ICD) shock on device-measured activity and patient-reported outcomes is unknown.
OBJECTIVE:
The purpose of this study was to analyze the acute and long-term effects of ICD shock on objective behavioral data (ie, device-based physical activity) and subjective patient-reported outcomes (eg, quality of life and shock

anxiety).
METHODS:
The PainFree Smart Shock Technology (SST) clinical trial included 2770 patients with a single- or dual-chamber ICD or cardiac resynchronization therapy - defibrillator device who were followed for 22 ± 9 months. Participants completed measures of quality of life (EuroQol-5D [EQ-5D] questionnaire) and shock anxiety (Florida Shock Anxiety Scale) at baseline, biannual visits, and monthly for 6 months after an ICD shock. Daily physical activity data were obtained from a built-in device accelerometer.
RESULTS:
The average daily activity was 185.3 ± 119.4 min/d. Activity was significantly reduced after an ICD shock (P < .0001) and recovered to a normal level after ~90 days. An ICD shock was also associated with decreased quality of life (EQ5-D health score) and increased EQ-5D anxiety scores, but it did not affect mobility, self-care, activity, or pain. Similarly, shock anxiety (Florida Shock Anxiety Scale) increased in shocked patients and remained significantly elevated at 24 months, regardless of appropriate or inappropriate shock delivery.
CONCLUSION:
ICD shocks have a long-lasting adverse effect on both objective, device-measured physical activity and subjective patient-reported outcomes of quality of life and shock anxiety. Successful management of patients with an ICD requires attention to clinically relevant behavioral and psychological outcomes to expedite recovery and return to activities of daily living.

Impactfactor 4.743

Defining and Measuring a Standard Set of Patient-Relevant Outcomes in Coronary Artery Disease

Daeter EJ, Timmermans MJ, Hirsch A, Lipsic E, **Houterman S**; Meetbaar Beter advisory board, **van Veghel D**, van der Nat PB

Am J Cardiol. 2018 Jun 15;121(12):1477-1488

Systematic outcome measurement enables to continuously improve treatment results and stimulates dissemination of best practices. For patients with coronary artery disease, no examples yet exist of standard sets of patient-relevant outcome measures that have already been fully implemented at a large scale in clinical care. The aim of this paper is twofold: (1) to share the standard set of outcome measures as developed by Meetbaar Beter, and (2) to show how the standard set is presented and published to support improvement of cardiac care. A step-wise approach was followed by an expert panel to construct a standard set of outcome measures. This resulted in a comprehensive set of relevant outcome measures, comprising 4 generic and 11 treatment-specific outcomes. Both short-term and long-term outcomes measures up to 5 years of follow-up were included. Relevant initial conditions were selected to enable case-mix adjustment. The standard set has been implemented in 21 hospitals across the Netherlands. The results and experiences have been used to fine-tune the set in 4 reporting cycles in 2012 to 2016, using an annual maintenance cycle. Currently about 83,000 percutaneous coronary interventions and 30,000 coronary artery bypass graftings are included in the dataset, covering the majority of all percutaneous coronary interventions and coronary artery bypass graftings in the Netherlands. In conclusion, Meetbaar Beter has defined and implemented a comprehensive set of patient-relevant outcome measures for coronary artery disease, and the variation of the results among the centers indicates that there are sufficient opportunities to further improve cardiac care in the Netherlands.

Impactfactor 3.171

Design and rationale of the Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen (MASTER DAPT) Study

Frigoli E, Smits P, Vranckx P, Ozaki Y, Tijssen J, Jüni P, Morice MC, Onuma Y, Windecker S, Frenk A, Spaulding C, Chevalier B, Barbato E, **Tonino P**, Hildick-Smith D, Roffi M, Kornowski R, Schultz C, Lesiak M, Iñiguez A, Colombo A, Alasnag M, Mullasari A, James S, Stankovic G, Ong PJL, Rodriguez AE, Mahfoud F, Bartunek J, Moschovitis A, Laanmets P, Leonardi S, Heg D, Sunnåker M, Valgimigli M

Am Heart J. 2018 Nov 22; 209:97-105

BACKGROUND:
The optimal duration of antiplatelet therapy in high-bleeding risk (HBR) patients with coronary artery disease treated with newer-generation drug-eluting bioresorbable polymer-coated stents remains unclear.
DESIGN:
MASTER DAPT (clinicaltrial.govNCT03023020) is an investigator-initiated, open-label, multicenter, randomized controlled trial comparing an abbreviated versus a standard duration of antiplatelet therapy after bioresorbable polymer-coated Ultimaster (TANSEI) sirolimus-eluting stent implantation in approximately 4,300 HBR patients recruited from =100 interventional cardiology centers globally. After a mandatory 30-day dual-antiplatelet therapy (DAPT) run-in phase, patients are randomized to (a) a single antiplatelet regimen until study completion or up to 5?months in patients with clinically indicated oral anticoagulation (experimental 1-month DAPT group) or (b) continue DAPT for at least 5?months in patients without or 2 in patients with concomitant indication to oral anticoagulation, followed by a single antiplatelet regimen (standard antiplatelet regimen). With a final sample size of 4,300 patients, this study is powered to assess the noninferiority of the abbreviated antiplatelet regimen with

respect to the net adverse clinical and major adverse cardiac and cerebral events composite end points and if satisfied for the superiority of abbreviated as compared to standard antiplatelet therapy duration in terms of major or clinically relevant nonmajor bleeding. Study end points will be adjudicated by a blinded Clinical Events Committee.
CONCLUSIONS:
The MASTER DAPT study is the first randomized controlled trial aiming at ascertaining the optimal duration of antiplatelet therapy in HBR patients treated with sirolimus-eluting bioresorbable polymer-coated stent implantation.

Impactfactor 4.171

Early initiation of extracorporeal life support in refractory out-of-hospital cardiac arrest: Design and rationale of the INCEPTION trial

Bol ME, Suverein MM, Lorusso R, Delnoij TSR, Brandon Bravo Bruinsma GJ, **Otterspoor L**, Kuijpers M, Lam KY, Vlaar APJ, Elzo Kraemer CV, van der Heijden JJ, Scholten E, Driessen AHG, Montero Cabezas JM, Rittersma SZH, Heijnen BG, Taccone FS, Essers B, Delhaas T, Weerwind PW, Roekaerts PMHJ, Maessen JG, van de Poll MCG
Am Heart J. 2018 Dec 14;210:58-68. [Epub ahead of print]

patients. These studies, however, are hampered by their non-randomized, observational design and are mostly single-center. A multicenter, randomized controlled trial is urgently warranted to evaluate the effectiveness of ECPR.
HYPOTHESIS:
We hypothesize that early initiation of ECPR in refractory out-of-hospital cardiac arrest (OHCA) improves the survival rate with favorable neurological status.
STUDY DESIGN:
The INCEPTION trial is an investigator-initiated, prospective, multicenter trial that will randomly allocate 110 patients to either continued CPR or ECPR in a 1:1 ratio. Patients eligible for inclusion are adults (= 70?years) with witnessed OHCA presenting with an initial rhythm of ventricular fibrillation (VF) or ventricular tachycardia (VT), who received bystander basic life support and who fail to achieve sustained return of spontaneous circulation within 15?minutes of cardiopulmonary resuscitation by emergency medical services. The primary endpoint of the study is 30-day survival rate with favorable neurological status, defined as 1 or 2 on the Cerebral Performance Category score. The secondary endpoints include 3, 6 and 12-month survival rate with favorable neurological status and the cost-effectiveness of ECPR compared to CCPR.
SUMMARY:
The INCEPTION trial aims to determine the clinical benefit for the use of ECPR in patients with refractory OHCA presenting with VF/VT. Additionally, the feasibility and cost-effectiveness of ECPR will be evaluated.

Impactfactor 4.171

Electrical latency predicts the optimal left ventricular endocardial pacing site: results from a multicentre international registry.

Sieniewicz BJ, Behar JM, Sohal M, Gould J, Claridge S, Porter B, Niederer S, Gamble JHP, Betts TR, Jais P, Derval N, Spragg DD, Steendijk P, **van Gelder BM**, **Bracke FA**, Rinaldi CA.
Europace. 2018 Dec 1 20(12):1989-1996.

Aims:
The optimal site for biventricular endocardial (BIVENDO) pacing remains undefined. Acute haemodynamic response (AHR) is reproducible marker of left ventricular (LV) contractility, best expressed as the change in the maximum rate of LV pressure (LV-dp/dtmax), from a baseline state. We examined the relationship between factors known to impact LV contractility, whilst delivering BIVENDO pacing at a variety of LV endocardial (LVENDO) locations.
Methods and results:
We compiled a registry of acute LVENDO pacing studies from five international centres: Johns Hopkins-USA, Bordeaux-France, Eindhoven-The Netherlands, Oxford-United Kingdom, and Guys and St Thomas' NHS Foundation Trust, London-UK. In all, 104 patients incorporating 687 endocardial and 93 epicardial pacing locations were studied. Mean age was 66?±?11?years, mean left ventricular ejection fraction 24.6?±?7.7% and mean QRS duration of 163?±?30?ms. In all, 50% were ischaemic [ischaemic cardiomyopathy (ICM)]. Scarred segments were associated with worse haemodynamics (dp/dtmax; 890?mmHg/s vs. 982?mmHg/s, P?<?0.01). Delivering BiVENDO pacing in areas of electrical latency was associated with greater improvements in AHR (P?<?0.01). Stimulating late activating tissue (LVLED?>50%) achieved greater increases in AHR than non-late activating tissue (LVLED?<?50%) (8.6?±?9.6% vs. 16.1?±?16.2%, P?=?0.002). However, the LVENDO pacing location with the latest Q-LV, was associated with the optimal AHR in just 62% of cases.
Conclusions:
Identifying viable LVENDO tissue which displays late electrical activation is crucial to identifying the optimal

BiVENDO pacing site. Stimulating late activating tissue (LVLED >50%) yields greater improvements in AHR however, the optimal location is frequently not the site of latest activation.

Impactfactor *5.231*

Endocardial center motion for quantification of left ventricular discoordination in heart failure using cine MRI

Saporito S, **Houthuizen P**, Aben JMM, Westenberg JJM, van Den Bosch HCM, **van Assen HC**, Mischi M.Physiol Meas. 2018 Feb 28 39(2):025009

OBJECTIVE:
To compare a novel cardiovascular magnetic resonance technique for the assessment of left ventricular (LV) mechanical discoordination by characterizing the endocardial center motion (ECM) in short-axis cine MRI in healthy volunteers and heart failure patients with left bundle branch block (HF-LBBB).
APPROACH:
To evaluate ECM analysis as mechanical discoordination measure, we retrospectively compared spatial and temporal features of the ECM between a group of healthy volunteers (n??=??14) and conduction defect patients (HF-LBBB, n??=??31). We tracked the center of the endocardial borders on short-axis view MRI cine loops during the cardiac cycle. From the ECM trajectory we calculated the overall traveled distance, the enclosed area, the eccentricity of the trajectory, and the maximum traveled distance. The ECM can be visualized in spatial coordinates as well as by its temporal behavior. We evaluated the classification performance of these measures for LBBB detection. We also quantified the coherence of the ECM on the longitudinal direction by considering the variability of the ECM measures between different short-axis slices.
MAIN RESULTS:
Patients with LBBB showed significantly higher traveled distance (p??<??0.0001), enclosed area (p??<??0.002), eccentricity (p??<??0.02), and peak displacement (p??<??0.02) of the endocardial center. Patients with positive late gadolinium enhancement showed a higher variability of ECM measures across different slices (p??<??0.05).
SIGNIFICANCE:
ECM analysis is feasible and it allows the assessment of left ventricular mechanical discoordination. Differences in ECM measures permit one to distinguish between LBBB and healthy volunteers.

Impactfactor *2.006*

Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

Xaplanteris P, Fournier S, **Pijls NH**, Fearon WF, Barbato E, **Tonino PA**, Engstrøm T, Kääb S, Dambrink JH, Rioufol G, Toth GG, Piroth Z, Witt N, Fröbert O, Kala P, Linke A, Jagic N, Mates M, Mavromatis K, Samady H, Irimpen A, Oldroyd K, Campo G, Rothenbühler M, Jüni P, De Bruyne B; FAME 2 Investigators

N Engl J Med. 2018 Jul 19;379(3):250-259

BACKGROUND:
We hypothesized that fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) would be superior to medical therapy as initial treatment in patients with stable coronary artery disease.
METHODS:
Among 1220 patients with angiographically significant stenoses, those in whom at least one stenosis was hemodynamically significant (FFR, =0.80) were randomly assigned to FFR-guided PCI plus medical therapy or to medical therapy alone. Patients in whom all stenoses had an FFR of more than 0.80 received medical therapy and were entered into a registry. The primary end point was a composite of death, myocardial infarction, or urgent revascularization.
RESULTS:
A total of 888 patients underwent randomization (447 patients in the PCI group and 441 in the medical-therapy group). At 5 years, the rate of the primary end point was lower in the PCI group than in the medical-therapy group (13.9% vs. 27.0%; hazard ratio, 0.46; 95% confidence interval [CI], 0.34 to 0.63; P<0.001). The difference was driven by urgent revascularizations, which occurred in 6.3% of the patients in the PCI group as compared with 21.1% of those in the medical-therapy group (hazard ratio, 0.27; 95% CI, 0.18 to 0.41). There were no significant differences between the PCI group and the medical-therapy group in the rates of death (5.1% and 5.2%, respectively; hazard ratio, 0.98; 95% CI, 0.55 to 1.75) or myocardial infarction (8.1% and 12.0%; hazard ratio, 0.66; 95% CI, 0.43 to 1.00). There was no significant difference in the rate of the primary end point between the PCI group and the registry cohort (13.9% and 15.7%, respectively; hazard ratio, 0.88; 95% CI, 0.55 to 1.39). Relief from angina was more pronounced after PCI than after medical therapy.
CONCLUSIONS:
In patients with stable coronary artery disease, an initial FFR-guided PCI strategy was associated with a significantly lower rate of the primary composite end point of death, myocardial infarction, or urgent revascularization at 5 years than medical therapy alone. Patients without hemodynamically significant stenoses had a favorable long-term outcome with medical therapy alone.

Impactfactor *79.258*

Fractional Flow Reserve and Quality-of-Life Improvement After Percutaneous Coronary Intervention in Patients With Stable Coronary Artery Disease

Nishi T, Piroth Z, De Bruyne B, Jagic N, Möbius-Winkler S, Kobayashi Y, Derimay F, Fournier S, Barbato E, **Tonino P**, Jüni P, **Pijls NH**, Fearon WF

Circulation. 2018 Oct 23;138(17):1797-1804

BACKGROUND:
Whether the benefit in quality of life (QOL) after percutaneous coronary intervention depends on the severity of the stenosis as determined by fractional flow reserve (FFR) remains unknown. This study sought to investigate the relationship between FFR values and improvement in QOL.
METHODS:
From the FAME 1 and 2 trials (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation), we identified 706 stable patients with coronary artery disease who had at least 1 lesion with an FFR=0.80 that was treated with percutaneous coronary intervention and 185 patients with coronary artery disease who had no lesion with an FFR=0.80 and were treated medically who served as a reference group. QOL was assessed by the European Quality of Life-5 Dimensions index at baseline, 1 month, and 1 year. We assessed the relationship between QOL improvement (defined as the change in European Quality of Life-5 Dimensions index from baseline) and FFR as a continuous value and according to abnormal FFR tertile.
RESULTS:
QOL improved significantly after percutaneous coronary intervention in each abnormal FFR tertile, whereas it did not change in the reference group. The lowest abnormal FFR subgroup had the greatest improvement in QOL at 1 month (P<0.001). In mixed-effects models for repeated measures, lower FFR (P=0.002 for 1 month and 0.049 for 1 year), greater delta FFR (P=0.021 for 1 month and 0.025 for 1 year), and higher angina class (P=0.001 for 1 month and <0.001 for 1 year) were associated with the greatest magnitude of QOL improvement at both 1 month and 1 year.
CONCLUSIONS:
Among patients with stable coronary artery disease, FFR and angina severity predict QOL improvement after percutaneous coronary intervention.

Impactfactor *18.880*

Health insurance outcome-based purchasing: The case of hospital contracting for cardiac interventions in the Netherlands

D. van Veghel, D. N. Schulz, A. H. M. van Straten, **T. A. Simmers**, A. Lenssen, **L. Kuijten-Slegers**, F. van Eenennaam, M. A. Soliman Hamad, B. A. de Mol & **L. R. C. Dekker**

INTERNATIONAL JOURNAL OF HEALTHCARE MANAGEMENT, 2018;11(4):371-8

Innovative forms of value-based purchasing contracts, based on outcome instead of volume, are imperative to face the imminent cost crisis in health care. The objective of this study was to design and implement a model for an outcome-based purchasing contract between a hospital and a health insurance company. The model was implemented in 2015. A study cohort (n = 14,944) from patients with coronary artery disease or atrial fibrillation treated in 2014 was compared to a historical reference cohort from patients treated between 2010 and 2013. The outcome measures and the model are based on Porter's value-based healthcare principles. Improvements in outcomes were observed, leading to a financial incentive to be spent on further quality improvement. Implementation of this model is a first step towards enabling inclusion of patient-relevant outcomes in purchasing for healthcare. It aligns the focus of health insurance companies and hospitals on patient value.

Impactfactor --

Impact of ultra-thin struts on restenosis after chronic total occlusion recanalization: Insights from the randomized PRISON IV trial

Zivelonghi C, **Teeuwen K**, Agostoni P, van der Schaaf RJ, Ribichini F, Adriaenssens T, Kelder JC, Tijssen JGP, Henriques JPS, Suttorp MJ

J Interv Cardiol. 2018 Oct 31(5):580-587. doi: 10.1111/joic.12516. Epub 2018 May 1

OBJECTIVES:
The PRISON-IV trial showed inferior outcome in patients with chronic total occlusions (CTOs) treated with the ultrathin-struts (60?µm for stent diameter =3?mm, 81µm >3?mm) hybrid-sirolimus eluting stents (SES) compared with everolimus eluting stents (EES, 81?µm). The aim of this study is to investigate if the use of smaller stents (=3?mm) was responsible for the inferior outcome reported in the trial.
METHODS:
In the PRISON-IV trial 330 patients with CTO lesion were randomized 1:1 to receive either hybrid-SES or EES. The hybrid-SES failed to reach the non-inferiority primary endpoint of in-segment late lumen loss (LLL) at 9-month angiographic follow-up. In this sub-analysis, we divided the population according to the different size of stents

implanted in those receiving only stents with diameter =3?mm (Group-A, 178 patients), only stents >3?mm (Group-B, 59 patients), and those receiving stents of both sizes (Group-C, 93 patients).
RESULTS:
Baseline and procedural characteristics were comparable in the three groups. At angiographic follow-up, most of the adverse outcomes occurred in Group A, with higher incidence of binary restenosis in the Hybrid-SES versus EES (10.3% vs 1.3%, P?=?0.03) and augmented in-stent diameter stenosis (26.04?±?18.59% vs 21.24?±?12.84, P?=?0.06). Similarly, optical coherence tomography (OCT), which was performed in 60 patients at follow-up, documented a mild trend toward lower values of minimum in stent area in Hybrid-SES arm of Group A (4.4?±?1.02mm2 vs 5.0?±?1.28mm2, respectively, P?=?0.16).
CONCLUSIONS:
The present analysis suggests that the inferior performance of the ultra-thin hybrid-SES in CTO-PCI is particularly pronounced when smaller stent (=3?mm diameter) are adopted, if compared with EES.

Impactfactor 1.728

Long-term impact of chronic total occlusion recanalisation in patients with ST-elevation myocardial infarction

Elias J, van Dongen IM, Råmunddal T, Laanmets P, Eriksen E, Meuwissen M, **Michels HR**, Bax M, Ioanes D, Suttorp MJ, Strauss BH, Barbato E, Marques KM, Claessen BEPM, Hirsch A, van der Schaaf RJ, Tijssen JGP, Henriques JPS, Hoebers LP; EXPLORE investigators: **Koolen JJ**

Heart. 2018 Sep;104(17):1432-1438. Epub 2018 Feb 20

BACKGROUND:
During primary percutaneous coronary intervention (PCI), a concurrent chronic total occlusion (CTO) is found in 10% of patients with ST-elevation myocardial infarction (STEMI). Long-term benefits of CTO-PCI have been suggested; however, randomised data are lacking. Our aim was to determine mid-term and long-term clinical outcome of CTO-PCI versus CTO-No PCI in patients with STEMI with a concurrent CTO.
METHODS:
The Evaluating Xience and left ventricular function in PCI on occlusiOns afteR STEMI (EXPLORE) was a multicentre randomised trial that included 302 patients with STEMI after successful primary PCI with a concurrent CTO. Patients were randomised to either CTO-PCI or CTO-No PCI. The primary end point of the current study was occurrence of major adverse cardiac events (MACE): cardiac death, coronary artery bypass grafting and MI. Other end points were 1-year left ventricular function (LVF); LV-ejection fraction and LV end-diastolic volume and angina status.
RESULTS:
The median long-term follow-up was 3.9 (2.1-5.0) years. MACE was not significantly different between both arms (13.5% vs 12.3%, HR 1.03, 95%?CI 0.54 to 1.98; P=0.93). Cardiac death was more frequent in the CTO-PCI arm (6.0% vs 1.0%, P=0.02) with no difference in all-cause mortality (12.9% vs 6.2%, HR 2.07, 95%?CI 0.84 to 5.14; P=0.11). One-year LVF did not differ between both arms. However, there were more patients with freedom of angina in the CTO-PCI arm at 1?year (94% vs 87%, P=0.03).
CONCLUSIONS:
In this randomised trial involving patients with STEMI with a concurrent CTO, CTO-PCI was not associated with a reduction in long-term MACE compared to CTO-No PCI. One-year LVF was comparable between both treatment arms. The finding that there were more patients with freedom of angina after CTO-PCI at 1-year follow-up needs further investigation.

Impactfactor 5.420

Long-term prognostic value of quantitative myocardial perfusion in patients with chest pain and normal coronary arteries

Monroy-Gonzalez AG, **Tio RA**, de Groot JC, Boersma HH, Prakken NH, De Jongste MJL, Alexanderson-Rosas E, Slart RHJA

J Nucl Cardiol. 2018 Oct 4.[Epub ahead of print]

BACKGROUND:
Patients with chest pain and no obstructive coronary artery disease have shown a high incidence of major adverse cardiovascular events (MACE). We evaluated the role of absolute myocardial perfusion quantification in predicting all-cause mortality and MACE during long-term follow-up in this group of patients.
METHODS:
We studied 79 patients who underwent Nitrogen-13 ammonia PET for quantification of global myocardial blood flow (MBF) and myocardial flow reserve (MFR) due to suspected impaired myocardial perfusion. Patients with coronary artery disease (i.e.,?>?30% stenosis in one or more coronary arteries) were excluded. We assessed all-cause mortality and MACE. MACE was defined as the composite incidence of death, myocardial infarction (MI), or hospitalization due to heart failure.
RESULTS:
Median follow-up was 8 (IQR: 3-14) years. Univariate Cox regression showed that only MFR (P?=?0.01) was a predictor of all-cause mortality. Univariate Cox regression analysis showed that both MFR and Stress MBF were

predictors of the composite endpoint of MACE (P?<?0.001 and P?=?0.01, respectively).
CONCLUSION:
Quantitative assessment of myocardial perfusion may predict all-cause mortality and MACE in patients with chest pain and normal coronary arteries in the long-term follow-up.

Impactfactor *3.847*

Myocardial bridging of the left anterior descending coronary artery is associated with reduced myocardial perfusion reserve: a (13)N-ammonia PET study

Monroy-Gonzalez AG, Alexanderson-Rosas E, Prakken NHJ, Juarez-Orozco LE, Walls-Laguarda L, Berrios-Barcenas EA, Meave-Gonzalez A, Groot JC, Slart RHJA, **Tio RA**

Int J Cardiovasc Imaging. 2018 Sep 28. [Epub ahead of print]

Myocardial Bridging (MB) refers to the band of myocardium that abnormally overlies a segment of a coronary artery. This paper quantitatively evaluates the influence of MB of the left anterior descending artery (LAD) on myocardial perfusion of the entire left ventricle. We studied 131 consecutive patients who underwent hybrid rest/stress 13N-ammonia positron emission tomography (PET) and coronary computed tomography angiography (CCTA) due to suspected myocardial ischemia. Patients with previous myocardial infarction and/or significant coronary artery disease (=?50% stenosis) were excluded. Myocardial perfusion measurements were compared between patients with and without LAD-MB. Additionally, we evaluated the relationship between anatomical characteristics (length and depth) of LAD-MB and myocardial perfusion measurements. 17 (13%) patients presented a single LAD-MB. Global myocardial perfusion reserve (MPR) was lower in patients with LAD-MB than in patients without LAD-MB (1.9?±?0.5 vs. 2.3?±?0.6, p?<?0.01). Global stress myocardial blood flow (MBF) was similar in patients with and without LAD-MB (2.2?±?0.4 vs. 2.3?±?0.7 ml/g/min, p?=?0.40). Global rest MBF was higher in patients with LAD-MB than in patients without LAD-MB (1.2?±?0.3 vs. 1.0?±?0.2 ml/g/min, p?<?0.01). Global rest MBF, stress MBF, and MPR quantifications were similar in patients with superficial and deep LAD-MB (all p?=?NS). We did not find any correlation between length and global rest MBF, stress MBF nor MPR (r?=?-?0.14, p?=?0.59; r?=?0.44, p?=?0.07; and r?=?0.45, p?=?0.07 respectively). Quantitative myocardial perfusion suggests that LAD-MB may be related to impaired perfusion reserve, an indicator of microvascular dysfunction. Anatomical characteristics of LAD-MB were not related to changes in myocardial perfusion.

Impactfactor *2.036*

Myocardial bridging, a trigger for Takotsubo syndrome

Triantafyllis AS, de Ridder S, **Teeuwen K, Otterspoor LC**

Neth Heart J. 2018 Nov;26(11):573-574

Geen abstract beschikbaar

Impactfactor *1.476*

Perforation of a saphenous vein graft anastomosed at a Y-configuration to the left internal mammary artery.

Triantafyllis AS, **Haeck JDE**, **van Dijk EGJA**, **Brueren GRG**, Spartalis E, **Tonino PAL**

Cardiovasc Revasc Med. 2018 Oct 16. pii: S1553-8389(18)30440-8. [Epub ahead of print]

Perforation of a saphenous vein graft (SVG) is a rare, yet dreadful complication during percutaneous coronary intervention (PCI). Perforation of a SVG arising at a Y-construction from the left internal mammary artery (LIMA) can be catastrophic since manipulations and material delivery through the single LIMA inflow can aggravate ischemia and accelerate hemodynamic collapse. Prior CABG and pericardial obliteration should not offer reassurance against tamponade, since coronary perforation in these patients may cause the development of loculated pericardial effusions, a complication associated with high mortality. Treating physicians must be alert for potential periprocedural pitfalls during PCI in post-CABG patients and these should be taken into consideration during interventional planning, procedure and follow-up.

Impactfactor --

Performance of idarucizumab as antidote of dabigatran in daily clinical practice

van der Wall SJ, van Rein N, van den Bemt B, Kruip MJHA, Meijer K, Te Boome LCJ, **Simmers TA**, Alings AMW, Tieleman R, Klok FA, Huisman MV

Europace. 2018 Oct 17. [Epub ahead of print]

Aims:
Because practice-based data on the usage of idarucizumab for urgent dabigatran reversal is unavailable, we evaluated the appropriateness of idarucizumab usage, its haemostatic effectiveness and clinical outcomes.
Methods and results:
An observational cohort study was performed including consecutive patients who were treated with idarucizumab between 2016 and 2018. Appropriate usage was assessed with predefined criteria. Post-

reversal effectiveness was evaluated according to International Society on Thrombosis and Haemostasis (ISTH) recommendations. Patients were followed for 90?days for occurrence of thromboembolism, (re-)bleeding and death. Idarucizumab was used in 88 patients, of whom 53 (60%) presented with severe bleeding (20 gastrointestinal and 18 intracranial) and 35 (40%) requiring urgent surgical intervention. Use of idarucizumab was judged inappropriate in 25 patients (28%). Effective haemostasis was achieved in 32 of 48 (67%) bleeding patients in whom assessment was possible. Seven of 16 patients with major bleeding who did not achieve effective haemostasis (five intracranial) died, compared with two of 32 patients with effective haemostasis (relative risk 7.0, 95% confidence interval 1.6-30). Four patients (4.2%) developed thromboembolism [2 (2.1%) within 30?days] and four patients (4.2%) re-bleeding, all within 10?days. Seventeen patients (19%) died; 10 (11%) within 5?days.
Conclusion:
In this practice-based cohort, idarucizumab use was considered inappropriate in 28% of patients. Effective haemostasis was achieved in two-third of bleeding patients and was associated with lower mortality risk. Clinical outcomes were similar to those observed in the RE-VERSE AD trial, comprising re-bleeds and thromboembolism, and a high-mortality rate.

Impactfactor 5.231

Pressure gradient vs. flow relationships to characterize the physiology of a severely stenotic aortic valve before and after transcatheter valve implantation

Johnson NP, Zelis JM, Tonino PAL, Houthuizen P, Bouwman RA, **Brueren GRG**, Johnson DT, **Koolen JJ**, Korsten HHM, **Wijnbergen IF, Zimmermann FM**, Kirkeeide RL, **Pijls NHJ**, Gould KL

Eur Heart J. 2018 Jul 21 39(28):2646-2655

Aims:
Echocardiography and tomographic imaging have documented dynamic changes in aortic stenosis (AS) geometry and severity during both the cardiac cycle and stress-induced increases in cardiac output. However, corresponding pressure gradient vs. flow relationships have not been described.
Methods and results:
We recruited 16 routine transcatheter aortic valve implantations (TAVI's) for graded dobutamine infusions both before and after implantation; 0.014? pressure wires in the aorta and left ventricle (LV) continuously measured the transvalvular pressure gradient (?P) while a pulmonary artery catheter regularly assessed cardiac output by thermodilution. Before TAVI, ?P did not display a consistent relationship with transvalvular flow (Q). Neither linear resistor (median R2 0.16) nor quadratic orifice (median R2?<?0.01) models at rest predicted stress observations; the severely stenotic valve behaved like a combination. The unitless ratio of aortic to left ventricular pressures during systolic ejection under stress conditions correlated best with post-TAVI flow improvement. After TAVI, a highly linear relationship (median R2 0.96) indicated a valid valve resistance.
Conclusion:
Pressure loss vs. flow curves offer a fundamental fluid dynamic synthesis for describing aortic valve pathophysiology. Severe AS does not consistently behave like an orifice (as suggested by Gorlin) or a resistor, whereas TAVI devices behave like a pure resistor. During peak dobutamine, the ratio of aortic to left ventricular pressures during systolic ejection provides a 'fractional flow reserve' of the aortic valve that closely approximates the complex, changing fluid dynamics. Because resting assessment cannot reliably predict stress haemodynamics, 'valvular fractional flow' warrants study to explain exertional symptoms in patients with only moderate AS at rest.

Impactfactor 23.425

Privacy of patient data in quality-of-care registries in cardiology and cardiothoracic surgery: the impact of the new general data protection regulation EU-law

Wierda E, Eindhoven DC, Schalij MJ, Borleffs CJ, Amoroso G, **van Veghel D**, Mitchell CR, de Mol BA, Hirsch A, Ploem MC

Eur Heart J Qual Care Clin Outcomes. 2018 Oct 1;4(4):239-245

Quality-of-care registries have been shown to improve quality of healthcare and should be facilitated and encouraged. The data of these registries are also very valuable for medical data research. While fully acknowledging the importance of re-using already available data for research purposes, there are concerns about how the applicable privacy legislation is dealt with. These concerns are also articulated in the new European law on privacy, the 'General Data Protection Regulation' (GDPR) which has come into force on 25 May 2018. The aim of this review is to examine what the implications of the new European data protection rules are for quality-of-care registries in Europe while providing examples of three quality-of-care registries in the field of cardiology and cardiothoracic surgery in Europe. A general overview of the European and national legal framework (relevant data protection and privacy legislation) applying to quality-of-care registries is provided. One of the main rules is that non-anonymous patient data may, in principle, not be used for research without the patient's informed consent. When patient data are solely and strictly used for quality control and improvement, this rule does not apply. None

of the described registries (NHR, SWEDEHEART, and NICOR) currently ask specific informed consent of patients before using their data in the registry, but they do carry out medical data research. Application of the GDPR implies that personal data may only be used for medical data research after informing patients and obtaining their explicit consent.

Impactfactor --

Prognostic Value of the Residual SYNTAX Score After Functionally Complete Revascularization in ACS

Kobayashi Y, Lønborg J, Jong A, Nishi T, De Bruyne B, Høfsten DE, Kelbæk H, Layland J, Nam CW, **Pijls NH**, **Tonino PA**, Warnøe J, Oldroyd KG, Berry C7, Engstrøm T, Fearon WF; DANAMI-3-PRIMULTI, FAME, and FAMOUS-NSTEMI Study Investigators

J Am Coll Cardiol. 2018 Sep 18;72(12):1321-1329

BACKGROUND:

The residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (RSS) quantitatively assesses angiographic completeness of revascularization after percutaneous coronary intervention (PCI) and has been shown to be a predictor of events after angiography-guided PCI. In stable patients undergoing functionally complete revascularization with fractional flow reserve (FFR) guidance, RSS did not predict outcome. Whether this is also true in patients with acute coronary syndromes (ACS) is unknown.

OBJECTIVES:

The purpose of this study was to determine whether the RSS could predict outcomes in patients with ACS.

METHODS:

From the DANAMI-3-PRIMULTI (Primary PCI in Patients With ST-elevation Myocardial Infarction and Multivessel Disease: Treatment of Culprit Lesion Only or Complete Revascularization), FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation), and FAMOUS-NSTEMI (Fractional Flow Reserve Versus Angiographically Guided Management to Optimise Outcomes in Unstable Coronary Syndromes) trials, 547 patients presented with ACS and underwent functionally complete revascularization. Major adverse cardiac events (MACE) were defined as the composite endpoint of all-cause death, nonfatal myocardial infarction, and any repeat revascularization. The RSS was based on the recalculation of the SYNTAX score after PCI. We compared differences in 2-year outcome by the RSS subgroups: 0, 1 to <5, 5 to <10, =10 (RSS = 0 represents angiographically complete revascularization).

RESULTS:

The study population consisted of 271 patients with unstable angina/non-ST-segment elevation myocardial infarction and 276 with ST-segment elevation myocardial infarction. The mean RSS was 6.7 ± 5.8. MACE at 2 years occurred in 69 patients (12.6%). Patients with and without MACE had similar RSS after PCI (RSS: 7.2 ± 5.5 vs. 6.6 ± 5.9; p = 0.23). Kaplan-Meier curve analysis showed a similar incidence of MACE regardless of the RSS subgroups (p = 0.54). With and without adjustment of clinical variables, RSS was not a significant predictor of MACE or of each component of MACE.

CONCLUSIONS:

After complete revascularization of functionally significant stenosis by FFR, the extent of residual angiographic disease is not associated with subsequent ischemic events in patients presenting with ACS. These results suggest that the concept of functionally complete revascularization is applicable even in ACS patients. (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation [F.A.M.E.] NCT00267774; Fractional Flow Reserve Versus Angiographically Guided Management to Optimise Outcomes in Unstable Coronary Syndromes [FAMOUS NSTEMI] NCT01764334; Primary PCI in Patients With ST-elevation Myocardial Infarction and Multivessel Disease: Treatment of Culprit Lesion Only or Complete Revascularization [DANAMI-3-PRIMULTI]; NCT01960933).

Impactfactor *16.834*

Quantitative myocardial perfusion evaluation with positron emission tomography and the risk of cardiovascular events in patients with coronary artery disease: a systematic review of prognostic studies.

Juárez-Orozco LE, **Tio RA**, Alexanderson E, Dweck M, Vliegenthart R, El Moumni M, Prakken N, Gonzalez-Godinez I, Slart RHJA

Eur Heart J Cardiovasc Imaging. 2018 Oct 1 19(10):1179-1187

Aims:

To evaluate the prognostic value of quantitative myocardial perfusion imaging with positron emission tomography (PET) for adverse cardiovascular outcomes in patients with known or suspected coronary artery disease (CAD).

Methods and results:

A search in MEDLINE and Embase was conducted for studies that evaluated (i) myocardial perfusion in absolute terms with PET, (ii) prognostic value for the development of major adverse cardiovascular events (MACE), cardiac death, and/or all-cause mortality, and (iii) patients with known or suspected CAD. Studies were divided according to the radiotracer utilized and their included population (patients with and without previous infarction). Comprehensive description and a selected instance of pooling were performed. Eight studies (n?=?6804) were analysed and documented clear variability in population, quantitative PET variables operationalization [stress myocardial blood flow (sMBF) and flow reserve (MFR)], statistical covariate structure, follow-up, and radiotracer

utilized. MFR was independently associated with MACE in eight studies [range of adjusted hazard ratios (HRs): 1.19-2.93]. The pooling instance demonstrated that MFR significantly associates with the development of MACEs (HR: 1.92 [1.29, 2.84]; P?=?0.001). sMBF was only associated with MACE in two studies that evaluated it, and only one study documented sMBF as a better predictor than MFR.
Conclusion:
This systematic review demonstrates the prognostic value of quantitative myocardial perfusion evaluated with PET, in the form of MFR and sMBF, for the development of major adverse cardiovascular outcomes in populations with known or suspected CAD. In the qualitative comparison, MFR seems to outperform sMBF as an independent prognostic factor. Evidence is still lacking for assessing quantitative PET for the occurrence of cardiac death and all-cause mortality. There is clear heterogeneity in predictor operationalization and study performances.

Impactfactor *8.336*

Recovery of absolute coronary flow and resistance one week after percutaneous coronary intervention of a chronic totally occluded coronary artery using the novel RayFlow© infusion catheter
Keulards DCJ, Zimmermann FM, Pijls NHJ, Teeuwen K
EuroIntervention. 2018 Aug 3;14(5):e588-e589

Geen abstract beschikbaar

Impactfactor *4.417*

RegressionExplorer: Interactive Exploration of Logistic Regression Models with Subgroup Analysis
Dingen D, **Veer MV**, **Houthuizen P**, Mestrom EHJ, Korsten EHHM, Bouwman ARA, Wijk JV
IEEE Trans Vis Comput Graph. 2018 Sep 13. [Epub ahead of print]

We present RegressionExplorer, a Visual Analytics tool for the interactive exploration of logistic regression models. Our application domain is Clinical Biostatistics, where models are derived from patient data with the aim to obtain clinically meaningful insights and consequences. Development and interpretation of a proper model requires domain expertise and insight into model characteristics. Because of time constraints, often a limited number of candidate models is evaluated. RegressionExplorer enables experts to quickly generate, evaluate, and compare many different models, taking the workflow for model development as starting point. Global patterns in parameter values of candidate models can be explored effectively. In addition, experts are enabled to compare candidate models across multiple subpopulations. The insights obtained can be used to formulate new hypotheses or to steer model development. The effectiveness of the tool is demonstrated for two uses cases: prediction of a cardiac conduction disorder in patients after receiving a heart valve implant and prediction of hypernatremia in critically ill patients.

Impactfactor *3.078*

Response by Kobayashi et al to Letter Regarding Article "Three-Vessel Assessment of Coronary Microvascular Dysfunction in Patients with Clinical Suspicion of Ischemia: Prospective Observation Study With the Index of Microcirculatory Resistance"
Kobayashi Y, Fearon WF, Nishi T, Choi DH, Lee JM, Lee JH, **Zimmermann FM**, Jung JH, Lee HJ, Doh JH, Nam CW, Shin ES, Koo BK
Circ Cardiovasc Interv. 2018 Feb 11(2):e006302

geen abstract beschikbaar

Impactfactor *6.504*

Review on Factors Influencing Physician Guideline Adherence in Cardiology
Hoorn CJGM, Crijns HJGM, Dierick-van Daele ATM, **Dekker LRC**
Cardiol Rev. 2018 Apr 9. [Epub ahead of print]

Cardiovascular disease is the most common cause of death in Western countries. Physician adherence to guidelines is often suboptimal, resulting in impaired patient outcome and prognosis. Multiple studies have been conducted to evaluate patterns and the influencing factors of patient adherence, but little is known about factors influencing physician guideline adherence. This review aims to identify factors influencing physician guideline adherence relevant to cardiology and to provide insights and suggestions for future improvement. Physician adherence was measured as adherence to standard local medical practice and applicable guidelines. Female gender and older age had a negative effect on physician guideline adherence. In addition, independent of the type of heart disease, physicians without cardiologic specialization were linked to physician noncompliance. Also, guideline adherence in primary care centers was at a lower level compared to secondary or tertiary care centers. The importance of guideline adherence increases as patients age, and complex diseases and comorbidity arise. Appropriate resources and interventions, taking important factors for nonadherence in account, are necessary to improve guideline adoption and adherence in every level of the chain. This in turn should improve patient outcome.

Impactfactor *1.951*

[Risk of heart failure diminished thanks to stomach reduction in obesity] - Hartfalen afgenomen door maagverkleining bij obesitas

Botter B1, Koolen E, van Montfort G, **Bracke F**, Bouwman A, Buise M

Ned Tijdschr Geneeskd. 2018;162:D1972

BACKGROUND:
Obesity is a chronic disease and a risk factor for heart failure. In end-stage heart failure, heart transplantation may be the only available treatment option, but obesity is a contraindication for this treatment because of its unfavourable prognosis. Bariatric surgery and its subsequent weight loss may affect the indication for transplantation in patients with heart failure and morbid obesity.
CASE DESCRIPTION:
A 46-year-old patient with morbid obesity and heart failure underwent gastric sleeve resection in preparation of a heart transplantation. Without it, he would not have been considered eligible for transplantation because of his obesity. The bariatric intervention was also intended to use weight loss as a way to reduce the symptoms of his heart failure and to make rehabilitation possible. One year after surgery, the condition of the patient had improved so much that heart transplantation was no longer necessary.
CONCLUSION:
Bariatric surgery is safe for morbidly obese patients with severe heart failure and may sometimes even avoid heart transplantation.

Impactfactor --

Sex Differences in Adenosine-Free Coronary Pressure Indexes: A CONTRAST Substudy

Shah SV, **Zimmermann FM**, Johnson NP, Nishi T, Kobayashi Y, Witt N, Berry C, Jeremias A, Koo BK, Esposito G8, Rioufol G, Park SJ, Oldroyd KG, Barbato E, **Pijls NH**, De Bruyne B, Fearon WF; CONTRAST Study Investigators

JACC Cardiovasc Interv. 2018 Aug 13;11(15):1454-1463

OBJECTIVES:
The goal of this study was to investigate sex differences in adenosine-free coronary pressure indexes.
BACKGROUND:
Several adenosine-free coronary pressure wire indexes have been proposed to assess the functional significance of coronary artery lesions; however, there is a theoretical concern that sex differences may affect diagnostic performance because of differences in resting flow and distal myocardial mass.
METHODS:
In this CONTRAST (Can Contrast Injection Better Approximate FFR Compared to Pure Resting Physiology?) substudy, contrast fractional flow reserve (cFFR), obtained during contrast-induced submaximal hyperemia, the instantaneous wave-free ratio (iFR), and distal/proximal coronary pressure ratio (Pd/Pa) were compared with fractional flow reserve (FFR) in 547 men and 216 women. Using FFR =0.8 as a reference, the diagnostic performance of each index was compared.
RESULTS:
Men and women had similar diameter stenosis (p = 0.78), but women were less likely to have FFR =0.80 than men (42.5% vs. 51.5%, p = 0.04). Sensitivity was similar among cFFR, iFR, and Pd/Pa when comparing women and men, respectively (cFFR, 77.5% vs. 75.3%; p = 0.69; iFR, 84.9% vs. 79.4%; p = 0.30; Pd/Pa, 78.8% vs. 77.3%; p = 0.78). cFFR was more specific than iFR or Pd/Pa regardless of sex (cFFR, 94.3% vs. 95.8%; p = 0.56; iFR, 75.6% vs. 80.1%; p = 0.38; Pd/Pa, 80.6% vs. 78.7%; p = 0.69). By receiver-operating characteristic curve analysis, cFFR provided better diagnostic accuracy than resting indexes irrespective of sex (p = 0.0001).
CONCLUSIONS:
Despite the theoretical concern, the diagnostic sensitivity and specificity of cFFR, iFR, and Pd/Pa did not differ between the sexes. Irrespective of sex, cFFR provides the best diagnostic performance

Impactfactor 9.881

Stress myocardial blood flow correlates with ventricular function and synchrony better than myocardial perfusion reserve: A Nitrogen-13 ammonia PET study

Juárez-Orozco LE, Alexanderson E, Dierckx RA, Boersma HH, Hillege JL, Zeebregts CJ, Martínez-Aguilar MM, Jordán-Ríos A, Ayala-German AG, Prakken N, **Tio RA**, Slart RH

J Nucl Cardiol. 2018 Jun;25(3):797-806

BACKGROUND:
Cardiac PET quantifies stress myocardial blood flow (MBF) and perfusion reserve (MPR), while ECG-gated datasets can measure components of ventricular function simultaneously. Stress MBF seems to outperform MPR in the detection of significant CAD. However, it is uncertain which perfusion measurement is more related to ventricular function. We hypothesized that stress MBF correlates with ventricular function better than MPR in patients studied for suspected myocardial ischemia.
METHODS:
We studied 248 patients referred to a rest and adenosine-stress Nitrogen-13 ammonia PET. We performed a multivariate analysis using systolic function (left ventricular ejection fraction, LVEF), diastolic function (mean filling

rate in diastole, MFR/3), and synchrony (Entropy) as the outcome variables, and stress MBF, MPR, and relevant covariates as the predictors. Secondarily, we repeated the analysis for the subgroup of patients with and without a previous myocardial infarction (MI).

RESULTS:

166 male and 82 female patients (mean age 63 ± 11 and 67 ± 11 year, respectively) were included. 60% of the patients presented hypertension, 57% dyslipidemia, 21% type 2 diabetes mellitus, 45% smoking, and 34.7% a previous MI. Mean stress MBF was 1.99 ± 0.75 mL/g/min, MPR = 2.55 ± 0.89, LVEF = 61.6 ± 15%, MFR/3 = 1.12 ± 0.38 EDV/s, and Entropy = 45.6 ± 11.3%. There was a significant correlation between stress MBF (P < .001) and ventricular function. This was stronger than the one for MPR (P = .063). Sex, age, diabetes, and extent of previous MI were also significant predictors. Results were similar for the analyses of the 2 subgroups.

CONCLUSION:

Stress MBF is better correlated with ventricular function than MPR, as evaluated by Nitrogen-13 ammonia PET, independently from other relevant cardiovascular risk factors and clinical covariates. This relationship between coronary vasodilatory capacity and ventricular function is sustained across groups with and without a previous MI.

Impactfactor 3.847

Subgroup Analysis Comparing Ultrathin, Bioresorbable Polymer Sirolimus-Eluting Stents Versus Thin, Durable Polymer Everolimus-Eluting Stents in Acute Coronary Syndrome Patients

Roguin A, Kandzari DE, Marcusohn E, **Koolen JJ,** Doros G, Massaro JM, Garcia-Garcia HM, Bennett J, Gharib EG, Cutlip DE, Waksman R

Circ Cardiovasc Interv. 2018 Oct;11(10):e007331

BACKGROUND:

Presentation with acute coronary syndromes (ACS) constitutes a high-risk subset of patients with worse outcome after percutaneous coronary intervention. We report clinical outcomes in subjects with ACS from the BIOFLOW V trial (BIOTRONIK - A Prospective Randomized Multicenter Study to Assess the Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in the Treatment of Subjects With up to Three De Novo or Restenotic Coronary Artery Lesions) comparing an ultrathin strut (60 µm) bioresorbable polymer sirolimus-eluting stent (BP-SES) with a thin strut (81 µm) durable polymer everolimus-eluting stent (DP-EES).

METHODS AND RESULTS:

Among 1334 patients randomized to 2:1 treatment with either BP-SES or DP-EES, 677 (50.7%) ACS patients without ST-segment-elevation myocardial infarction (MI; 454 BP-SES and 223 DP-EES) were identified in the retrospective post hoc analysis. The primary end point of 12-month target lesion failure, individual component end points, and stent thrombosis were evaluated. Recurrent MI was defined as a =50% increase of creatine kinase-myocardial band or in the absence of creatine kinase-myocardial band, troponin >50% increase over previous level and >3× the upper limit of normal). All events were adjudicated by a blinded independent clinical events committee. Overall, baseline clinical, angiographic, and procedural characteristics of the ACS population were similar between the 2 treatment groups. At 12 months, target lesion failure occurred in 5.6% (24/426) of BP-SES patients versus 11.0% (23/209) in DP-EES patients (P=0.02); target lesion failure composite components were cardiac death, 0% versus 1.0% (P=0.11); target vessel-related MI, 3.5% versus 9.7% (P=0.003); and clinically driven target lesion revascularization, 2.8% versus 3.4% (P=0.80). Spontaneous target vessel MI was 0.5% (2/425) for BP-SES versus 2.4% (5/206) for DP-EES (P=0.041). Stent thrombosis rates at 1 year were similar (0.5% versus 1.0%; P=0.601).

CONCLUSIONS:

In the ACS subgroup population of the BIOFLOW V study, treatment with BP-SES compared with DP-EES was associated with a significantly lower rate of 12-month target lesion failure, a difference driven by significantly lower periprocedural MI and spontaneous MI. These findings support treatment with an ultrathin strut BP-SES in ACS patients undergoing percutaneous coronary intervention.

Impactfactor 6.504

Sympathetic denervation in patients with ischemic cardiomyopathy and risk on ventricular tachy-arrhythmias. A pilot study

Noordzij W, Elvan A, Demirel F, Jager PL, **Tio RA**, Slart RH

Q J Nucl Med Mol Imaging. 2018 Dec;62(4):429-435

BACKGROUND:

Patients with ischemic cardiomyopathy (ICM) are at risk for ventricular arrhythmias and are protected by an implantable cardioverter defibrillator (ICD). Visualization of cardiac sympathetic innervation may play an additional role to left ventricular ejection fraction (LVEF) in identifying those patients who will benefit from ICD therapy. The purpose of this study was to detect the role of sympathetic denervation in the genesis of ventricular arrhythmias in ICM patients.

METHODS:

Twenty patients with ICM and LVEF <30% were included in this pilot study. Included patients were equally stratified into two groups: no history of arrhythmias (group A) and recurrent arrhythmias (group B). All patients

underwent cardiac sympathetic denervation (using carbon-11 labelled meta-hydroxy-ephedrine ([11C]-mHED)), myocardial ischemia and viability detection. Patients were followed up to one year after the imaging studies.
RESULTS:
Mean age was 63±7.5 years. Mean global retention of [11C]-mHED was 0.055±0,012 min-1, and was not different between the two patient groups: 0.056±0.011 min-1 vs. 0.054±0.013 min-1 for group A vs. group B, respectively. During follow-up, seven patients developed ventricular arrhythmias, and four patients died. No difference in [11C]-mHED retention was found between patients with and without ventricular arrhythmia during follow-up. However, size of denervated area was larger in patients who died during follow-up: 10±1 segments vs. 6±2 segments, P=0.002.
CONCLUSIONS:
Cardiac sympathetic innervation is impaired in patients with ischemic cardiomyopathy. All-cause mortality occurred in those patients with large areas of [11C]-mHED defect.

Impactfactor *2,368*

The Hemodynamic Effects of Different Pacing Modalities After Cardiopulmonary Bypass in Patients With Reduced Left Ventricular Function

Gielgens RCW, Herold IHF, van Straten AHM, **van Gelder BM**, **Bracke FA**, Korsten HHM, Soliman Hamad MA, Bouwman RA

J Cardiothorac Vasc Anesth. 2018 Feb 32(1):259-266. . Epub 2017 Jul 8

OBJECTIVES:
Patients with decreased left ventricular function undergoing cardiac surgery have a greater chance of difficult weaning from cardiopulmonary bypass and a poorer clinical outcome. Directly after weaning, interventricular dyssynchrony, paradoxical septal motion, and even temporary bundle-branch block might be observed. In this study, the authors measured arterial dP/dtmax, mean arterial pressure (MAP), and cardiac index using transpulmonary thermodilution, pulse contour analysis, and femoral artery catheter and compared the effects between right ventricular (A-RV) and biventricular (A-BiV) pacing on these parameters.
DESIGN:
Prospective study.
SETTING:
Single-center study.
PARTICIPANTS:
The study comprised 17 patients with a normal or prolonged QRS duration and a left ventricular ejection fraction =35% who underwent coronary artery bypass grafting with or without valve replacement.
INTERVENTIONS:
Temporary pacing wires were placed on the right atrium and both ventricles. Different pacing modalities were used in a standardized order.
MEASUREMENTS AND MAIN RESULTS:
A-BiV pacing compared with A-RV pacing demonstrated higher arterial dP/dtmax values (846 ± 646 mmHg/s v 800 ± 587 mmHg/s, p = 0.023) and higher MAP values (77 ± 19 mmHg v 71 ± 18 mmHg, p = 0.036).
CONCLUSION:
In patients with preoperative decreased left ventricular function undergoing coronary artery bypass grafting, A-BiV pacing improve the arterial dP/dtmax and MAP in patients with both normal and prolonged QRS duration compared with standard A-RV pacing. In addition, arterial dP/dtmax and MAP can be used to evaluate the effect of intraoperative pacing. In contrast to previous studies using more invasive techniques, transpulmonary thermodilution is easy to apply in the perioperative clinical setting.

Impactfactor *1.574*

The Impact of Curriculum Design in the Acquisition of Knowledge of Oncology: Comparison Among Four Medical Schools

Cecilio-Fernandes D, Aalders WS Bremers AJ, **Tio RA**, de Vries J

J Cancer Educ. 2018 Oct;33(5):1110-1114

Geen abstract beschikbaar

Impactfactor *--*

The Impact of Massed and Spaced-Out Curriculum in Oncology Knowledge Acquisition

Cecilio-Fernandes D, Aalders WS, de Vries J, **Tio RA**

J Cancer Educ. 2018 Aug;33(4):922-925

Starting in 2009, cancer has been the leading cause of death in the Netherlands. Oncology is therefore an important part of the medical curriculum in undergraduate education. It is crucial that medical students know about cancer, since doctors will encounter many cases of oncology. We have compared the influence that teaching oncology has when spread over a 3-year curriculum versus concentrated in one semester. The participants comprised 525 medical students from one medical school with comprehensive integrated curricula.

Of those, 436 followed the massed curriculum, with oncology concentrated in one semester. The remaining 89 students followed a spaced-out curriculum, in which oncology was spread out over 3 years. To measure students' knowledge, we used their progress test results from 2009 to 2012. All questions about oncology were categorized and selected. Because of our unbalanced sample and missing data and to reduce the chances for a type II error, we compared the growth of oncology questions using mixed effect models. A cubic growth model with an unstructured covariance matrix fitted our data best. At the start, students in the spaced-out curriculum scored higher on oncology questions. The initial growth was faster for the spaced-out curriculum students, whereas the acceleration over time was slower compared to the massed curriculum students. At the end of the growth curve, the knowledge of the massed curriculum students increased faster. In the last test, the massed curriculum students outperformed those in the spaced-out curriculum. The way students acquired and applied their knowledge was similar in both curricula. It seems, however, that students benefitted more from massed than spaced-out education, which may be due to the comprehensive integrated teaching involved.

Impactfactor --

The Prognostic Value of RightÂ VentricularÂ Deformation Imaging inÂ EarlyÂ Arrhythmogenic RightÂ Ventricular Cardiomyopathy

Mast TP, Taha K, Cramer MJ, Lumens J, van der Heijden JF, Bouma BJ, van den Berg MP, Asselbergs FW, Doevendans PA, Teske AJ

JACC Cardiovasc Imaging. 2018 Mar 9. pii: S1936-878X(18)30118-9. [Epub ahead of print]

OBJECTIVES:

The aim of this study was to investigate the prognostic value of echocardiographic deformation imaging in arrhythmogenic right ventricular cardiomyopathy (ARVC) to optimize family screening protocols.

BACKGROUND:

ARVC is characterized by variable disease expressivity among family members, which complicates family screening protocols. Previous reports have shown that echocardiographic deformation imaging detects abnormal right ventricular (RV) deformation in the absence of established disease expression in ARVC.

METHODS:

First-degree relatives of patients with ARVC were evaluated according to 2010 task force criteria, including RV deformation imaging (n = 128). Relatives fulfilling structural task force criteria were excluded for further analysis. At baseline, deformation patterns of the subtricuspid region were scored as type I (normal deformation), type II (delayed onset, decreased systolic peak, and post-systolic shortening), or type III (systolic stretching and large post-systolic shortening). The final study population comprised relatives who underwent a second evaluation during follow-up. Disease progression was defined as the development of a new 2010 task force criterion during follow-up that was absent at baseline.

RESULTS:

Sixty-five relatives underwent a second evaluation after a mean follow-up period of 3.7 ± 2.1 years. At baseline, 28 relatives (43%) had normal deformation (type I), and 37 relatives (57%) had abnormal deformation (type II or III) in the subtricuspid region. Disease progression occurred in 4% of the relatives with normal deformation at baseline and in 43% of the relatives with abnormal deformation at baseline ($p < 0.001$). Positive and negative predictive values of abnormal deformation were, respectively, 43% (95% confidence interval: 27% to 61%) and 96% (95% confidence interval: 82% to 100%).

CONCLUSIONS:

Normal RV deformation in the subtricuspid region is associated with absence of disease progression during nearly 4-year follow-up in relatives of patients with ARVC. Abnormal RV deformation seems to precede the established signs of ARVC. RV deformation imaging may potentially play an important role in ARVC family screening protocols.

Impactfactor *10.189*

Type D personality affects health-related quality of life in patients with lone atrial fibrillation by increasing symptoms related to sympathetic activation

Kupper N, van den Broek K, Haagh E, **van der Voort P**, Widdershoven J, Denollet J

J Psychosom Res. 2018 Dec;115:44-52

BACKGROUND:

Health-related quality of life (HRQoL) is impaired in patients with atrial fibrillation (AF), and even more so in patients with a Distressed personality type (Type D). It is unknown whether this extends to patients with 'lone AF'. Since chronic stress is associated with increased arousal, it might affect recurrences and thus HRQoL. The current study examined the influence of Type D on the trajectory of disease-specific and generic HRQoL, compared it with HRQoL in the general population, and assessed the mediating role of arousal symptoms (e.g., tachycardia, sweating).

METHODS:

159 patients with 'lone AF' (age: 61.6±0.8, 63% men, 3.3±5.0 years since diagnosis) filled out a survey on personality (Type D: DS14), quality of life (SF-36, AFQoL) and symptoms (ATSSS) of AF at inclusion, and 6, 12, and 18 months later. Linear mixed modeling was used.

RESULTS:
Generic HRQoL was reduced as compared to the general population, and all HRQoL scales remained stable across time. Type D personality was a significant predictor of worse disease-specific (estimate= -17.1 ; 95%CI:-23.9 - -10.2; p<.001), and generic HRQoL (estimatePCS=-5.5; 95%CI:-9.3 - -1.8; p=.004; estimateMCS=-14.8; 95%CI:-18.9- -10.6; p<.001), with arousal symptoms accounting for substantial change in the Type D estimate, suggesting partially shared variance between Type D and arousal symptoms in predicting HRQoL.
CONCLUSION:
HRQoL was stable across time, and systematically poorer in distressed 'lone AF' patients. Arousal symptoms partly explained the relation between Type D and HRQoL. Chronic distress may affect AF patients' HRQoL through sympathetic activation and accompanying complaints.

Impactfactor 2.947

Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents Versus Thin Durable Polymer Everolimus-Eluting Stents

Kandzari DE, **Koolen JJ**, Doros G, Massaro JJ, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE, Waksman R BIOFLOW V Investigators

J Am Coll Cardiol. 2018 Dec 25 72(25):3287-3297. Epub 2018 Sep 23

BACKGROUND:
Coronary drug-eluting stent development has introduced new metal alloys, changes in stent architecture, and bioresorbable polymers. Whether these advancements improve long-term clinical safety and efficacy has been inconsistent in prior studies.
OBJECTIVES:
The authors sought to compare late-term clinical outcomes among patients treated with an ultrathin strut (60 μm) bioresorbable polymer sirolimus-eluting stent (BP SES) and a thin strut (81 μm) durable polymer everolimus-eluting stent (DP EES) in a large randomized trial.
METHODS:
BIOFLOW V (Biotronik Prospective Randomized Multicenter Study to Assess the Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in the Treatment of Subjects with Up to Three De Novo or Restenotic Coronary Artery Lesions V) was an international randomized trial comparing coronary revascularization with BP SES and DP EES regarding the primary endpoint of 12-month target lesion failure (TLF). Analysis of pre-specified 2-year clinical outcomes was performed.
RESULTS:
Among 1,334 patients randomized to treatment with BP SES (n = 884) or DP EES (n = 450), the 2-year TLF rate was 7.5% for BP SES and 11.9% for DP EES (-4.33% treatment difference; 95% confidence interval: -8.16% to -0.91%; p = 0.015), driven by differences in target vessel myocardial infarction (MI) (5.3% vs. 9.5%; p = 0.01) and ischemia-driven target lesion revascularization (2.6% vs. 4.9%; p = 0.04). Rates of cardiac death or MI were 7.0% versus 10.4% for BP SES and DP EES, respectively (p = 0.047). Late/very late definite stent thrombosis was statistically lower for BP SES compared with DP EES (0.1% vs. 1.0%; p = 0.045).
CONCLUSIONS:
In a large randomized trial, significant differences in both TLF and target vessel-related MI persisted through 2 years, favoring treatment with BP SES over DP EES. Significantly lower cumulative target lesion revascularization and late/very late stent thrombosis were also observed with BP SES. (Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in Subjects With Coronary Artery Lesions [BIOFLOW-V]; NCT02389946).

Impactfactor 16.834

Validation of a novel non-hyperaemic index of coronary artery stenosis severity: the Resting Full-cycle Ratio (VALIDATE RFR) study

Svanerud J, Ahn JM, Jeremias A, **van 't Veer M**, Gore A, Maehara A, Crowley A, **Pijls NHJ**, De Bruyne B, Johnson NP, Hennigan B, Watkins S, Berry C, Oldroyd KG, Park SJ, Ali ZA

EuroIntervention. 2018 Sep 20;14(7):806-814

AIMS:
Randomised controlled trials have reported instantaneous wave-free ratio (iFR) to be non-inferior to fractional flow reserve (FFR) for major adverse cardiovascular events at one year; however, iFR is limited by sensitive landmarking of the pressure waveform, and the assumption that maximal flow and minimal resistance occur during a fixed period of diastole. We sought to validate the resting full-cycle ratio (RFR), a novel non-hyperaemic index of coronary stenosis severity based on unbiased identification of the lowest distal coronary pressure to aortic pressure ratio (Pd/Pa), independent of the ECG, landmark identification, and timing within the cardiac cycle.
METHODS AND RESULTS:
VALIDATE-RFR was a retrospective study designed to derive and validate the RFR. The primary endpoint was the agreement between RFR and iFR. RFR was retrospectively determined in 651 waveforms in which iFR was measured using a proprietary Philips/Volcano wire. RFR was highly correlated to iFR (R2=0.99, p<0.001), with a

mean bias of -0.002 (95% limits of agreement -0.023 to 0.020). The diagnostic performance of RFR versus iFR was diagnostic accuracy 97.4%, sensitivity 98.2%, specificity 96.9%, positive predictive value 94.5%, negative predictive value 99.0%, area under the receiver operating characteristic curve of 0.996, and diagnostically equivalent within 1% (mean difference -0.002; 95% CI: -0.009 to 0.006, p=0.03). The RFR was detected outside diastole in 12.2% (341/2,790) of all cardiac cycles and 32.4% (167/516) of cardiac cycles in the right coronary artery where the sensitivity of iFR compared to FFR was lowest (40.6%).
CONCLUSIONS:
RFR is diagnostically equivalent to iFR but unbiased in its ability to detect the lowest Pd/Pa during the full cardiac cycle, potentially unmasking physiologically significant coronary stenoses that would be missed by assessment dedicated to specific segments of the cardiac cycle.

Impactfactor *4.417*

What is the cause of P-wave undersensing in this CRT-D device?

Schroemges J, **Bracke FA, van Gelder BM**

Neth Heart J. 2018 Aug;26(7-8):409-410

Geen abstract beschikbaar

Impactfactor *1.476*

What is the cause of P-wave undersensing in this CRT-D device?

Schroemges J, **Bracke FA, van Gelder BM**

Neth Heart J. 2018 Aug;26(7-8):413-414

Geen abstract beschikbaar

Impactfactor *1.476*

Yellow traffic lights and grey zone fractional flow reserve values: stop or go?

Johnson NP, **Zimmermann FM**

Eur Heart J. 2018 May 7 39(18):1620-1622

Geen abstract beschikbaar

Impactfactor *23.425*

Chirurgie

A collective review of biological versus synthetic mesh-reinforced cruroplasty during laparoscopic Nissen fundoplication

Castelijns PSS, **Ponten JEH**, van de Poll MCG, **Nienhuijs SW**, **Smulders JF**

J Minim Access Surg. 2018 Apr-Jun;14(2):87-94

Background:
Laparoscopic cruroplasty and fundoplication have become the gold standard in the treatment of hiatal hernia and gastro-oesophageal reflux disease (GERD). The use of a mesh-reinforcement of the cruroplasty has been proven effective; although, there is a lack of evidence considering which type of mesh is superior. The aim of this study was to compare recurrence rates after mesh reinforced cruroplasty using biological versus synthetic meshes.
Methods:
We performed a systematic review of all clinical trials published between January 2004 and September 2015 describing the application of a mesh in the hiatal hernia repair during Nissen fundoplication for both GERD and hiatal hernia. The primary outcome was the recurrence rate, and secondary outcomes were complication rate, mortality and symptomatic outcome.
Results:
We included 16 studies and extracted data regarding 1089 mesh operated patients of whom 385 received a biological mesh and 704 a synthetic mesh. The mean follow-up was 53.4 months. The recurrence rate in the synthetic mesh group was 6.8% compared to 16.1% in the biological mesh group ($P < 0.05$). The complication rate was 5.1% and 4.6% ($P = 0.694$), respectively, and there were 12 mesh-related complications. No mesh-related mortality was reported.
Conclusion:
Mesh reinforcement of hiatal hernia repair seems safe in the short-term follow-up. The available literature suggests no clear advantage of biological over synthetic meshes. Regarding cost-efficiency and short-term results, the use of synthetic nonabsorbable meshes might be advocated.

Impactfactor: 1.137

A Delphi Consensus of the Crucial Steps in Gastric Bypass and Sleeve Gastrectomy Procedures in the Netherlands

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Obes Surg. 2018 Sep;28(9):2634-2643

PURPOSE:
Bariatric procedures are technically complex and skill demanding. In order to standardize the procedures for research and training, a Delphi analysis was performed to reach consensus on the practice of the laparoscopic gastric bypass and sleeve gastrectomy in the Netherlands.
METHODS:
After a pre-round identifying all possible steps from literature and expert opinion within our study group, questionnaires were send to 68 registered Dutch bariatric surgeons, with 73 steps for bypass surgery and 51 steps for sleeve gastrectomy. Statistical analysis was performed to identify steps with and without consensus. This process was repeated to reach consensus of all necessary steps.
RESULTS:
Thirty-eight participants (56%) responded in the first round and 32 participants (47%) in the second round. After the first Delphi round, 19 steps for gastric bypass (26%) and 14 for sleeve gastrectomy (27%) gained full consensus. After the second round, an additional amount of 10 and 12 sub-steps was confirmed as key steps, respectively. Thirteen steps in the gastric bypass and seven in the gastric sleeve were deemed advisable. Our expert panel showed a high level of consensus expressed in a Cronbach's alpha of 0.82 for the gastric bypass and 0.87 for the sleeve gastrectomy.
CONCLUSIONS:
The Delphi consensus defined 29 steps for gastric bypass and 26 for sleeve gastrectomy as being crucial for correct performance of these procedures to the standards of our expert panel. These results offer a clear framework for the technical execution of these procedures.

Impactfactor: 3.895

A Dutch Nationwide Bariatric Quality Registry: DATO

Poelemeijer YQ, Liem RS, **Nienhuijs SW**

Obes Surg. 2018 Jun;28(6):1602-1610

INTRODUCTION:
In the Netherlands, the number of bariatric procedures increased exponentially in the 90s. To ensure and improve the quality of bariatric surgery, the nationwide Dutch Audit for Treatment of Obesity (DATO) was established in 2014. The audit was coordinated by the Dutch Institute for Clinical Auditing (DICA). This article provides a review of the aforementioned process in establishing a nationwide registry in the Netherlands.

MATERIALS AND METHODS:
In collaboration with the DATO's scientific committee and other stakeholders, an annual list of several external quality indicators was formulated. This list consists of volume, process, and outcome indicators. In addition to the annual external indicators, the database permits individual hospitals to analyze their own data. The dashboard provides several standardized reports and detailed quality indicators, which are updated on a weekly base.
RESULTS:
Since the start, all 18 Dutch bariatric centers participated in the nationwide audit. A total of 21,941 cases were registered between 2015 and 2016. By 2016, the required variables were registered in 94.3% of all cases. A severe complicated course was seen in 2.87%, and mortality in 0.05% in 2016. The first-year follow-up shows a >?20% TWL in 86.1% of the registered cases.
DISCUSSION:
The DATO has become rapidly a mature registry. The well-organized structure of the national audit institution DICA and governmental funding were essential. However, most important were the bariatric teams themselves. The authors believe reporting the results from the registry has already contributed to more knowledge and acceptance by other health care providers.

Impactfactor: 3.895

A Modified Technique to Create a Standardized Floppy Nissen Fundoplication Without a Bougie

Castelijns PSS, van de Poll MCG, **Smulders JF**

J Laparoendosc Adv Surg Tech A. 2018 Jul 28(7):853-858. Epub 2018 Feb 21

INTRODUCTION:
Nissen fundoplication is frequently applied in the surgical treatment of patients with gastroesophageal reflux disease (GERD). When the gastroesophageal junction remains too large or becomes too narrow, persistent GERD or dysphagia may occur. To assure a correct size of the gastroesophageal junction, the fundoplication can be created over a bougie. However, this increases the risk of esophageal perforation. Therefore, we have modified a previously described technique to create a standardized fundoplication without the use of a bougie. In this article, we describe this technique and demonstrate the initial results.
MATERIALS AND METHODS:
We describe a technique to create a standardized Nissen fundoplication. After suture repair of the hiatal hernia, three marking sutures were placed on the gastric fundus, based on an equilateral triangle. The size of this triangle determines the final diameter of the fundoplication. With these measurements, we assure sufficient patency, minimize rotation, and create a more reproducible fundoplication that may reduce postoperative dysphagia.
RESULTS:
We have operated 15 patients according to this technique. Mean operative time was 69.5 (SD 8.4) minutes, no complications occurred. There was no early dysphagia and the mean length of stay was 1.3 days (1-2). Quality of life after 1 year was excellent.
CONCLUSIONS:
This modified method for standardized Nissen fundoplication is safe and might reduce postoperative dysphagia. Quality of life after 1 year is excellent. The effect on postoperative dysphagia and the reproducibility of this technique should be established in a large prospective study.

Impactfactor: 1.257

A prospective cohort study assessing differences in cosmetic appreciation of lateralization while smiling in patients with a peripheral facial palsy

Luijmes RE, Beurskens CHG, **Pouwels S**, Ingels KJAO

Laterality. 2018 Jul;23(4):381-390. Epub 2017 Apr 26

We investigated the differences in cosmetic appreciation of patients with a left and a right peripheral facial palsy (PFP) while smiling. Smiling pictures of patients with a facial palsy with House-Brackmann II-VI were reversed as a mirror image and offered as a pair of pictures, together with the true image. Twenty-six patients with a PFP and 24 medical professionals familiar with facial palsy were asked to choose the most attractive photograph. Patients rated their own pictures. Medical professionals preferred pictures of patients with a right and left PFP in, respectively, a mean of 43.00?±?12.25% and 57.00?±?12.28% (p?=?.005). Patients with a right PFP chose their mirror and true image in 65% and 35% in smiling pictures (p?=?.01). Patients with a left PFP facial palsy chose their mirror and true image in 58% and 42% in smiling pictures (p?=?.02). The House-Brackmann score and age of the patients did not influence preferences of medical professionals and patients. We have found that medical professionals have a significant preference for pictures of patients with a left PFP. Patients with a left PFP and right PFP significantly prefer their mirror image in smiling pictures.

Impactfactor: 1.388

A structured training program for minimally invasive esophagectomy for esophageal cancer- a Delphi consensus study in Europe

Visser E, van Rossum PSN, van Veer H, Al-Naimi K, Chaudry MA, Cuesta MA, Gisbertz SS, Gutschow CA, Hölscher AH, **Luyer MDP**, Mariette C, Moorthy K, **Nieuwenhuijzen GAP**, Nilsson M, Räsänen JV, Schneider PM, Schröder W, Cheong E, van Hillegersberg R

Dis Esophagus. 2018 Mar 1;31(3)

Evidence suggests that structured training programs for laparoscopic procedures can ensure a safe standard of skill acquisition prior to independent practice. Although minimally invasive esophagectomy (MIO) is technically demanding, no consensus on requirements for training for the MIO procedure exists. The aim of this study is to determine essential steps required for a structured training program in MIO using the Delphi consensus methodology. Eighteen MIO experts from 13 European hospitals were asked to participate in this study. The consensus process consisted of two structured meetings with the expert panel, and two Delphi questionnaire rounds. A list of items required for training MIO were constructed for three key domains of MIO, including (1) requisite criteria for units wishing to be trained and (2) to proctor MIO, and (3) a framework of a MIO training program. Items were rated by the experts on a scale 1-5, where 1 signified 'not important' and 5 represented 'very important.' Consensus for each domain was defined as achieving Cronbach alpha =0.70. Items were considered as fundamental when =75% of experts rated it important (4) or very important (5). Both Delphi rounds were completed by 16 (89%) of the 18 invited experts, with a median experience of 18 years with minimally invasive surgery. Consensus was achieved for all three key domains. Following two rounds of a 107-item questionnaire, 50 items were rated as essential for training MIO. A consensus among European MIO experts on essential items required for training MIO is presented. The identified items can serve as directive principles and core standards for creating a comprehensive training program for MIO.

Impactfactor: 2.702

Abdominal Drainage and Amylase Measurement for Detection of Leakage After Gastrectomy for Gastric Cancer

Schots JPM, **Luyer MDP**, **Nieuwenhuijzen GAP**

J Gastrointest Surg. 2018 May 7. [Epub ahead of print]

PURPOSE:

To investigate the value of daily measurement of drain amylase for detecting leakage in gastric cancer surgery.

METHODS:

This was a retrospective analysis including all patients who underwent a gastrectomy for gastric cancer. From January 2013 until December 2015, an intra-abdominal drain was routinely placed. Drain amylase was measured daily. Receiver operator characteristic curves were created to assess the ability of amylase to predict leakage. Sensitivity, specificity, and negative and positive predictive value of amylase in drain fluid were determined. Leakage of the gastrojejunostomy or esophagojejunostomy, enteroenterostomy, duodenal stump, or pancreas was diagnosed by CT scan, endoscopy, or during re-operation. From January 2016 until April 2017, no drain was inserted. Surgical outcome and postoperative complications were compared between both groups.

RESULTS:

Median drain amylase concentrations were higher for each postoperative day in patients with leakage. The optimal cutoff value was 1000 IU/L (sensitivity 77.8%, specificity 98.2%, negative predictive value 96.6%). Sixty-seven consecutive procedures were performed with a drain and 40 procedures without. No differences in group characteristics were observed except for gender. Fourteen patients (13.1%) had a leakage. The incidence and severity of leakage were not different between the patients with and without a drain. There was no significant difference in time to diagnosis (1 vs. 0 days; p 0.34), mortality rate (7.5 vs. 2.5%; p 0.41), and median length of hospital stay (9 days in both groups; p 0.46).

CONCLUSION:

Daily amylase measurement in drain fluid does not influence the early recognition and management of leakage in gastric cancer surgery.

Impactfactor: 2.813

Acute malignant obstruction in patients with peritoneal carcinomatosis: The role of palliative surgery

de Boer NL, Hagemans JAW, Schultze BTA, Brandt-Kerkhof ARM, Madsen EVE, Verhoef C, **Burger JWA**

Eur J Surg Oncol. 2018 Dec 21. pii: S0748-7983(18)32037-7 [Epub ahead of print]

INTRODUCTION:

Patients with peritoneal carcinomatosis who do not have curative treatment options often develop acute obstructive symptoms and when conservative management fails, surgical treatment is the remaining option. However, palliative surgery is associated with high morbidity and mortality and the chance of success is unclear. The aim of this study was to evaluate outcomes of palliative surgery and to provide guidance for surgeons, medical oncologists and patients in their decision-making.

METHODS:

All consecutive patients who underwent palliative surgery for acute obstruction caused by peritoneal carcinomatosis between January 2005 and October 2017 where identified.

RESULTS:
In total 148 patients underwent surgery. Primary malignancy was colorectal cancer (28.4%), neuroendocrine tumor (20.3%), ovarian cancer (14.2%) or 'other' (37.2%). Median length of postoperative hospital stay was 16 days (IQR 9-24). More than half (58.1%) of the patients developed postoperative complications, 29.1% developed =2 complications. In-hospital mortality was 8.8%. Readmission (56.1%) and re-obstruction (35.0%) were common. Median overall survival was 119 days (IQR 48-420). Patients with a neuroendocrine tumor had a significantly better overall survival compared to other primary malignancies (p?<?0.001). Patients who developed an obstruction during or within 6 months after treatment with chemotherapy had a worse overall survival (p?<?0.001), compared to patients treated with chemotherapy longer than 6 months ago, or patients not treated with chemotherapy.
CONCLUSION:
Palliative surgery is associated with high rates of complications and readmission and re-obstruction are common. Comfort care is often a better option than surgery, especially in patients with disease progression under recent treatment with chemotherapy.

Impactfactor: 3.688

An economic evaluation of perioperative enteral nutrition in patients undergoing colorectal surgery (SANICS II study)

Pattamatta M, Evers SMAA, **Smeets BJJ**, **Peters EG**, **Luyer MDP**, Hiligsmann M

J Med Econ. 2018 Dec 7:1-14

AIMS:
The objective of this (trial based) economic evaluation was to assess, from a societal perspective, the cost-effectiveness of perioperative enteral nutrition compared with standard care in patients undergoing colorectal surgery.
MATERIALS AND METHODS:
Alongside the SANICS II randomized controlled trial, global quality of life, utilities (measured by EQ-5D-5L), healthcare costs, production losses, and patient and family costs were assessed at baseline, 3 months, and 6 months. Incremental cost effectiveness ratios (ICERs) (i.e. cost per increased global quality of life score or quality-adjusted life year [QALY] gained) and cost effectiveness acceptability curves were visualized.
RESULTS:
In total, 265 patients were included in the original trial (n?=?132 in the perioperative enteral nutrition group and n?=?133 in the standard care group). At 6 months, global quality of life (83 versus 83, p?=?0.357) did not differ significantly between the groups. The mean total societal costs for the intervention and standard care groups were €14,673 and €11,974 respectively but did not reach the statistical significance (p?=?0.109). The intervention resulted in an ICER of -€6276 per point increase in the global quality of life score. The gain in QALY was marginal (0.003) with an additional cost of €2,941 and the ICUR (Incremental cost utility ratio) was estimated at €980,333.
LIMITATIONS:
The cost elements for all the participating centers reflect the reference prices from the Netherlands. Patient-reported questionnaires may have resulted in recall bias. Sample size was limited by exclusion of patients who did not complete questionnaires at least at two time points. A power analysis based on costs and health related quality of life (HRQoL) was not performed. The economic impact could not be analyzed at 1 month postoperatively where the effects could potentially be higher.
CONCLUSIONS:
This study suggests that perioperative nutrition is not beneficial for the patients in terms of quality of life and is not cost effective.

Impactfactor: 2.264

Assessing the value of eHealth for bariatric surgery (BePatient trial): study protocol for a randomized controlled trial

Versteegden DP, **Van Himbeeck MJ**, **Nienhuijs SW**

Trials. 2018 Nov 14;19(1):625.

BACKGROUND:
The expansion of digital devices and widespread access to the Internet has opened up opportunities to provide patients with more personal information. It can be hypothesized that eHealth in addition to standard care could enhance clinical outcomes such as increased weight loss, co-morbidity reduction, and commitment to the program. The beneficial value of incorporating eHealth applications as standard postoperative care is yet to be established. In this trial, the value of different levels of eHealth are assessed.
METHODS/DESIGN:
Two hundred adult patients with a body mass index (BMI) =?40 kg/m2, or =?35 kg/m2 with obesity-related co-morbidity, undergoing sleeve gastrectomy or gastric bypass will be enrolled in this randomized controlled trial. Patients will be randomly assigned to one of the groups: receiving standard care (control group, n =?100); have access to an online eHealth platform in addition to the previous group (online group, n =?50); or receive wireless monitoring devices in addition to previous groups (device group, n =?50). The total follow-up period is two years

postoperatively. Primary outcome is weight loss in terms of BMI. Secondary outcomes include: quality of life; return-to-work time; co-morbidity reduction; additional contacts; and ease of use of devices.

DISCUSSION:

In this trial, the value of different levels of eHealth will be assessed. This addresses an important aspect of a changing healthcare environment.

Impactfactor: 2.067

Basilic vein transposition for unsuitable upper arm hemodialysis needle access segment may attenuate concurrent hand ischemia

Gerrickens MWM, Vaes RHD, Govaert B, **Teijink JAW**, Scheltinga MR

Hemodial Int. 2018 Jul 22(3):335-341. Epub 2018 Mar 8

INTRODUCTION:

Some hemodialysis patients with a brachial arteriovenous fistula (AVF) have an unsuitable upper arm needle access segment (NAS) necessitating basilic vein transposition (BVT). It was frequently observed that a portion of these patients spontaneously experienced a warmer and less painful dialysis hand after BVT. Aim of this study was to determine whether BVT for an inadequate NAS attenuated hemodialysis access-induced distal ischemia in patients with a brachial AVF.

METHODS:

Patients with a brachial AVF and an unsuitable NAS also reporting hand ischemia and scheduled to undergo BVT between 2005 and 2016 in a single facility were studied. Hand ischemia was graded as proposed in a 2016 consensus meeting. Hand ischemic questionnaire (HIQ-) scores (0 points, no ischemia-500 points, maximal ischemia), digital brachial index (DBI, ischemia <0.6) and access flow (mL/min) before and after BVT were compared. The cephalic vein and all side branches of the basilic vein were ligated during the BVT.

FINDINGS:

Ten patients were studied (8 males, 61 [54-75] years). BVT was performed 8 [4-10] months following the initial AVF construction. HIQ-scores dropped from 220 [71-285] to 9 [0-78] (P?=?0.043) postoperatively, whereas DBI increased from 0.51 [0.39-0.67] to 0.85 [0.68-0.97] (P?=?0.012). DBI and HIQ-scores were inversely correlated (R2 =71%, P?=?0.001). Access flows dropped significantly (Flowpre 1120 mL/min [1100-2300] vs. Flowpost 700 mL/min [600-1760]; P?=?0.018). Surgery-associated complications were absent and dialysis continued uninterruptedly. Eight patients reported total recovery from hand ischemia six weeks postoperatively.

DISCUSSION:

Basilic vein transposition for an unsuitable upper arm needle access segment may attenuate hand ischemia in patients with a brachial AVF previously reporting hemodialysis access-induced distal ischemia.

Impactfactor: 1.237

Cardiac structure and function before and after bariatric surgery: a clinical overview

Lascaris B, Pouwels S, Houthuizen P, Dekker LR, **Nienhuijs SW**, Bouwman RA, Buise MP

Clin Obes. 2018 Dec;8(6):434-443

Obesity, defined as a body mass index of =30 kg/m2 , is the most common chronic metabolic disease worldwide and its prevalence has been strongly increasing. Obesity has deleterious effects on cardiac function. The purpose of this review is to evaluate the effects of obesity and excessive weight loss due to bariatric surgery on cardiac function, structural changes and haemodynamic responses of both the left and right ventricle.

Impactfactor --

Comparison of 2 Perioperative Management Protocols and Their Influence on Postoperative Recovery after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Standard Parenteral Nutrition Selective Bowel Decontamination and Suprapubic Catheters?

Elekonawo FMK, van der Meeren MMD, **Simkens GA**, de Wilt JHW, **de Hingh IH**, Bremers AJA

Dig Surg. 2018 Jul 6:1-8. [Epub ahead of print]

BACKGROUND:

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is associated with considerable postoperative morbidity, including ileus and infectious complications. Perioperative care is believed to be an important factor for the development and treatment of postoperative morbidity.

PATIENTS AND METHODS:

Data on case-matched patients from a retrospective database of 2 Dutch HIPEC centres was compared. Patient selection and procedures were identical in both hospitals although perioperative management items differ slightly. In centre B, immediate total parenteral nutrition (TPN), suprapubic urine bladder catheter placement (SPCs) and selective decontamination of the digestive-tract are standard care for CRS-HIPEC patients, while in centre A, they are not.

RESULTS:

From a total of 223 patients, 68 consecutive patients from centre B were compared to 68 matched patients from centre A. TPN was administered to 54.4% of patients in centre A because of prolonged ileus, whereas it was standard

of care in centre B. In all, 105 (77.2%) patients experienced postoperative complications including 17.6% who had a grades III-IV complication. The incidence of grade III-V complications was 18 (26.4%) in centre A and 8 (11.8%) in centre B (p = 0.03). Median hospital stay was 12 days (7-84) in A and 11(6-80) in centre B (p = 0.546). CONCLUSIONS:

Gastrointestinal recovery after CRS-HIPEC seems to take longer as compared to other surgical procedures. Between the 2 centres, a significant difference in severe complications was found, while standard TPN, selective bowel decontamination and SPCs were the only identified differences in perioperative care.

Impactfactor: 2.031

CRITICS-II: a multicentre randomised phase II trial of neo-adjuvant chemotherapy followed by surgery versus neo-adjuvant chemotherapy and subsequent chemoradiotherapy followed by surgery versus neo-adjuvant chemoradiotherapy followed by surgery in resectable gastric cancer

Slagter AE, Jansen EP, van Laarhoven HW, van Sandick JW, van Grieken NCT, Sikorska K, Cats A, Muller-Timmermans P, Hulshof MC, Boot H, Los M8, Beerepoot LV, Peters FP, Hospers GA, van Etten B, Hartgrink HH, van Berge Henegouwen MI, **Nieuwenhuijzen GA**, van Hillegersberg R, van der Peet DL, Grabsch HI, Verheij M

BMC Cancer. 2018 Sep 10;18(1):877

BACKGROUND:

Although radical surgery remains the cornerstone of cure in resectable gastric cancer, survival remains poor. Current evidence-based (neo)adjuvant strategies have shown to improve outcome, including perioperative chemotherapy, postoperative chemoradiotherapy and postoperative chemotherapy. However, these regimens suffer from poor patient compliance, particularly in the postoperative phase of treatment. The CRITICS-II trial aims to optimize preoperative treatment by comparing three treatment regimens: (1) chemotherapy, (2) chemotherapy followed by chemoradiotherapy and (3) chemoradiotherapy.

METHODS:

In this multicentre phase II non-comparative study, patients with clinical stage IB-IIIC (TNM 8th edition) resectable gastric adenocarcinoma are randomised between: (1) 4 cycles of docetaxel+oxaliplatin+capecitabine (DOC), (2) 2 cycles of DOC followed by chemoradiotherapy (45Gy in combination with weekly paclitaxel and carboplatin) or (3) chemoradiotherapy. Primary endpoint is event-free survival, 1 year after randomisation (events are local and/or regional recurrence or progression, distant recurrence, or death from any cause). Secondary endpoints include: toxicity, surgical outcomes, percentage radical (R0) resections, pathological tumour response, disease recurrence, overall survival, and health related quality of life. Exploratory endpoints include translational studies on predictive and prognostic biomarkers.

DISCUSSION:

The aim of this study is to select the most promising among three preoperative treatment arms in patients with resectable gastric adenocarcinoma. This treatment regimen will subsequently be compared with the standard therapy in a phase III trial.

Impactfactor: 3.288

Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Metastases From a Small Bowel Adenocarcinoma: Multi-Institutional Experience

Liu Y, Yonemura Y, Levine EA, Glehen O, Goere D, Elias D, Morris DL, Sugarbaker PH, Tuech JJ, Cashin P, Spiliotis JD, **de Hingh I**, Ceelen W, Baumgartner JM, Piso P, Katayama K, Deraco M, Kusamura S, Pocard M, Quenet F, Fushita S BIG-RENAPE Group

Ann Surg Oncol. 2018 May 25(5):1184-1192

BACKGROUND:

The multi-institutional registry in this study evaluated the outcome after cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) for patients with peritoneal metastases (PM) from small bowel adenocarcinoma (SBA).

METHODS:

A multi-institutional data registry including 152 patients with PM from SBA was established. The primary end point was overall survival (OS) after CRS plus HIPEC.

RESULTS:

Between 1989 and 2016, 152 patients from 21 institutions received a treatment of CRS plus HIPEC. The median follow-up period was 20 months (range 1-100 months). Of the 152 patients, 70 (46.1%) were women with a median age of 54 years. The median peritoneal cancer index (PCI) was 10 (mean 12; range 1-33). Completeness of cytoreduction (CCR) 0 or 1 was achieved for 134 patients (88.2%). After CRS and HIPEC, the median OS was 32 months (range 1-100 months), with survival rates of 83.2% at 1 year, 46.4% at 3 years, and 30.8% at 5 years. The median disease-free survival after CCR 0/1 was 14 months (range 1-100 months). The treatment-related mortality rate was 2%, and 29 patients (19.1%) experienced grades 3 or 4 operative complications. The period between detection of PM and CRS plus HIPEC was 6 months or less (P = 0.008), and multivariate analysis identified absence of lymph node metastasis (P = 0.037), well-differentiated tumor (P = 0.028), and PCI of 15 or lower (P = 0.003) as independently associated with improved OS.

CONCLUSION:
The combined treatment strategy of CRS plus HIPEC achieved prolonged survival for selected patients who had PM from SBA with acceptable morbidity and mortality.

Impactfactor: 3.857

Defining the Key Competencies in Radiation Protection for Endovascular Procedures: A Multispecialty Delphi Consensus Study

Doyen B, Maurel B, Cole J, Maertens H, Mastracci T, Van Herzeele I; PRET (Principles of Radiation protection within Endovascular Team) group: **Teijink JA**

Eur J Vasc Endovasc Surg. 2018 Feb;55(2):281-287

OBJECTIVES:
Radiation protection training courses currently focus on broad knowledge topics which may not always be relevant in daily practice. The goal of this study was to determine the key competencies in radiation protection that every endovascular team member should possess and apply routinely, through multispecialty clinical content expert consensus.
METHODS:
Consensus was obtained through a two round modified Delphi methodology. The expert panel consisted of European vascular surgeons, interventional radiologists, and interventional cardiologists/angiologists experienced in endovascular procedures. An initial list of statements, covering knowledge skills, technical skills and attitudes was created, based on a literature search. Additional statements could be suggested by the experts in the first Delphi round. Each of the statements had to be rated on a 5- point Likert scale. A statement was considered to be a key competency when the internal consistency was greater than alpha = 0.80 and at least 80% of the experts agreed (rating 4/5) or strongly agreed (rating 5/5) with the statement. Questionnaires were emailed to panel members using the Surveymonkey service.
RESULTS:
Forty-one of 65 (63.1%) invited experts agreed to participate in the study. The response rates were 36 out of 41 (87.8%): overall 38 out of 41(92.6%) in the first round and 36 out of 38 (94.7%) in the second round. The 71 primary statements were supplemented with nine items suggested by the panel. The results showed excellent consensus among responders (Cronbach's alpha = 0.937 first round; 0.958 s round). Experts achieved a consensus that 30 of 33 knowledge skills (90.9%), 23 of 27 technical skills (82.1%), and 15 of 20 attitudes (75.0%) should be considered as key competencies.
CONCLUSIONS:
A multispecialty European endovascular expert panel reached consensus about the key competencies in radiation protection. These results may serve to create practical and relevant radiation protection training courses in the future, enhancing radiation safety for both patients and the entire endovascular team.

Impactfactor 3.877

Definitive chemoradiation or surgery in elderly patients with potentially curable esophageal cancer in the Netherlands: a nationwide population-based study on patterns of care and survival

Koëter M, van Putten M, Verhoeven RHA, Lemmens VEPP, **Nieuwenhuijzen GAP**

Acta Oncol. 2018 Sep 57(9):1192-1200. Epub 2018 Mar 12

BACKGROUND:
The aim of our study was to describe treatment patterns and the impact on overall survival among elderly patients (75 years and older) with potentially curable esophageal cancer.
MATERIAL AND METHODS:
Between 2003 and 2013, 13,244 patients from the nationwide population-based Netherlands Cancer Registry (NCR) were diagnosed with potentially curable esophageal cancer (cT2-3, X, any cN, cM0, X) of which 34% were elderly patients (n?=?4501).
RESULTS:
Surgical treatment with or without neoadjuvant treatment remained stable among elderly patients (around the 16% between 2003 and 2013). However, among younger patients, surgical treatment increased from 60.2 to 67.0%. The use of definitive chemoradiation (dCRT) increased in elderly patients from 1.9 to 19.5% and in younger patients from 5.2 to 17.2%. Due to the increase in dCRT, treatment with curative intent doubled in the elderly from 17 to 37.1%. Multivariable Cox regression revealed that elderly patients with an adenocarcinoma receiving surgery alone or dCRT had a significantly worse overall survival compared to those receiving surgery with neoadjuvant chemo (radio) therapy (nCRT/CT) (HR: 1.7 95% CI 1.4-2.0 and HR: 1.9 95% CI 1.5-2.3). However, among elderly with squamous cell carcinoma overall survival was comparable between dCRT, surgery alone and surgery with nCRT/CT.
CONCLUSIONS:
Survival was comparable among elderly patients with squamous cell carcinoma who underwent surgery with nCRT/CT, surgery alone or received dCRT, while elderly patients with an adenocarcinoma who underwent surgery with nCRT/CT had a better overall survival when compared with surgery alone or dCRT. Therefore, dCRT can be considered as a reasonable alternative for surgery among potentially curable elderly patients with esophageal

squamous cell carcinoma. However, in elderly patients with esophageal adenocarcinoma surgery with nCRT/CT is still preferable regarding overall survival.

Impactfactor: 3.473

Detection of residual disease after neoadjuvant chemoradiotherapy for oesophageal cancer (preSANO): a prospective multicentre, diagnostic cohort study

Noordman BJ, Spaander MC, Valkema R, Wijnhoven BP, van Berge Henegouwen MI, Shapiro J, Biermann K, van der Gaast A, van Hillegersberg R, Hulshof MC, Krishnadath KK, Lagarde SM, **Nieuwenhuijzen GA**, Oostenbrug LE, Siersema PD, Schoon EJ, Sosef MN, Steyerberg EW, van Lanschot JJ; SANO study group: Curvers WL

Lancet Oncol. 2018 Jul;19(7):965-974

BACKGROUND: After neoadjuvant chemoradiotherapy for oesophageal cancer, roughly half of the patients with squamous cell carcinoma and a quarter of those with adenocarcinoma have a pathological complete response of the primary tumour before surgery. Thus, the necessity of standard oesophagectomy after neoadjuvant chemoradiotherapy should be reconsidered for patients who respond sufficiently to neoadjuvant treatment. In this study, we aimed to establish the accuracy of detection of residual disease after neoadjuvant chemoradiotherapy with different diagnostic approaches, and the optimal combination of diagnostic techniques for clinical response evaluations.

METHODS: The preSANO trial was a prospective, multicentre, diagnostic cohort study at six centres in the Netherlands. Eligible patients were aged 18 years or older, had histologically proven, resectable, squamous cell carcinoma or adenocarcinoma of the oesophagus or oesophagogastric junction, and were eligible for potential curative therapy with neoadjuvant chemoradiotherapy (five weekly cycles of carboplatin [area under the curve 2 mg/mL per min] plus paclitaxel [50 mg/m2 of body-surface area] combined with 41·4 Gy radiotherapy in 23 fractions) followed by oesophagectomy. 4-6 weeks after completion of neoadjuvant chemoradiotherapy, patients had oesophagogastroduodenoscopy with biopsies and endoscopic ultrasonography with measurement of maximum tumour thickness. Patients with histologically proven locoregional residual disease or no-pass during endoscopy and without distant metastases underwent immediate surgical resection. In the remaining patients a second clinical response evaluation was done (PET-CT, oesophagogastroduodenoscopy with biopsies, endoscopic ultrasonography with measurement of maximum tumour thickness, and fine-needle aspiration of suspicious lymph nodes), followed by surgery 12-14 weeks after completion of neoadjuvant chemoradiotherapy. The primary endpoint was the correlation between clinical response during clinical response evaluations and the final pathological response in resection specimens, as shown by the proportion of tumour regression grade (TRG) 3 or 4 (>10% residual carcinoma in the resection specimen) residual tumours that was missed during clinical response evaluations. This study was registered with the Netherlands Trial Register (NTR4834), and has been completed.

FINDINGS: Between July 22, 2013, and Dec 28, 2016, 219 patients were included, 207 of whom were included in the analyses. Eight of 26 TRG3 or TRG4 tumours (31% [95% CI 17-50]) were missed by endoscopy with regular biopsies and fine-needle aspiration. Four of 41 TRG3 or TRG4 tumours (10% [95% CI 4-23]) were missed with bite-on-bite biopsies and fine-needle aspiration. Endoscopic ultrasonography with maximum tumour thickness measurement missed TRG3 or TRG4 residual tumours in 11 of 39 patients (28% [95% CI 17-44]). PET-CT missed six of 41 TRG3 or TRG4 tumours (15% [95% CI 7-28]). PET-CT detected interval distant histologically proven metastases in 18 (9%) of 190 patients (one squamous cell carcinoma, 17 adenocarcinomas).

INTERPRETATION: After neoadjuvant chemoradiotherapy for oesophageal cancer, clinical response evaluation with endoscopic ultrasonography, bite-on-bite biopsies, and fine-needle aspiration of suspicious lymph nodes was adequate for detection of locoregional residual disease, with PET-CT for detection of interval metastases. Active surveillance with this combination of diagnostic modalities is now being assessed in a phase 3 randomised controlled trial (SANO trial; Netherlands Trial Register NTR6803).

Impactfactor: 36.418

Determination of Endograft Apposition Position and Expansion in the Aortic Neck Predicts Type Ia Endoleak and Migration After Endovascular Aneurysm Repair

Schuurmann RCL, van Noort K, Overeem SP, van Veen R, Ouriel K, Jordan WD Jr, Muhs BE, **'t Mannetje YW**, Reijnen MMPJ, Fioole B, Unlu C, Brummel P, de Vries JPM

J Endovasc Ther. 2018 Jun 25(3):366-375. Epub 2018 Mar 26

PURPOSE:

To describe the added value of determining changes in position and apposition on computed tomography angiography (CTA) after endovascular aneurysm repair (EVAR) to detect early caudal displacement of the device and to prevent type Ia endoleak.

METHODS:

Four groups of elective EVAR patients were selected from a dataset purposely enriched with type Ia endoleak and migration (>10 mm) cases. The groups included cases of late type Ia endoleak (n=36), migration (n=9), a type II endoleak (n=16), and controls without post-EVAR complications (n=37). Apposition of the endograft fabric with the aortic neck, shortest distance between the fabric and the renal arteries, expansion of the main body (or dilatation of the aorta in the infrarenal sealing zone), and tilt of the endograft toward the aortic axis were determined on the

first postoperative and the last available CTA scan without type Ia endoleak or migration. Differences in these endograft dimensions were compared between the first vs last scan and among the 4 groups.
RESULTS:
No significant differences in endograft configurations were observed among the groups on the first postoperative CTA scan. On the last CTA scan before a complication arose, the position of the fabric relative to the renal arteries, expansion of the main body, and apposition of the fabric with the aortic neck were significantly different between the type Ia endoleak (median follow-up 15 months) and migration groups (median follow-up 23 months) compared with the control group (median follow-up 19 months). Most endograft dimensions had changed significantly compared with the first postoperative CTA scan for all groups. Apposition had increased in the control group but had decreased significantly in the type Ia endoleak and migration groups.
CONCLUSION:
Progressive changes in dimensions of the endograft within the infrarenal neck could be detected on regular CTA scans before the complication became urgent in many patients.

Impactfactor: 2.732

Diagnosing internal herniation after laparoscopic Roux-en-Y gastric bypass: usefulness of systematically reviewing CT scans using ten signs

Ederveen JC**, van Berckel MMG, Jol S, Nienhuijs SW,** Nederend J

Eur Radiol. 2018 Sep 28(9):3583-3590. Epub 2018 Mar 2

OBJECTIVES:
To evaluate if systematically reviewing CT scans using ten signs leads to a better accuracy in diagnosing internal herniation (IH), compared to the original report. Also, the difference in accuracy was analysed between experience levels.
METHODS:
Patients were retrospectively included if they had undergone laparoscopic gastric bypass surgery between 2011 and 2014, and if additional radiological examination was performed for suspected IH between 2011 and 2016. Out of 1475 patients who had undergone laparoscopic gastric bypass surgery, 183 patients had one or more additional radiological examinations. A total of 245 CT scans were performed. All were reassessed by an abdominal radiologist, a radiology resident and intern. Assessment was done using ten signs from previous literature. Overall suspicion of IH was graded using a 5-point Likert scale. Accuracy was calculated using two-way contingency tables. Interobserver agreement was calculated using Fleiss' kappa.
RESULTS:
After 70 reoperations an IH was diagnosed in 48.6% (34/70). There was an increase in specificity for diagnosing IH with reoperation as reference from 52.8% (19/36; 95% CI 35.7-69.2%) in the original report to 86.1% (31/36; 95% CI 74.8-97.4%) for the radiologist (p = 0.002), 77.8% (28/36; 95% CI 64.2-91.4%) for the resident (p = 0.026) and 77.8% (28/36; 95% CI 64.2-91.4%) for the intern (p = 0.026). Interobserver agreement was good.
CONCLUSIONS:
Systematically reviewing CT scans using a list of ten CT signs can improve specificity and thereby reduce unnecessary reoperations, especially in a high pre-test probability population. The tool can be easily taught to less experienced readers.
KEYPOINTS:
• Computed tomography is useful to diagnose internal herniation(IH) after gastric bypass surgery • Ten signs are described to improve CT diagnosis of IH • Systematically reviewing CT scans improves specificity • There is no difference in experience levels when using these ten signs.

Impactfactor: 2.843

Diagnostic performance of gadofosveset-enhanced axillary MRI for nodal (re)staging in breast cancer patients: results of a validation study

van Nijnatten TJA, **Schipper RJ**, Lobbes MBI, van Roozendaal LM, Vöö SA, Moossdorff M, Paiman ML, de Vries B, Keymeulen KBMI, Wildberger JE, Smidt ML, Beets-Tan RGH

Clin Radiol. 2018 Feb 73(2):168-175. Epub 2017 Oct 10

AIM:
To evaluate diagnostic performance of gadofosveset (GDF)-enhanced magnetic resonance imaging (MRI) in addition to T2-weighted (T2W) MRI for nodal (re)staging in newly diagnosed breast cancer patients.
MATERIALS AND METHODS:
Ninety patients underwent axillary T2W- and GDF-MRI. Two radiologists independently scored each lymph node; first on T2W-MRI, subsequently adjusting their score on GDF-MRI. Diagnostic performance parameters were calculated on node-by-node and patient-by-patient validation with histopathology as the reference standard. Furthermore, learning curve analysis for reading GDF-MRI was performed.
RESULTS:
In patient-by-patient validation, overall reader performances for T2W- and GDF-MRI were similar with area under the receiver operating characteristic curves (AUC) of 0.75 and 0.77 (p=0.731) for reader 1 and 0.79 and 0.72

(p=0.156) for reader 2. For node-by-node validation, AUC values of T2W- and GDF-MRI were 0.76 and 0.82 (p=0.018) and 0.77 and 0.77 (p=0.998) for reader 1 and 2. The AUC for reader 1 was 0.71 for first one-third of nodes evaluated, improving to 0.80 and 0.95 for the next and last one-third, respectively. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) improved from 38%, 89%, 56%, and 79% to 60%, 93%, 64%, and 92%. The AUC of reader 2 improved from 0.69 to 0.79.

CONCLUSION:

The present study confirmed that GDF-MRI, in addition to T2W-MRI, has potential as a non-invasive method for nodal (re)staging in breast cancer.

Impactfactor: 2.282

Drug-Coated Balloon Treatment of Femoropopliteal Lesions for Patients With Intermittent Claudication and Ischemic Rest Pain: 2-Year Results From the IN.PACT Global Study

Micari A, Brodmann M, Keirse 3, Peeters P, Tepe G, Frost M, Wang H, Zeller T; IN.PACT Global Study Investigators: **Teijink JA**

JACC Cardiovasc Interv. 2018 May 28;11(10):945-953

OBJECTIVES:

The IN.PACT Global Study is the largest prospective, multicenter, independently adjudicated trial to evaluate a paclitaxel drug-coated balloon in patients with lifestyle-limiting claudication and/or ischemic rest pain due to atherosclerotic disease of the femoropopliteal artery and includes complex lesions beyond what are typically included in randomized controlled trials.

BACKGROUND:

Randomized controlled trials have demonstrated the safety and efficacy of drug-coated balloons for the treatment of Trans-Atlantic Inter-Society Consensus Document II A and B lesions, but there is a need for large-scale prospective studies to evaluate a broader range of lesions.

METHODS:

The IN.PACT Global Study enrolled 1,535 subjects, and 1,406 (1,773 lesions) were included in the pre-defined clinical cohort analysis. Freedom from clinically driven target lesion revascularization was evaluated at 24 months. The safety composite endpoint was freedom from device- and procedure-related death through 30 days and freedom from target limb major amputation and clinically driven target vessel revascularization within 24 months.

RESULTS:

Mean lesion length was 12.1 cm, 35.5% were total occlusions, and 18.0% had in-stent restenosis. Freedom from clinically driven target lesion revascularization at 24 months was 83.3%, the composite safety endpoint was met in 81.7%, the 2-year all-cause mortality rate was 7.0%, and the major target limb amputation rate was 0.7%. Increased lesion length and the presence of de novo in-stent restenosis or coronary artery disease were associated with increased risk for clinically driven target lesion revascularization by 24 months.

CONCLUSIONS:

This real-world study of femoropopliteal artery disease treatment with drug-coated balloons confirmed positive findings reported from more strictly designed randomized controlled trials and showed that outcomes are durable in this population up to 2 years after treatment.

Impactfactor: 9.881

Early outcomes with a single-sided access endovascular stent

Hofmann M, Pecoraro F, Planer D, Pfammatter T, Puippe G, Bettex D, Veith FJ, Lachat M, Chaykovska L; FIM and PIVOTAL trialists: **van Sambeek MR**

J Vasc Surg. 2018 Jul;68(1):83-90.e2

OBJECTIVE:

The objective of this study was to report the 1-year follow-up study results of the new Horizon stent graft (Endospan, Herzliya, Israel) from two different prospective consecutive trials. The Horizon abdominal aortic aneurysm stent graft system is a 14F profile system requiring only a single access site. It consists of three modules, introduced separately: base limb (iliac to iliac limb); distal aortic limb; and proximal aortic limb with a bare suprarenal crown and active fixation.

METHODS:

Data from the first in man (FIM) clinical study with 10 patients enrolled and the pivotal study with 30 patients were analyzed. Outcomes measured were freedom from major adverse events (MAEs) including all-cause mortality, myocardial infarction, renal failure, respiratory failure, paraplegia, stroke, bowel ischemia, and procedural blood loss =1000 mL. Performance end points included successful delivery and deployment of the device, freedom from aneurysm growth =5 mm, type I or type III endoleak, stent graft occlusion, conversion to open surgery, rupture, and stent graft migration.

RESULTS:

In the FIM study, one conversion to open surgery with >1000 mL of blood loss was registered perioperatively. In the pivotal study, no perioperative MAE was registered. Overall, at 1-year follow-up, two deaths and one aneurysm growth unrelated to endoleak were registered.

CONCLUSIONS:

The results of both the FIM and pivotal studies demonstrated that 39 of 40 procedures were successful for delivery and deployment of the Horizon stent graft. No MAE was registered during the follow-up. The primary safety and performance end points were met in both studies.

Impactfactor: 2.758

Effect of Early vs Late Start of Oral Intake on Anastomotic Leakage Following Elective Lower Intestinal Surgery: A Systematic Review

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Nutr Clin Pract. 2018; 33 (6): 803-812. Epub 2017 dec 14

BACKGROUND: Experimental and clinical studies have demonstrated a beneficial effect of early enteral nutrition (EN) on anastomotic leakage following colorectal surgery. Early oral intake is a common form of early EN with various clinical benefits, but the effect on anastomotic leakage is unclear. This systematic review investigates the effect of early vs late start of oral intake on anastomotic leakage following lower intestinal surgery.METHODS:

A systematic literature search was performed using the PubMed, Embase, Medline, and Cochrane databases. Randomized controlled trials were included that compared early (within 24 hours) vs late start of oral intake following elective surgery of the small bowel, colon, or rectum. Meta-analysis was performed for anastomotic leakage, overall complications, length of stay, and mortality. Sensitivity analysis was performed in which studies of inferior methodological quality were excluded.

RESULTS: Nine studies including 879 patients met eligibility criteria. Early start of oral intake significantly reduced overall complications (odds ratio [OR], 0.65; 95% confidence interval [CI], 0.46-0.93; P = .02), length of stay (mean difference, -0.89; 95% CI, -1.22 to -0.57; P < .001), and anastomotic leakage (OR, 0.40; 95% CI, 0.17-0.95; P = .04) compared with late start of oral intake. However, in the sensitivity analysis only the overall reduction of length of stay remained significant.

CONCLUSION: The effect of early oral intake on anastomotic leakage is unclear as existing studies are heterogeneous and at risk of bias. High-quality studies are needed to study the potential benefit of EN on anastomotic healing.

Impactfactor: 2.591

Effect of Neoadjuvant Chemoradiotherapy on Health-Related Quality of Life in Esophageal or Junctional Cancer: Results From the Randomized CROSS Trial

Noordman BJ, Verdam MGE, Lagarde SM, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, van Laarhoven HWM, **Nieuwenhuijzen GAP**, Hospers GAP, Bonenkamp JJ, Cuesta MA, Blaisse RJB, Busch OR, Ten Kate FJW, Creemers GM, Punt CJA, Plukker JTM, Verheul HMW, Spillenaar Bilgen EJ, van Dekken H, van der Sangen MJC, Rozema T, Biermann K, Beukema JC, Piet AHM, van Rij CM, Reinders JG, Tilanus HW, Steyerberg EW, van der Gaast A, Sprangers MAG, van Lanschot JJB

J Clin Oncol. 2018 Jan 20 36(3):268-275

Purpose To compare pre-agreed health-related quality of life (HRQOL) domains in patients with esophageal or junctional cancer who received neoadjuvant chemoradiotherapy (nCRT) followed by surgery or surgery alone. Secondary aims were to examine the effect of nCRT on HRQOL before surgery and the effect of surgery on HRQOL. Patients and Methods Patients were randomly assigned to nCRT (carboplatin plus paclitaxel with concurrent 41.4-Gy radiotherapy) followed by surgery or surgery alone. HRQOL was measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) and -Oesophageal Cancer Module (QLQ-OES24) questionnaires pretreatment and at 3, 6, 9, and 12 months postoperatively. The nCRT group also received preoperative questionnaires. Physical functioning (PF; QLQ-C30) and eating problems (EA; QLQ-OES24) were chosen as predefined primary end points. Predefined secondary end points were global QOL (GQOL; QLQ-C30), fatigue (FA; QLQ-C30), and emotional problems (EM; QLQ-OES24). Results A total of 363 patients were analyzed. No statistically significant differences in postoperative HRQOL were found between treatment groups. In the nCRT group, PF, EA, GQOL, FA, and EM scores deteriorated 1 week after nCRT (Cohen's d: -0.93, P < .001; 0.47, P < .001; -0.84, P < .001; 1.45, P < .001; and 0.32, P = .001, respectively). In both treatment groups, all end points declined 3 months postoperatively compared with baseline (Cohen's d: -1.00, 0.33, -0.47, -0.34, and 0.33, respectively; all P < .001), followed by a continuous gradual improvement. EA, GQOL, and EM were restored to baseline levels during follow-up, whereas PF and FA remained impaired 1 year postoperatively (Cohen's d: 0.52 and -0.53, respectively; both P < .001). Conclusion Although HRQOL declined during nCRT, no effect of nCRT was apparent on postoperative HRQOL compared with surgery alone. In addition to the improvement in survival, these findings support the view that nCRT according to the Chemoradiotherapy for Esophageal Cancer Followed by Surgery Study-regimen can be regarded as a standard of care.

Impactfactor 26.303

Endovascular revascularisation versus conservative management for intermittent claudication

Fakhry F, Fokkenrood HJ, Spronk S, **Teijink JA**, Rouwet EV, Hunink MGM

Cochrane Database Syst Rev. 2018 Mar 8;3:CD010512

BACKGROUND:

Intermittent claudication (IC) is the classic symptomatic form of peripheral arterial disease affecting an estimated 4.5% of the general population aged 40 years and older. Patients with IC experience limitations in their ambulatory function resulting in functional disability and impaired quality of life (QoL). Endovascular revascularisation has been proposed as an effective treatment for patients with IC and is increasingly performed.

OBJECTIVES:

The main objective of this systematic review is to summarise the (added) effects of endovascular revascularisation on functional performance and QoL in the management of IC.

SEARCH METHODS:

For this review the Cochrane Vascular Information Specialist (CIS) searched the Specialised Register (February 2017) and the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 1). The CIS also searched trials registries for details of ongoing and unpublished studies.

SELECTION CRITERIA:

Randomised controlled trials (RCTs) comparing endovascular revascularisation (± conservative therapy consisting of supervised exercise or pharmacotherapy) versus no therapy (except advice to exercise) or versus conservative therapy (i.e. supervised exercise or pharmacotherapy) for IC.

DATA COLLECTION AND ANALYSIS:

Two review authors independently selected studies, extracted data, and assessed the methodological quality of studies. Given large variation in the intensity of treadmill protocols to assess walking distances and use of different instruments to assess QoL, we used standardised mean difference (SMD) as treatment effect for continuous outcome measures to allow standardisation of results and calculated the pooled SMD as treatment effect size in meta-analyses. We interpreted pooled SMDs using rules of thumb (< 0.40 = small, 0.40 to 0.70 = moderate, > 0.70 = large effect) according to the Cochrane Handbook for Systematic Reviews of Interventions. We calculated the pooled treatment effect size for dichotomous outcome measures as odds ratio (OR).

MAIN RESULTS:

We identified ten RCTs (1087 participants) assessing the value of endovascular revascularisation in the management of IC. These RCTs compared endovascular revascularisation versus no specific treatment for IC or conservative therapy or a combination therapy of endovascular revascularisation plus conservative therapy versus conservative therapy alone. In the included studies, conservative treatment consisted of supervised exercise or pharmacotherapy with cilostazol 100 mg twice daily. The quality of the evidence ranged from low to high and was downgraded mainly owing to substantial heterogeneity and small sample size.Comparing endovascular revascularisation versus no specific treatment for IC (except advice to exercise) showed a moderate effect on maximum walking distance (MWD) (SMD 0.70, 95% confidence interval (CI) 0.31 to 1.08; 3 studies; 125 participants; moderate-quality evidence) and a large effect on pain-free walking distance (PFWD) (SMD 1.29, 95% CI 0.90 to 1.68; 3 studies; 125 participants; moderate-quality evidence) in favour of endovascular revascularisation. Long-term follow-up in two studies (103 participants) showed no clear differences between groups for MWD (SMD 0.67, 95% CI -0.30 to 1.63; low-quality evidence) and PFWD (SMD 0.69, 95% CI -0.45 to 1.82; low-quality evidence). The number of secondary invasive interventions (OR 0.81, 95% CI 0.12 to 5.28; 2 studies; 118 participants; moderate-quality evidence) was also not different between groups. One study reported no differences in disease-specific QoL after two years.Data from five studies (n = 345) comparing endovascular revascularisation versus supervised exercise showed no clear differences between groups for MWD (SMD -0.42, 95% CI -0.87 to 0.04; moderate-quality evidence) and PFWD (SMD -0.05, 95% CI -0.38 to 0.29; moderate-quality evidence). Similarliy, long-term follow-up in three studies (184 participants) revealed no differences between groups for MWD (SMD -0.02, 95% CI -0.36 to 0.32; moderate-quality evidence) and PFWD (SMD 0.11, 95% CI -0.26 to 0.48; moderate-quality evidence). In addition, high-quality evidence showed no difference between groups in the number of secondary invasive interventions (OR 1.40, 95% CI 0.70 to 2.80; 4 studies; 395 participants) and in disease-specific QoL (SMD 0.18, 95% CI -0.04 to 0.41; 3 studies; 301 participants).Comparing endovascular revascularisation plus supervised exercise versus supervised exercise alone showed no clear differences between groups for MWD (SMD 0.26, 95% CI -0.13 to 0.64; 3 studies; 432 participants; moderate-quality evidence) and PFWD (SMD 0.33, 95% CI -0.26 to 0.93; 2 studies; 305 participants; moderate-quality evidence). Long-term follow-up in one study (106 participants) revealed a large effect on MWD (SMD 1.18, 95% CI 0.65 to 1.70; low-quality evidence) in favour of the combination therapy. Reports indicate that disease-specific QoL was comparable between groups (SMD 0.25, 95% CI -0.05 to 0.56; 2 studies; 330 participants; moderate-quality evidence) and that the number of secondary invasive interventions (OR 0.27, 95% CI 0.13 to 0.55; 3 studies; 457 participants; high-quality evidence) was lower following combination therapy.Two studies comparing endovascular revascularisation plus pharmacotherapy (cilostazol) versus pharmacotherapy alone provided data showing a small effect on MWD (SMD 0.38, 95% CI 0.08 to 0.68; 186 participants; high-quality evidence), a moderate effect on PFWD (SMD 0.63, 95% CI 0.33 to 0.94; 186 participants; high-quality evidence), and a moderate effect on disease-specific QoL (SMD 0.59, 95% CI 0.27 to 0.91; 170 participants; high-quality evidence) in favour of combination therapy. Long-term follow-up in one study (47 participants) revealed a moderate effect on MWD (SMD 0.72, 95% CI 0.09 to 1.36; P = 0.02) in favour of combination therapy and no clear differences in

PFWD between groups (SMD 0.54, 95% CI -0.08 to 1.17; P = 0.09). The number of secondary invasive interventions was comparable between groups (OR 1.83, 95% CI 0.49 to 6.83; 199 participants; high-quality evidence)
AUTHORS' CONCLUSIONS:
In the management of patients with IC, endovascular revascularisation does not provide significant benefits compared with supervised exercise alone in terms of improvement in functional performance or QoL. Although the number of studies is small and clinical heterogeneity underlines the need for more homogenous and larger studies, evidence suggests that a synergetic effect may occur when endovascular revascularisation is combined with a conservative therapy of supervised exercise or pharmacotherapy with cilostazol: the combination therapy seems to result in greater improvements in functional performance and in QoL scores than are seen with conservative therapy alone.

Impactfactor: --

Enteral nutrition during major surgery: how to proceed after SANICS II - Authors' reply

Luyer MDP, all authors.

Lancet Gastroenterol Hepatol. 2018 Jul;3(7):455.

Geen abstract beschikbaar.

Impactfactor: --

Epidemiology of injuries, treatment (costs) and outcome in burn patients admitted to a hospital with or without dedicated burn centre (Burn-Pro): protocol for a multicentre prospective observational study

Van Lieshout EM, Van Yperen DT, Van Baar ME,, Polinder S, Boersma D, Cardon AY, De Rijcke PA, Guijt M, Klem TM, Lansink KW, Ringburg AN, Staarink M, Van de Schoot L, **Van der Veen AH**, Van Eijck FC, Van Eerten PV, Vegt PA, Vos DI, Waleboer M, Verhofstad MH, Van der Vlies CH

BMJ Open. 2018 Nov 15;8(11):e023709

INTRODUCTION:
The Emergency Management of Severe Burns (EMSB) referral criteria have been implemented for optimal triaging of burn patients. Admission to a burn centre is indicated for patients with severe burns or with specific characteristics like older age or comorbidities. Patients not meeting these criteria can also be treated in a hospital without burn centre. Limited information is available about the organisation of care and referral of these patients. The aims of this study are to determine the burn injury characteristics, treatment (costs), quality of life and scar quality of burn patients admitted to a hospital without dedicated burn centre. These data will subsequently be compared with data from patients with<10%?total bodysurface area (TBSA) burned who are admitted (or secondarily referred) to a burn centre. If admissions were in agreement with the EMSB, referral criteria will also be determined.
METHODS AND ANALYSIS:
In this multicentre, prospective, observational study (cohort study), the following two groups of patients will be followed: 1) all patients (no age limit) admitted with burn-related injuries to a hospital without a dedicated burn centre in the Southwest Netherlands or Brabant Trauma Region and 2) all patients (no age limit) with<10%?TBSA burned who are primarily admitted (or secondarily referred) to the burn centre of Maasstad Hospital. Data on the burn injury characteristics (primary outcome), EMSB compliance, treatment, treatment costs and outcome will be collected from the patients' medical files. At 3?weeks and at 3, 6 and 12 months after trauma, patients will be asked to complete the quality of life questionnaire (EuroQoL-5D), and the patient-reported part of the Patient and Observer Scar Assessment Scale (POSAS). At those time visits, the coordinating investigator or research assistant will complete the observer-reported part of the POSAS.
ETHICS AND DISSEMINATION:
This study has been exempted by the medical research ethics committee Erasmus MC (Rotterdam, The Netherlands). Each participant will provide written consent to participate and remain encoded during the study. The results of the study are planned to be published in an international, peer-reviewed journal.

Impactfactor: *2.413*

Evaluation of PET and laparoscopy in STagIng advanced gastric cancer: a multicenter prospective study (PLASTIC-study)

Brenkman HJF, Gertsen EC, Vegt E, van Hillegersberg R, van Berge Henegouwen MI, Gisbertz SS, **Luyer MDP**, **Nieuwenhuijzen GAP**, van Lanschot JJB, Lagarde SM, de Steur WO, Hartgrink HH, Stoot JHMB, Hulsewe KWE, Spillenaar Bilgen EJ, van Det MJ, Kouwenhoven EA, van der Peet DL, Daams F, van Sandick JW, van Grieken NCT, Heisterkamp J, van Etten B, Haveman JW, Pierie JP, Jonker F, Thijssen AY, Belt EJT, van Duijvendijk P, Wassenaar E, van Laarhoven HWM, Wessels FJ, Haj Mohammad N, van Stel HF, Frederix GWJ, Siersema PD, Ruurda JP, PLASTIC Study Group

BMC Cancer. 2018 Apr 20;18(1):450

BACKGROUND:
Initial staging of gastric cancer consists of computed tomography (CT) and gastroscopy. In locally advanced (cT3-4)

gastric cancer, fluorodeoxyglucose positron emission tomography with CT (FDG-PET/CT or PET) and staging laparoscopy (SL) may have a role in staging, but evidence is scarce. The aim of this study is to evaluate the impact and cost-effectiveness of PET and SL in addition to initial staging in patients with locally advanced gastric cancer.

METHODS:

This prospective observational cohort study will include all patients with a surgically resectable, advanced gastric adenocarcinoma (cT3-4b, N0-3, M0), that are scheduled for treatment with curative intent after initial staging with gastroscopy and CT. The modalities to be investigated in this study is the addition of PET and SL. The primary outcome of this study is the proportion of patients in whom the PET or SL lead to a change in treatment strategy. Secondary outcome parameters are: diagnostic performance, morbidity and mortality, quality of life, and cost-effectiveness of these additional diagnostic modalities. The study recently started in August 2017 with a duration of 36 months. At least 239 patients need to be included in this study to demonstrate that the diagnostic modalities are break-even. Based on the annual number of gastrectomies in the participating centers, it is estimated that approximately 543 patients are included in this study.

DISCUSSION:

In this study, it is hypothesized that performing PET and SL for locally advanced gastric adenocarcinomas results in a change of treatment strategy in 27% of patients and an annual cost-reduction in the Netherlands of €916.438 in this patient group by reducing futile treatment. The results of this study may be applicable to all countries with comparable treatment algorithms and health care systems.

Impactfactor: 3.288

FA 01.02: The effect of postoperative complications after mie on long-term survival: a retrospective, multi-center cohort studiy

Fransen L, Berkelmans G, Asti E, Van Berge Henegouwen M, Berlth F, Bonavina L, Brown A, Bruns C, Gisbertz S, Grimminger P, Gutschow C, Hölscher A, Kauppi J, Lagarde SM, Mercer S, Moons J, Nafteux P, Nilsson M, Palazzo F, Pattyn P, Philippron A, Raptis D, Räsänen J, Rosato E, Rouvelas I, Schmidt H7, Schneider P, Schröder W, Wijnhoven BPL, **Nieuwenhuijzen GA, Luyer M**

Dis Esophagus. 2018 Sep 1;31(13):1

Background:

Esophagectomy has a high incidence of postoperative morbidity. Complications lead to a decreased short-term survival, however the influence of those complications on long-term survival is still unclear. Most of the performed studies are small, single center cohort series with inconclusive or conflicting results. Minimally invasive esophagectomy (MIE) has been shown to be associated with a reduced postoperative morbidity. In this study, the influence of complications on long-term survival for patients with esophageal cancer undergoing a MIE were investigated.

Methods:

Data was collected from the EsoBenchmark database, a collaboration of 13 high-volume centers routinely performing MIE. Patients were included in this database from June 1, 2011 until May 31, 2016. Complications were scored according to the Clavien-Dindo (CD) classification for surgical complications. Major complications were defined as a CD grade = 3. The data were corrected for 90-day mortality to correct for the short-term effect of postoperative complications on mortality. Overall survival was analyzed using the Kaplan Meier, log rank- and (uni- and multivariable) Cox-regression analyses.

Results:

A total of 926 patients were eligible for analysis. Mean follow-up time was 30.8 months (SD 17.9). Complications occurred in 543 patients (59.2%) of which 39.3% had a major complication. Anastomotic leakage (AL) occurred in 135 patients (14.5%) of which 9.2% needed an intervention (CD grade = 3). A significant worse long-term survival was observed in patients with any AL (HR 1.73, 95% CI 1.29-2.32, P < 0.001) and for patients with AL CD grade =3 (HR 1.86, 95% CI 1.32-2.63, P < 0.001). Major cardiac complications occurred in 18 patients (1.9%) and were related to a decreased long-term survival (HR 2.72, 95% CI 1.38-5.35, p 0.004). For all other complications, no significant influence on long-term survival was found.

Conclusion:

The occurrence and severity of anastomotic leakage and cardiac complications after MIE negatively affect long-term survival of esophageal cancer patients.

Impactfactor: 2.702

Factors affecting outcomes following pelvic exenteration for locally recurrent rectal cancer

PelvEx Collaborative: **Rutten HJ, Burger JW**

Br J Surg. 2018 May;105(6):650-657

BACKGROUND:

Pelvic exenteration for locally recurrent rectal cancer (LRRC) is associated with variable outcomes, with the majority of data from single-centre series. This study analysed data from an international collaboration to determine robust parameters that could inform clinical decision-making.

METHODS:
Anonymized data on patients who had pelvic exenteration for LRRC between 2004 and 2014 were accrued from 27 specialist centres. The primary endpoint was survival. The impact of resection margin, bone resection, node status and use of neoadjuvant therapy (before exenteration) was assessed.
RESULTS:
Of 1184 patients, 614 (51·9 per cent) had neoadjuvant therapy. A clear resection margin (R0 resection) was achieved in 55·4 per cent of operations. Twenty-one patients (1·8 per cent) died within 30?days and 380 (32·1 per cent) experienced a major complication. Median overall survival was 36?months following R0 resection, 27?months after R1 resection and 16?months following R2 resection (P?<?0·001). Patients who received neoadjuvant therapy had more postoperative complications (unadjusted odds ratio (OR) 1·53), readmissions (unadjusted OR 2·33) and radiological reinterventions (unadjusted OR 2·12). Three-year survival rates were 48·1 per cent, 33·9 per cent and 15 per cent respectively. Bone resection (when required) was associated with a longer median survival (36 versus 29?months; P?<?0·001). Node-positive patients had a shorter median overall survival than those with node-negative disease (22 versus 29?months respectively). Multivariable analysis identified margin status and bone resection as significant determinants of long-term survival.
CONCLUSION:
Ngative margins and bone resection (where needed) were identified as the most important factors influencing overall survival. Neoadjuvant therapy before pelvic exenteration did not affect survival, but was associated with higher rates of readmission, complications and radiological reintervention.

Impactfactor: 5.433

Factors influencing health-related quality of life after gastrectomy for cancer

Brenkman HJF, Tegels JJW2Ruurda JP, **Luyer MDP**, Kouwenhoven EA, Draaisma WA, van der Peet DL, Wijnhoven BPL, Stoot JHMB, van Hillegersberg R; LOGICA Study Group

Gastric Cancer. 2018 May;21(3):524-532. Epub 2017 Oct 24

AIM:
Insight in health-related quality of life (HRQoL) may improve clinical decision making and inform patients about the long-term effects of gastrectomy. This study aimed to evaluate and identify factors associated with HRQoL after gastrectomy.
METHODS:
This cross-sectional study used prospective databases from seven Dutch centers (2001-2015) including patients who underwent gastrectomy for cancer. Between July 2015 and November 2016, European Organization for Research and Treatment of Cancer HRQoL questionnaires QLQ-C30 and QLQ-STO22 were sent to all surviving patients without recurrence. The QLQ-C30 scores were compared to a Dutch reference population using a one-sample t test. Spearman's rank test was used to correlate time after surgery to HRQoL, and multivariable linear regression was performed to identify factors associated with HRQoL.
RESULTS:
A total of 222 of 274 (81.0%) patients completed the questionnaires. Median follow-up was 29 months (range, 3-171) and 86.9% of patients had a follow-up >1 year. The majority of patients had undergone neoadjuvant treatment (64.4%) and total gastrectomy (52.7%). Minimally invasive gastrectomy (MIG) was performed in 50% of the patients. Compared to the general population, gastrectomy patients scored significantly worse on most functional and symptom scales ($p < 0.001$) and slightly worse on global HRQoL (78 vs. 74, $p = 0.012$). Time elapsed since surgery did not correlate with global HRQoL (Spearman's ? = 0.06, $p = 0.384$). Distal gastrectomy, neoadjuvant treatment, and MIG were associated with better HRQoL ($p < 0.050$).
CONCLUSION:
After gastrectomy, patients encounter functional impairments and symptoms, but experience only a slightly impaired global HRQoL. Distal gastrectomy, the ability to receive neoadjuvant treatment, and MIG may be associated with HRQoL benefits.

Impactfactor: 5.045

Factors Predicting Lower Leg Chronic Exertional Compartment Syndrome in a Large Population

de Bruijn JA, van Zantvoort APM, van Klaveren D, Winkes MB, van der Cruijsen-Raaijmakers M, Hoogeveen AR, **Teijink JAW**, Scheltinga MR

Int J Sports Med. 2018 Jan 39(1):58-66

Knowledge about lower leg chronic exertional compartment syndrome (CECS) is largely obtained from highly selected populations. Patient characteristics may therefore not be appropriate for the general population. Our purpose was to describe a heterogeneous population of individuals suspected of lower leg CECS and to identify predictors of CECS. Charts of individuals who were analyzed for exercise-induced lower leg pain in a referral center between 2001 and 2013 were retrospectively studied. Patients were included if history and physical examination were suggestive of CECS and if they had undergone a dynamic intracompartmental pressure measurement. Six hundred ninety-eight of 1411 individuals were diagnosed with CECS in one or more of three lower leg muscle compartments (anterior tibial, deep flexor, lateral). Prevalence of CECS peaked around the age of 20-25 years and

decreased thereafter, although a plateau around 50 years was found. Age, gender, bilateral symptoms, previous lower leg pathology, sports (running and skating) and tender muscle compartments were identified as independent predictors of lower leg CECS. The proposed predictive model has moderate discriminative ability (AUC 0.66) and good calibration over the complete range of predicted probabilities. The predictive model, displayed as a nomogram, may aid in selecting individuals requiring an invasive dynamic intracompartmental muscle pressure measurement.

Impactfactor: 2.453

Failure to Rescue - a Closer Look at Mortality Rates Has No Added Value for Hospital Comparisons but Is Useful for Team Quality Assessment in Abdominal Aortic Aneurysm Surgery in The Netherlands

Lijftogt N, Karthaus EG, Vahl A, van Zwet EW, van der Willik EM, Tollenaar RAEM, Hamming JF, Wouters MWJM; Dutch Society of Vascular Surgery; Steering Committee of the Dutch Surgical Aneurysm Audit; Dutch Institute for Clinical Auditing: **van Sambeek MR, Teijink JA**

Eur J Vasc Endovasc Surg. 2018 Nov;56(5):652-661

OBJECTIVES:

Failure to rescue (FTR) is a composite quality indicator, defined as the proportion of deceased patients following major complications. The aims of this study were to compare FTR with mortality for hospital comparisons in abdominal aortic aneurysm (AAA) surgery in The Netherlands and investigate hospital volume and associated factors.

METHODS:

Patients prospectively registered between 2013 and 2015 in the Dutch Surgical Aneurysm Audit (DSAA) were analysed. FTR was analysed for AAA patients and subgroups elective (EAAA) and acute (AAAA; symptomatic or ruptured) aneurysms. Variables and hospital volume were analysed by uni- and multivariable regression analysis. Adjusted hospital comparisons for mortality, major complications, and FTR were presented in funnel plots. Isomortality lines were constructed when presenting FTR and major complication rates.

RESULTS:

A total of 9258 patients were analysed in 61 hospitals: 7149 EAAA patients (77.2%) and 2109 AAAA patients (22.8%). There were 2785 (30.1%) patients with complications (unadjusted range 5-65% per hospital): 2161 (77.6%) with major and 624 (28.4%) patients with minor complications. Overall mortality was 6.6% (adjusted range 0-16% per hospital) and FTR was 28.4% (n = 613) (adjusted range 0-60% per hospital). Glasgow Coma Scale, age, pulse, creatinine, electrocardiography, and operative setting were independently associated with FTR. Hospital volume was not associated with FTR. In AAAA patients hospital volume was significantly associated with a lower adjusted major complication and mortality rate (OR 0.62, 95% CI 0.49-0.78; and 0.64, 95% CI 0.48-0.87). Four hospitals had a significant lower adjusted FTR with different major complication rates on different isomortality lines.

CONCLUSIONS:

There was more variation in FTR than in mortality between hospitals. FTR identified the same best performing hospitals as for mortality and therefore was of limited additional value in measuring quality of care for AAA surgery. FTR can be used for internal quality improvement with major complications in funnel plots and diagrams with isomortality lines.

Impactfactor: 3.877

Fasciotomy for Lateral Lower-leg Chronic Exertional Compartment Syndrome

van Zantvoort AP, de Bruijn JA, Hundscheid HP, van der Cruijsen-Raaijmakers M, **Teijink JA**, Scheltinga MR

Int J Sports Med. 2018 Dec;39(14):1081-1087

Exercise-induced lower leg pain may be caused by chronic exertional compartment syndrome (CECS). Anterior or deep posterior compartments are usually affected. Knowledge about CECS of the lateral compartment (lat-CECS) is limited and outcome after fasciotomy is unknown. The purpose of this study is to report on success rates of fasciotomy in patients with lat-CECS. Surgical success rates in patients with lat-CECS diagnosed with a dynamic intracompartmental pressure (ICP) measurement were studied using a questionnaire (success: excellent or good as judged by the patient; unsuccessful: moderate, fair or poor). We conducted ICP measurements in 247 patients for suspected lat-CECS, of whom 78 were positively diagnosed. Following exclusion (n=11), 30 of the eligible 67 patients completed the questionnaire. Bilateral (70%, n=21/30) exertional pain (97%, n=29) and a feeling of tightness (93%, n=28) were the most frequently reported symptoms. Four years after fasciotomy, severity and frequency of symptoms had dropped significantly. Long-term surgical success was reported by 33% (n=10; excellent n=4, good n=6). Seventy-three percent (n=22) had resumed sports activities (9 same level, 13 lower level). In conclusion, a fasciotomy for lat-CECS was successful in the long term in just one of three operated patients in this retrospective study.

Impactfactor: 2.453

Gore Iliac Branch Endoprosthesis for treatment of bilateral common iliac artery aneurysms

Maldonado TS, Mosquera NJ, Lin P, Bellosta R, Barfield M, Moussa A, Rhee R, Schermerhorn ML, Weinberger J, Wikkeling M, Heyligers J, Veith FJ, Milner R, Reijnen MP; Gore Bilateral IBE Study Group: **van Sambeek MRJ**

Vasc Surg. 2018 Jul;68(1):100-108.e3

OBJECTIVE:
The Gore Iliac Branch Endoprosthesis (IBE; W. L. Gore & Associates, Flagstaff, Ariz) has recently been approved by the Food and Drug Administration for treatment of common iliac artery (CIA) aneurysms. Despite early excellent results in clinical trial, none of 63 patients were treated for bilateral iliac aneurysms. The goal of this study was to examine real-world experience using the Gore IBE for bilateral CIA aneurysms.
METHODS:
A retrospective review of an international multicenter (16 U.S., 8 European) experience using the Gore IBE to treat bilateral CIA aneurysms was performed. Cases were limited to those occurring after Food and Drug Administration approval (February 2016) in the United States and after CE mark approval (November 2013) in Europe. Demographics of the patients, presentation, anatomic characteristics, and procedural details were captured.
RESULTS:
There were 47 patients (45 men; mean age, 68 years; range, 41-84 years) treated with bilateral Gore IBEs (27 U.S., 20 European). Six patients (12.7%) were symptomatic and 12 (25.5%) patients were treated primarily for CIA aneurysm (aorta <5.0 cm). Mean CIA diameter was 40.3 mm. Four patients had aneurysmal internal iliac arteries (IIAs). Two of these were sealed proximally at the IIA aneurysm neck and two required coil embolization of IIA branches to achieve seal in the largest first-order branches. Technical success was achieved in 46 patients (97.9%). No type I or type III endoleaks were noted. There was no significant perioperative morbidity or mortality. IIA branch adjunctive stenting was required in four patients (one IIA distal dissection, three kinks). On follow-up imaging available for 40 patients (85.1%; mean, 6.5 months; range, 1-36 months), 12 type II endoleaks (30%) and no type I or type III endoleaks were detected. Two of 80 (2.5%) IIA branches imaged were occluded; one was intentionally sacrificed perioperatively.
CONCLUSIONS:
Preservation of bilateral IIAs in repair of bilateral CIA aneurysms can be performed safely with excellent technical success and short-term patency rates using the Gore IBE device. Limb and branch occlusions are rare, usually are due to kinking, and can almost always be treated successfully with stenting.

Impactfactor: 2.758

Health-related quality of life and cost-effectiveness analysis of gum chewing in patients undergoing colorectal surgery: results of a randomized controlled trial

Pattamatta M, **Smeets BJJ**, Evers SMAA, **Rutten HJT, Luyer MDP**, Hiligsmann M

Acta Chir Belg. 2018 Jan 30:1-8.

BACKGROUND:
Postoperative ileus (POI) and anastomotic leakage (AL) following colorectal surgery severely increase healthcare costs and decrease quality of life. This study evaluates the effects of reducing POI and AL via perioperative gum chewing compared to placebo (control) on in-hospital costs, health-related quality of life (HRQoL), and assesses cost-effectiveness.
METHODS:
In patients undergoing elective, open colorectal surgery, changes in HRQoL were assessed using EORTC-QLQ-C30 questionnaires and costs were estimated from a hospital perspective. Incremental cost-effectiveness ratios were estimated.
RESULTS:
In 112 patients, mean costs for ward stay were significantly lower in the gum chewing group when compared to control (€3522 (95% CI €3034-€4010) versus €4893 (95% CI €3843-€5942), respectively, p?=?.020). No differences were observed in mean overall in-hospital costs, or in mean change in any of the HRQoL scores or utilities. Gum chewing was dominant (less costly and more effective) compared to the control in more than 50% of the simulations for both POI and AL.
CONCLUSION:
Reducing POI and AL via gum chewing reduced costs for ward stay, but did not affect overall in-hospital costs, HRQoL, or mapped utilities. More studies with adequate sample sizes using validated questionnaires at standardized time points are needed.

Impactfactor: 0.420

Hospital of Diagnosis Influences the Probability of Receiving Curative Treatment for Esophageal Cancer

van Putten M, **Koëter M**, van Laarhoven HWM, Lemmens VEPP, Siersema PD, Hulshof MCCM, Verhoeven RHA, **Nieuwenhuijzen GAP**

Ann Surg. 2018 Feb 267(2):303-310

OBJECTIVE:
The aim of this article was to study the influence of hospital of diagnosis on the probability of receiving curative treatment and its impact on survival among patients with esophageal cancer (EC).
BACKGROUND:
Although EC surgery is centralized in the Netherlands, the disease is often diagnosed in hospitals that do not perform this procedure.
METHODS:
Patients with potentially curable esophageal or gastroesophageal junction tumors diagnosed between 2005 and 2013 who were potentially curable (cT1-3,X, any N, M0,X) were selected from the Netherlands Cancer Registry. Multilevel logistic regression was performed to examine the probability to undergo curative treatment (resection with or without neoadjuvant treatment, definitive chemoradiotherapy, or local tumor excision) according to hospital of diagnosis. Effects of variation in probability of undergoing curative treatment among these hospitals on survival were investigated by Cox regression.
RESULTS:
All 13,017 patients with potentially curable EC, diagnosed in 91 hospitals, were included. The proportion of patients receiving curative treatment ranged from 37% to 83% and from 45% to 86% in the periods 2005-2009 and 2010-2013, respectively, depending on hospital of diagnosis. After adjustment for patient- and hospital-related characteristics these proportions ranged from 41% to 77% and from 50% to 82%, respectively (both P < 0.001). Multivariable survival analyses showed that patients diagnosed in hospitals with a low probability of undergoing curative treatment had a worse overall survival (hazard ratio = 1.13, 95% confidence interval 1.06-1.20; hazard ratio = 1.15, 95% confidence interval 1.07-1.24).
CONCLUSIONS:
The variation in probability of undergoing potentially curative treatment for EC between hospitals of diagnosis and its impact on survival indicates that treatment decision making in EC may be improved.
Impactfactor: *1.536*

[Hospital of diagnosis influences the probability of receiving curative treatment for oesophageal and gastric cancer] | Ziekenhuis van diagnose beïnvloedt kans op curatieve behandeling voor slokdarm- en maagkanker *

van Putten M, Verhoeven RHA, **Koëter M**, van Laarhoven HWM, van Sandick JW, Plukker JTM, Siersema PD, Hulshof MCCM, Wijnhoven BPL, Lemmens VEPP, **Nieuwenhuijzen GAP**

Ned Tijdschr Geneeskd. 2018;162:D1970

OBJECTIVE:
The aim of these studies was to examine the influence of hospital of diagnosis on the probability of receiving curative treatment and its impact on survival among oesophageal and gastric cancer.
DESIGN:
Although oesophageal and gastric cancer surgery is centralised in the Netherlands, the disease is often diagnosed in hospitals that do not perform this procedure.
METHOD:
Patients with potentially curable oesophageal or gastric cancer tumours diagnosed between 2005 and 2013 were selected from the Netherlands Cancer Registry. The probability to undergo curative treatment was examined for each hospital of diagnosis after adjustment for case-mix. Effects of variation in probability of undergoing curative treatment among these hospitals on survival were investigated Cox regression.
RESULTS:
All 13,017 patients with potentially curable oesophageal and 5,620 patients with potentially curable gastric cancer, diagnosed in 91 hospitals, were included. After adjustment, the proportion of oesophageal cancer patients receiving curative treatment ranged from 50% to 82% and from 48% to 78% for patients with gastric cancer in 2010-2013, depending on hospital of diagnosis (both P < 0.001). Furthermore, patients diagnosed in hospitals with a low probability of undergoing curative treatment had a worse overall survival in the period 2010-2013 (oesophageal cancer hazard ratio (HR): 1,15; 95%-CI: 1,07-1,24; gastric cancer HR: 1,21; 95%-CI: 1,04-1,41).
CONCLUSION:
The variation in probability of undergoing potentially curative treatment for oesophageal and gastric cancer between hospitals of diagnosis and its impact on survival indicates that treatment decision-making for these patients may be improved. Regional expert multidisciplinary team meetings in this field may improve the selection of patients for curative treatment.
Impactfactor: *--*

** Dit artikel is een bewerking van een eerdere publicatie in Annals of Surgery (2018;267:303-10) met als titel 'Hospital of diagnosis influences the probability of receiving curative treatment for esophageal cancer' en in British Journal of Surgery (2016;103:233-41) met als titel 'Hospital of diagnosis and probability of having surgical treatment for resectable gastric cancer'. Afgedrukt met toestemming.*

Hospital variation and the impact of postoperative complications on the use of perioperative chemo(radio)therapy in resectable gastric cancer. Results from the Dutch Upper GI Cancer Audit

Schouwenburg MG, Busweiler LAD, Beck N, Henneman D, Amodio S, van Berge Henegouwen MI, Cats A, van Hillegersberg R, van Sandick JW, Wijnhoven BPL, Wouters MWJ, **Nieuwenhuijzen GAP,** Dutch Upper GI Cancer Audit group

Eur J Surg Oncol. 2018 Apr 44(4):532-538. Epub 2018 Jan 12

BACKGROUND:
Dutch national guidelines on the diagnosis and treatment of gastric cancer recommend the use of perioperative chemotherapy in patients with resectable gastric cancer. However, adjuvant chemotherapy is often not administered. The aim of this study was to evaluate hospital variation on the probability to receive adjuvant chemotherapy and to identify associated factors with special attention to postoperative complications.
METHODS:
All patients who received neoadjuvant chemotherapy and underwent an elective surgical resection for stage IB-IVa (M0) gastric adenocarcinoma between 2011 and 2015 were identified from a national database (Dutch Upper GI Cancer Audit). A multivariable linear mixed model was used to evaluate case-mix adjusted hospital variation and to identify factors associated with adjuvant therapy.
RESULTS:
Of all surgically treated gastric cancer patients who received neoadjuvant chemotherapy (n = 882), 68% received adjuvant chemo(radio)therapy. After adjusting for case-mix and random variation, a large hospital variation in the administration rates for adjuvant was observed (OR range 0.31-7.1). In multivariable analysis, weight loss, a poor health status and failure of neoadjuvant chemotherapy completion were strongly associated with an increased likelihood of adjuvant therapy omission. Patients with severe postoperative complications had a threefold increased likelihood of adjuvant therapy omission (OR 3.07 95% CI 2.04-4.65).
CONCLUSION:
Despite national guidelines, considerable hospital variation was observed in the probability of receiving adjuvant chemo(radio)therapy. Postoperative complications were strongly associated with adjuvant chemo(radio)therapy omission, underlining the need to further reduce perioperative morbidity in gastric cancer surgery.

Impactfactor: 3.688

Hospital volume and outcome in rectal cancer patients; results of a population-based study in the Netherlands

Hagemans JAW, Alberda WJ, Verstegen M, de Wilt JHW, Verhoef C, Elferink MA, **Burger JWA**

Eur J Surg Oncol. 2018 Dec 26. pii: S0748-7983(18)32040-7. [Epub ahead of print]

BACKGROUND:
Clinically staged T1-3 rectal cancer (cT1-3) is generally treated by total mesorectal excision(TME) with or without neoadjuvant therapy and sometimes requires beyond TME-surgery, whereas cT4 rectal cancer often requires both. This study evaluates the outcome of cT1-3 and cT4 rectal cancer according to hospital volume.
METHODS:
Patients undergoing rectal cancer surgery between 2005 and 2013 in the Netherlands were included from the National Cancer Registry. Hospitals were divided into low(1-20), medium(21-50) and high(>50 resections/year) volume for cT1-3 and low(1-4), medium(5-9) and high(=10 resections/year) volume for cT4 rectal cancer. Cox-proportional hazards model was used for multivariable analysis of overall survival (OS).
RESULTS:
A total of 14.050 confirmed cT1-3 patients and 2.104 cT4 patients underwent surgery. In cT1-3 rectal cancer, there was no significant difference in 5-year OS related to high, medium and low hospital volume (70% vs. 69% vs. 69%). In cT4 rectal cancer, treatment in a high volume cT4 hospital was associated with a survival benefit compared to low volume cT4 hospitals (HR 0.81 95%CI 0.67-0.98) adjusted for non-treatment related confounders, but this was not significant after adjustment for neoadjuvant treatment. Patients with cT4-tumours treated in high volume hospitals had a significantly lower age, more synchronous metastases, more patients treated with neoadjuvant therapy and a higher pT-stage.
CONCLUSION:
Hospital volume was not associated with survival in cT1-3 rectal cancer. In cT4 rectal cancer, treatment in high volume cT4 hospitals was associated with improved survival compared to low volume cT4 hospitals, although this association lost statistical significance after correction for neoadjuvant treatment.

Impactfactor: 3.688

Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, **de Hingh IHJT**, van der Velden J, Arts HJ, Massuger LFAG, Aalbers AGJ, Verwaal VJ, Kieffer JM, Van de Vijver KK, van Tinteren H, Aaronson NK, Sonke GS

N Engl J Med. 2018 Jan 18 378(3):230-240

BACKGROUND:
Treatment of newly diagnosed advanced-stage ovarian cancer typically involves cytoreductive surgery and systemic chemotherapy. We conducted a trial to investigate whether the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to interval cytoreductive surgery would improve outcomes among patients who were receiving neoadjuvant chemotherapy for stage III epithelial ovarian cancer.
METHODS:
In a multicenter, open-label, phase 3 trial, we randomly assigned 245 patients who had at least stable disease after three cycles of carboplatin (area under the curve of 5 to 6 mg per milliliter per minute) and paclitaxel (175 mg per square meter of body-surface area) to undergo interval cytoreductive surgery either with or without administration of HIPEC with cisplatin (100 mg per square meter). Randomization was performed at the time of surgery in cases in which surgery that would result in no visible disease (complete cytoreduction) or surgery after which one or more residual tumors measuring 10 mm or less in diameter remain (optimal cytoreduction) was deemed to be feasible. Three additional cycles of carboplatin and paclitaxel were administered postoperatively. The primary end point was recurrence-free survival. Overall survival and the side-effect profile were key secondary end points.
RESULTS:
In the intention-to-treat analysis, events of disease recurrence or death occurred in 110 of the 123 patients (89%) who underwent cytoreductive surgery without HIPEC (surgery group) and in 99 of the 122 patients (81%) who underwent cytoreductive surgery with HIPEC (surgery-plus-HIPEC group) (hazard ratio for disease recurrence or death, 0.66; 95% confidence interval [CI], 0.50 to 0.87; P=0.003). The median recurrence-free survival was 10.7 months in the surgery group and 14.2 months in the surgery-plus-HIPEC group. At a median follow-up of 4.7 years, 76 patients (62%) in the surgery group and 61 patients (50%) in the surgery-plus-HIPEC group had died (hazard ratio, 0.67; 95% CI, 0.48 to 0.94; P=0.02). The median overall survival was 33.9 months in the surgery group and 45.7 months in the surgery-plus-HIPEC group. The percentage of patients who had adverse events of grade 3 or 4 was similar in the two groups (25% in the surgery group and 27% in the surgery-plus-HIPEC group, P=0.76).
CONCLUSIONS:
Among patients with stage III epithelial ovarian cancer, the addition of HIPEC to interval cytoreductive surgery resulted in longer recurrence-free survival and overall survival than surgery alone and did not result in higher rates of side effects.

Impactfactor: 79.258

Impact of neoadjuvant chemoradiotherapy on health-related quality of life in long-term survivors of esophageal or junctional cancer: results from the randomized CROSS trial

Noordman BJ, Verdam MGE, Lagarde SM, Shapiro J, Hulshof MCCM, van Berge Henegouwen MI, Wijnhoven BPL, **Nieuwenhuijzen GAP**, Bonenkamp JJ, Cuesta MA, Plukker JTM, Spillenaar Bilgen EJ, Steyerberg EW, van der Gaast A, Sprangers MAG, van Lanschot JJB; CROSS Study Group

Ann Oncol. 2018 Feb 1;29(2):445-451

Background: Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard of care for patients with esophageal or junctional cancer, but the long-term impact of nCRT on health-related quality of life (HRQOL) is unknown. The purpose of this study is to compare very long-term HRQOL in long-term survivors of esophageal cancer who received nCRT plus surgery or surgery alone.
Patients and methods: Patients were randomly assigned to receive nCRT (carboplatin/paclitaxel with 41.4-Gy radiotherapy) plus surgery or surgery alone. HRQOL was measured using EORTC-QLQ-C30, EORTC-QLQ-OES24 and K-BILD questionnaires after a minimum follow-up of 6?years. To allow for examination over time, EORTC-QLQ-C30 and QLQ-OES24 questionnaire scores were compared with pretreatment and 12 months postoperative questionnaire scores. Physical functioning (QLQ-C30), eating problems (QLQ-OES24) and respiratory problems (K-BILD) were predefined primary end points. Predefined secondary end points were global quality of life and fatigue (both QLQ-C30).
Results: After a median follow-up of 105?months, 123/368 included patients (33%) were still alive (70 nCRT plus surgery, 53 surgery alone). No statistically significant or clinically relevant differential effects in HRQOL end points were found between both groups. Compared with 1-year postoperative levels, eating problems, physical functioning, global quality of life and fatigue remained at the same level in both groups. Compared with pretreatment levels, eating problems had improved (Cohen's d -0.37, P?=?0.011) during long-term follow-up, whereas physical functioning and fatigue were not restored to pretreatment levels in both groups (Cohen's d -0.56 and 0.51, respectively, both P?<?0.001).
Conclusions: Although physical functioning and fatigue remain reduced after long-term follow-up, no adverse impact of nCRT is apparent on long-term HRQOL compared with patients who were treated with surgery alone. In addition to the earlier reported improvement in survival and the absence of impact on short-term HRQOL, these results support the view that nCRT according to CROSS can be considered as a standard of care.

Impactfactor: 13.926

Impact of Surgical Approach on Long-term Survival in Esophageal Adenocarcinoma Patients With or Without Neoadjuvant Chemoradiotherapy

Noordman BJ, van Klaveren D, van Berge Henegouwen MI, Wijnhoven BPL, Gisbertz SS, Lagarde SM, van der Gaast A, Hulshof MCCM, Biermann K, Steyerberg EW, van Lanschot JJB; also on behalf of the CROSS-study group: **Nieuwenhuijzen GA,** Creemers GJ, Sangen MJ van der

Ann Surg. 2018 May;267(5):892-897

OBJECTIVE:

To compare overall survival in patients with esophageal adenocarcinoma who underwent transhiatal esophagectomy (THE) with limited lymphadenectomy or transthoracic esophagectomy (TTE) with extended lymphadenectomy with or without neoadjuvant chemoradiotherapy (nCRT).

BACKGROUND:

The application of neoadjuvant therapy might change the association between the extent of lymphadenectomy and survival in patients with esophageal adenocarcinoma. This may influence the choice of surgical approach in patients treated with nCRT.

METHODS:

Patients with potentially curable subcarinal esophageal adenocarcinoma treated with surgery alone or nCRT followed by surgery in 7 centers were included. The effect of surgical approach on overall survival, differentiated by the addition or omission of nCRT, was analyzed using a multivariable Cox regression model that included well-known prognostic factors and factors that might have influenced the choice of surgical approach.

RESULTS:

In total, 701 patients were included, of whom 318 had TTE with extended lymphadenectomy and 383 had THE with limited lymphadenectomy. TTE had differential effects on survival (P for interaction = 0.02), with a more favorable prognostic effect in patients who were treated with surgery alone [hazard ratio (HR) = 0.77, 95% confidence interval (CI) 0.58-1.03]. This association was statistically significant in a subgroup of patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 0.62, 95% CI 0.43-0.90). The favorable prognostic effect of TTE over THE was absent in the nCRT and surgery group (HR = 1.16, 95% CI 0.80-1.66) and in the subgroup of nCRT patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 1.00, 95% CI 0.61-1.68).

CONCLUSIONS:

Compared to surgery alone, the addition of nCRT may reduce the need for TTE with extended lymphadenectomy to improve long-term survival in patients with esophageal adenocarcinoma.

Impactfactor: 1.536

Improvement in quality of life after bariatric surgery: sleeve versus bypass

Versteegden DPA, Van Himbeeck MJJ, Nienhuijs SW

Surg Obes Relat Dis. 2018 Feb 14(2):170-174. Epub 2017 Oct 16

BACKGROUND:

Obesity is steadily growing to be the largest threat to human health in this century, not only increasing prevalence of obesity-related co-morbidity but also impairing health-related quality of life (QoL). Bariatric surgery has shown to improve co-morbidity as well as QoL.

OBJECTIVES:

To assess the differences in improvement in QoL for the 2 most performed procedures: laparoscopic sleeve gastrectomy (SG) and laparoscopic Roux-en-Y gastric bypass (RYGB).

SETTING:

Obesity center, the Netherlands.

METHODS:

All patients who underwent either SG or RYGB as a primary operation from January 2012 until January 2017 were eligible. Included, were only those who completed preoperatively and 1-year postoperatively the QoL questionnaire. The RAND 36-item Health Survey was used to assess QoL.

RESULTS:

A total of 1184 cases were included in analysis of which 666 patients underwent SG and 518 patients underwent RYGB. Groups significantly differed in body mass index, weight, waist circumference, prevalence of gastroesophageal reflux disease, obstructive sleep apnea syndrome, and hypertension. All QoL domains greatly improved after bariatric surgery. Physical functioning increased more in patients who underwent gastric bypass. This remained significant after correcting for differences between groups. Other domains were not significantly different.

CONCLUSION:

QoL is greatly improved at 1 year after bariatric surgery. The improvement was comparable after SG and RYGB, expect for more increase in physical functioning after RYGB. QoL could influence decision-making between SG and RYGB. So far, no clinically relevant differences were found. Future research should focus on both longer follow-up and more specific questionnaires.

Impactfactor: 3.900

Influence of Conversion and Anastomotic Leakage on Survival in Rectal Cancer Surgery; Retrospective Cross-sectional Study

Furnée EJ, Aukema TS, Oosterling SJ, Borstlap WA, Bemelman WA, Tanis PJ; Dutch Snapshot Research Group: **Brinkman DJ, Rutten HJ, Simkens GA**

J Gastrointest Surg. 2018 Sep 5 [Epub ahead of print]

BACKGROUND:
Conversion and anastomotic leakage in colorectal cancer surgery have been suggested to have a negative impact on long-term oncologic outcomes. The aim of this study in a large Dutch national cohort was to analyze the influence of conversion and anastomotic leakage on long-term oncologic outcome in rectal cancer surgery.
METHODS:
Patients were selected from a retrospective cross-sectional snapshot study. Patients with a benign lesion, distant metastasis, or unknown tumor or metastasis status were excluded. Overall (OS) and disease-free survival (DFS) were compared between laparoscopic, converted, and open surgery as well as between patients with and without anastomotic leakage.
RESULTS:
Out of a database of 2095 patients, 638 patients were eligible for inclusion in the laparoscopic, 752 in the open, and 107 in the conversion group. A total of 746 patients met the inclusion criteria and underwent low anterior resection with primary anastomosis, including 106 (14.2%) with anastomotic leakage. OS and DFS were significantly shorter in the conversion compared to the laparoscopic group (p?=?0.025 and p?=?0.001, respectively) as well as in anastomotic leakage compared to patients without anastomotic leakage (p?=?0.002 and p?=?0.024, respectively). In multivariable analysis, anastomotic leakage was an independent predictor of OS (hazard ratio 2.167, 95% confidence interval 1.322-3.551) and DFS (1.592, 1077-2.353). Conversion was an independent predictor of DFS (1.525, 1.071-2.172), but not of OS.
CONCLUSION:
Technical difficulties during laparoscopic rectal cancer surgery, as reflected by conversion, as well as anastomotic leakage have a negative prognostic impact, underlining the need to improve both aspects in rectal cancer surgery.

Impactfactor: 2.813

Influence of Helicobacter pylori infection on gastrointestinal symptoms and complications in bariatric surgery patients: a review and meta-analysis

Smelt HJM**, Smulders JF,** Gilissen LPL**, Said M**, Ugale S, Pouwels S

Surg Obes Relat Dis. 2018 Oct;14(10):1645-1657

BACKGROUND:
Numerous papers have discussed the importance of preoperative detection and eradication of Helicobacter pylori (HP) in bariatric patients.
OBJECTIVES:
This systematic review specifically focuses on the influence of HP infection on clinical symptoms, complications, and abnormal endoscopic findings in postbariatric patients.
METHODS:
A systematic search on the influence of HP infection on postoperative complications in bariatric surgery was conducted. The methodologic quality of the included studies was rated using the Newcastle-Ottawa rating scale. The agreement between the reviewers was assessed with Cohen's kappa. The included studies were assessed into 2 groups, studies with and without eradication therapy preoperatively.
RESULTS:
A total of 21 studies were included with a methodologic quality ranging from poor to good. The agreement between the reviewers, assessed with the Cohen's kappa, was .70. Overall, tendency in the included studies was that HP infection was associated with an increased risk for developing marginal ulcers and postoperative complications. A meta-analysis on the incidence of marginal ulcers and overall postoperative complications was conducted and showed, respectively, an odds ratio of .508 (.031-8.346) and 2.863 (.262-31.268).
CONCLUSIONS:
HP is frequently found in patients before and after bariatric and metabolic surgery. We assessed whether, according to the current literature, HP increases the risk for developing postoperative complications after surgery. This meta-analysis shows that a methodologically good study should be performed to clarify the role of HP in bariatric patients and the question of whether HP should be eradicated before surgery.

Impactfactor: 3.900

Intrathoracic stomach in hiatal hernia: the role of laparoscopic repair

Castelijns PS, **Ponten JE**, Bouvy ND, **Smulders JF**, van de Poll MC

Minerva Chir. 2018 Feb 73(1):64-76. Epub 2017 Dec 14

INTRODUCTION:
For decades, intrathoracic stomach has been an indication for surgical repair and over time laparoscopy has become standard treatment. However, there are still many aspects in the treatment of intrathoracic stomach that are

subject of debate. We performed a literature review to discuss the role of laparoscopy in intrathoracic stomach repair.
EVIDENCE ACQUISITION:
We performed an extensive literature search in Pubmed, Embase and Cochrane and reviewed studies from the last 5 years. To provide a complete overview, references from the found studies are also used. All data was compiled into a review format.
EVIDENCE SYNTHESIS:
Laparoscopic surgery is proven to be superior to open hiatal hernia repair in the treatment of intrathoracic stomach. The role of hernia sac excision, short esophagus, mesh reinforcement, fundoplication, complications and future perspectives are discussed in this review.
CONCLUSIONS:
Laparoscopy plays a major role in the treatment of intrathoracic stomach and regarding most aspects of the treatment. All available techniques have their advantages and disadvantages, and the decision on how to repair the intrathoracic stomach, remains a tailored based decision.

Impactfactor: 0.554

Investigation on the Effect of Spatial Compounding on Photoacoustic Images of Carotid Plaques in the In Vivo Available Rotational Range

Arabul MU, Heres HM, Rutten MC, **van Sambeek MR**, van de Vosse FN, Lopata RG

IEEE Trans Ultrason Ferroelectr Freq Control. 2018 Mar;65(3):440-447

Photoacoustic imaging (PAI) is a promising imaging modality due to its high optical specificity. However, the low signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of in vivo PA images are major challenges that prevent PAI from finding its place in clinics. This paper investigates the merit of spatial compounding of PA images in arterial phantoms and the achievable improvements of SNR, when in vivo conditions are mimicked. The analysis of the compounding technique was performed on a polyvinyl alcohol vessel phantom with black threads embedded in its wall. The in vivo conditions were mimicked by limiting the rotation range in ±30°, adding turbid surrounding medium, and filling the lumen with porcine blood. Finally, the performance of the technique was evaluated in ex vivo human carotid plaque samples. Results showed that spatial compounding elevates the SNR by 5-10 dB and CNR by 1-5 dB, depending on the location of the absorbers. This paper elucidates prospective in vivo PA characterization of carotid plaques by proposing a method to enhance PA image quality.

Impactfactor: 2.704

Invited comment to: rates of and methods used at reoperation for recurrence after primary inguinal hernia repair with Prolene Hernia System and Lichtenstein

Magnusson J, Gustafsson UO, Nygren J, Thorell A. **Nienhuijs SW**

Hernia. 2018 Jun22(3):445-446

Comment on:
Rates of and methods used at reoperation for recurrence after primary inguinal hernia repair with Prolene Hernia System and Lichtenstein. [Hernia. 2018]

Impactfactor: 2.417

Iterative cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases: A multi-institutional experience

Alzahrani NA, Valle SJ, Fisher OM, Sugarbaker PH, Yonemura Y, Glehen O, Goere D, Honore C, Brigand C, **de Hingh I**, **Verwaal VJ**, Deraco M, Baratti D, Kusamura S, Pocard M, Piso P, Maerz L, Marchal F, Moran B, Levine EA, Dumont F, Pezet D, et al

J Surg Oncol. 2018 Dec 16. [Epub ahead of print]

BACKGROUND AND OBJECTIVES:
The aims of this multi-institutional study were to assess the feasibility of iterative cytoreductive surgery (iCRS)/hyperthermic intraperitoneal chemotherapy, iCRS in colorectal peritoneal carcinomatosis (CRPC), evaluate survival, recurrence, morbidity and mortality outcomes, and identify prognostic factors for overall survival.
METHODS:
Patients with CRPC that underwent an iCRS, with or without intraperitoneal chemotherapy, from June 1993 to July 2016 at 13 institutions were retrospectively analyzed from prospectively maintained databases.
RESULTS:
The study comprised of 231 patients, including 126 females (54.5%) with a mean age at iCRS of 51.3 years. The iterative high-grade (3/4) morbidity and mortality rates were 23.4% and 1.7%, respectively. The median recurrence-free survival was 15.0 and 10.1 months after initial and iCRS, respectively. The median and 5-year survivals were 49.1 months and 43% and 26.4 months and 26% from the initial and iCRS, respectively. Independent negative predictors of survival from the initial CRS included peritoneal carcinomatosis index (PCI)?>?20 (P?=?0.02) and

lymph node positivity (P?=?0.04), and from iCRS, PCI?>?10 (P?=?0.03 for PCI 11-20; P?<?0.001 for PCI?>?20), high-grade complications (P?=?0.012), and incomplete cytoreduction (P?<?0.001).

CONCLUSION:

iCRS can provide long-term survival benefits to highly selected colorectal peritoneal carcinomatosis patients with comparable mortality and morbidity rates to the initial CRS procedure. Careful patient selection is necessary to improve overall outcomes.

Impactfactor: 2.886

Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial

Loozen CS, van Santvoort HC, van Duijvendijk P, Besselink MG, Gouma DJ, **Nieuwenhuijzen GA**, Kelder JC, Donkervoort SC, van Geloven AA, Kruyt PM, Roos D, Kortram K, Kornmann VN, Pronk A, van der Peet DL, Crolla RM, van Ramshorst B, Bollen TL, Boerma D

BMJ. 2018 Oct 8 363:k3965

OBJECTIVE:

To assess whether laparoscopic cholecystectomy is superior to percutaneous catheter drainage in high risk patients with acute calculous cholecystitis.

DESIGN:

Multicentre, randomised controlled, superiority trial.

SETTING:

11 hospitals in the Netherlands, February 2011 to January 2016.

PARTICIPANTS:

142 high risk patients with acute calculous cholecystitis were randomly allocated to laparoscopic cholecystectomy (n=66) or to percutaneous catheter drainage (n=68). High risk was defined as an acute physiological assessment and chronic health evaluation II (APACHE II) score of 7 or more.

MAIN OUTCOME MEASURES:

The primary endpoints were death within one year and the occurrence of major complications, defined as infectious and cardiopulmonary complications within one month, need for reintervention (surgical, radiological, or endoscopic that had to be related to acute cholecystitis) within one year, or recurrent biliary disease within one year.

RESULTS:

The trial was concluded early after a planned interim analysis. The rate of death did not differ between the laparoscopic cholecystectomy and percutaneous catheter drainage group (3% v 9%, P=0.27), but major complications occurred in eight of 66 patients (12%) assigned to cholecystectomy and in 44 of 68 patients (65%) assigned to percutaneous drainage (risk ratio 0.19, 95% confidence interval 0.10 to 0.37; P<0.001). In the drainage group 45 patients (66%) required a reintervention compared with eight patients (12%) in the cholecystectomy group (P<0.001). Recurrent biliary disease occurred more often in the percutaneous drainage group (53% v 5%, P<0.001), and the median length of hospital stay was longer (9 days v 5 days, P<0.001).

CONCLUSION:

Laparoscopic cholecystectomy compared with percutaneous catheter drainage reduced the rate of major complications in high risk patients with acute cholecystitis.

Impactfactor: 23.259

Laparoscopic pancreatoduodenectomy with open or laparoscopic reconstruction during the learning curve: a multicenter propensity score matched study

van Hilst J, de Rooij T, van den Boezem PB, Bosscha K, Busch OR, van Duijvendijk P, Festen S6, Gerhards MF, **de Hingh IH**, Karsten TM, Kazemier G, Lips DJ, **Luyer MD**, Nieuwenhuijs VB, Patijn GA, Stommel MW, Zonderhuis BM8, Daams F8, Besselink MG9; Dutch Pancreatic Cancer Group

HPB (Oxford). 2018 Dec 4. pii: S1365-182X(18)34529-5. doi: 10.1016/j.hpb.2018.11.003. [Epub ahead of print]

BACKGROUND:

Laparoscopic pancreatoduodenectomy with open reconstruction (LPD-OR) has been suggested to lower the rate of postoperative pancreatic fistula reported after laparoscopic pancreatoduodenectomy with laparoscopic reconstruction (LPD). Propensity score matched studies are, lacking.

METHODS:

This is a multicenter prospective cohort study including patients from 7 Dutch centers between 2014-2018. Patients undergoing LPD-OR were matched LPD patients in a 1:1 ratio based on propensity scores. Main outcomes were postoperative pancreatic fistulas (POPF) grade B/C and Clavien-Dindo grade =3 complications.

RESULTS:

A total of 172 patients were included, involving the first procedure for all centers. All 56 patients after LPD-OR could be matched to a patient undergoing LPD. With LPD-OR, the unplanned conversion rate was 21% vs. 9% with LPD (P < 0.001). Median blood loss (300 vs. 400 mL, P = 0.85), operative time (401 vs. 378 min, P = 0.62) and hospital stay (10 vs. 12 days, P = 0.31) were comparable for LPD-OR vs. LPD, as were Clavien-Dindo grade =3 complications (38% vs. 52%, P = 0.13), POPF grade B/C (23% vs. 21%, P = 0.82), and 90-day mortality (4% vs. 4%, P > 0.99).

CONCLUSION:

In this propensity matched cohort performed early in the learning curve, no benefit was found for LPD-OR, as compared to LPD.

Impactfactor: 3.131

Learning curves in minimally invasive esophagectomy

van Workum F, **Fransen L, Luyer MD**, Rosman C

World J Gastroenterol. 2018 Nov 28;24(44):4974-4978

Surgical innovation and pioneering are important for improving patient outcome, but can be associated with learning curves. Although learning curves in surgery are a recognized problem, the impact of surgical learning curves is increasing, due to increasing complexity of innovative surgical procedures, the rapid rate at which new interventions are implemented and a decrease in relative effectiveness of new interventions compared to old interventions. For minimally invasive esophagectomy (MIE), there is now robust evidence that implementation can lead to significant learning associated morbidity (morbidity during a learning curve, that could have been avoided if patients were operated by surgeons that have completed the learning curve). This article provides an overview of the evidence of the impact of learning curves after implementation of MIE. In addition, caveats for implementation and available evidence regarding factors that are important for safe implementation and safe pioneering of MIE are discussed.

Impactfactor: 3.300

Limited Adherence to Peripheral Arterial Disease Guidelines and Suboptimal Ankle Brachial Index Reliability in Dutch Primary Care

Hageman D, Pesser N, Gommans LNM, Willigendael EM, **van Sambeek MRHM**, Huijbers E, Snoeijen A, Scheltinga MRM, **Teijink JAW**

Eur J Vasc Endovasc Surg. 2018 Jun 55(6):867-873

OBJECTIVE/BACKGROUND:

The Dutch College of General Practitioners' guideline on peripheral arterial disease (PAD) provides clear recommendations on the management of PAD. An ankle brachial index (ABI) measurement, prescription of antiplatelet drugs and statins, and supervised exercise therapy (SET) for intermittent claudication (IC) are advised. The aims of this study were to determine the adherence of general practitioners (GPs) to their own guideline on PAD and to evaluate the reliability of primary care ABI measurements.

METHODS:

This was a cross-sectional study. All patients suspected of having symptomatic PAD who were referred by GPs to a large hospital in 2015 were evaluated regarding three of the guideline criteria: (i) ABI measurement; (ii) prescription of secondary prevention; (iii) initiation of SET. ABI values obtained in primary care and the hospital's vascular laboratory were compared using correlation coefficients and regression analysis. An abnormal ABI was defined as a value <.9 (normal ABI =.9).

RESULTS:

Of 308 potential patients with new onset PAD, 58% (n = 178) had undergone ABI measurement prior to referral. A modest correlation between ABI values obtained in primary care and the vascular laboratory was found (r = .63, p < .001). Furthermore, a moderate reliability was calculated (intraclass correlation coefficient 0.60, 95% confidence interval 0.49-0.69, p < .001). Of the new patients with an abnormal ABI, 59% used antiplatelet drugs and 55% used statins. A referral for SET was initiated by a GP in 10% of new PAD patients with IC symptoms.

CONCLUSIONS:

Adherence by Dutch GPs to their own society's PAD guideline has room for improvement. The reliability of ABI measurements is suboptimal, whereas rates of prescription of secondary prevention and initiation of SET as primary treatment for IC need upgrading.

Impactfactor: 3.877

Lipoedema in patients after bariatric surgery: report of two cases and review of literature

Pouwels S, Huisman S, Smelt HJM**, Said M, Smulders JF**

Clin Obes. 2018 Apr 8(2):147-150. doi: Epub 2018 Jan 25

Lipoedema is a disorder of adipose tissue that is characterized by abnormal subcutaneous fat deposition, leading to swelling and enlargement of the lower limbs as well as the trunk. This entity is often misdiagnosed as lymphoedema or obesity and, therefore, may be overlooked and missed in patients scheduled for bariatric surgery. Patients with lipoedema who undergo bariatric surgery may have to continue to have extensive lower extremity and trunk adiposity despite adequate weight loss. In this report, we present two patients who had extensive trunk and lower extremity adiposity, one of them before and the other after the bariatric surgery.

Impactfactor: --

Long-term Oncological and Functional Outcomes of Chemoradiotherapy Followed by Organ-Sparing Transanal Endoscopic Microsurgery for Distal Rectal Cancer: The CARTS Study

Stijns RCH, de Graaf EJR, Punt CJA, Nagtegaal ID, Nuyttens JJME, van Meerten E, Tanis PJ, **de Hingh IHJT**, van der Schelling GP, Acherman Y, Leijtens JWA, Bremers AJA, Beets GL, Hoff C, Verhoef C, Marijnen CAM, de Wilt JHW
JAMA Surg. 2018 Oct 10. [Epub ahead of print]

Importance:

Treatment of rectal cancer is shifting toward organ preservation aiming to reduce surgery-related morbidity. Short-term outcomes of organ-preserving strategies are promising, but long-term outcomes are scarce in the literature.

Objective:

To explore long-term oncological outcomes and health-related quality of life (HRQL) in patients with cT1-3N0M0 rectal cancer who underwent neoadjuvant chemoradiotherapy (CRT) followed by transanal endoscopic microsurgery (TEM).

Design, Setting, and Participants:

In this multicenter phase II feasibility study, patients with cT1-3N0M0 rectal cancer admitted to referral centers for rectal cancer throughout the Netherlands between February 2011 and September 2012 were prospectively included. These patients were to be treated with neoadjuvant CRT followed by TEM in case of good response. An intensive follow-up scheme was used to detect local recurrences and/or distant metastases. Data from validated HRQL questionnaires and low anterior resection syndrome questionnaires were collected. Data were analyzed from February 2011 to April 2017.

Main Outcomes and Measures:

The primary study outcome of the study was the number of ypT0-1 specimens by performing TEM. Secondary outcome parameters were locoregional recurrences and HRQL.

Results:

Of the 55 included patients, 30 (55%) were male, and the mean (SD) age was 64 (39-82) years. Patients were followed up for a median (interquartile range) period of 53 (39-57) months. Two patients (4%) died during CRT, 1 (2%) stopped CRT, and 1 (2%) was lost to follow-up. Following CRT, 47 patients (85%) underwent TEM, of whom 35 (74%) were successfully treated with local excision alone. Total mesorectal excision was performed in 16 patients (4 with inadequate responses, 8 with completion after TEM, and 4 with salvage for local recurrence). The actuarial 5-year local recurrence rate was 7.7%, with 5-year disease-free and overall survival rates of 81.6% and 82.8%, respectively. Health-related quality of life during follow-up was equal to baseline, with improved emotional well-being in patients treated with local excision (mean score at baseline, 72.0; 95% CI, 67.1-80.1; mean score at follow-up, 86.9; 95% CI, 79.2-94.7; P?=?.001). Major, minor, and no low anterior resection syndrome was experienced in 50%, 28%, and 22%, respectively, of patients with successful organ preservation.

Conclusions and Relevance:

In early-stage rectal cancer (cT1-3N0M0), CRT enables organ preservation with additional TEM surgery in approximately two-thirds of patients with good long-term oncological outcome and HRQL. This multimodality treatment triggers a certain degree of bowel dysfunction, and one-third of patients still undergo radical surgery and are overtreated by CRT.

Impactfactor: 8.498

Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

van der Valk MJ, Hilling DE, Bastiaannet E, Meershoek-Klein Kranenbarg E, Beets GL, Figueiredo NL, Habr-Gama A, Perez RO, Renehan AG, van de Velde CJ; IWWD Consortium: **Rutten HJ**
Lancet. 2018 Jun 23;391(10139):2537-2545.

BACKGROUND:

The strategy of watch and wait (W&W) in patients with rectal cancer who achieve a complete clinical response (cCR) after neoadjuvant therapy is new and offers an opportunity for patients to avoid major resection surgery. However, evidence is based on small-to-moderate sized series from specialist centres. The International Watch & Wait Database (IWWD) aims to describe the outcome of the W&W strategy in a large-scale registry of pooled individual patient data. We report the results of a descriptive analysis after inclusion of more than 1000 patients in the registry.

METHODS:

Participating centres entered data in the registry through an online, highly secured, and encrypted research data server. Data included baseline characteristics, neoadjuvant therapy, imaging protocols, incidence of local regrowth and distant metastasis, and survival status. All patients with rectal cancer in whom the standard of care (total mesorectal excision surgery) was omitted after neoadjuvant therapy were eligible to be included in the IWWD. For the present analysis, we only selected patients with no signs of residual tumour at reassessment (a cCR). We analysed the proportion of patients with local regrowth, proportion of patients with distant metastases, 5-year overall survival, and 5-year disease-specific survival.

FINDINGS:

Between April 14, 2015, and June 30, 2017, we identified 1009 patients who received neoadjuvant treatment and were managed by W&W in the database from 47 participating institutes (15 countries). We included 880 (87%)

patients with a cCR. Median follow-up time was 3·3 years (95% CI 3·1-3·6). The 2-year cumulative incidence of local regrowth was 25·2% (95% CI 22·2-28·5%), 88% of all local regrowth was diagnosed in the first 2 years, and 97% of local regrowth was located in the bowel wall. Distant metastasis were diagnosed in 71 (8%) of 880 patients. 5-year overall survival was 85% (95% CI 80·9-87·7%), and 5-year disease-specific survival was 94% (91-96%). INTERPRETATION:

This dataset has the largest series of patients with rectal cancer treated with a W&W approach, consisting of approximately 50% data from previous cohort series and 50% unpublished data. Local regrowth occurs mostly in the first 2 years and in the bowel wall, emphasising the importance of endoscopic surveillance to ensure the option of deferred curative surgery. Local unsalvageable disease after W&W was rare.

Impactfactor: 53.254

Long-term survival improvement in oesophageal cancer in the Netherlands

van Putten M, de Vos-Geelen J, **Nieuwenhuijzen GAP**, Siersema PD, Lemmens VEPP, Rosman C, **van der Sangen** MJC, Verhoeven RHA

Eur J Cancer. 2018 May 94:138-147. Epub 2018 Mar 20

BACKGROUND:

Treatment for oesophageal cancer has evolved due to developments including the centralisation of surgery and introduction of neoadjuvant treatment. Therefore, this study evaluated trends in stage distribution, treatment and survival of oesophageal cancer patients in the last 26 years in the Netherlands.

PATIENTS AND METHODS:

Patients with oesophageal cancer diagnosed in the period 1989-2014 were selected from the Netherlands Cancer Registry. Patients were divided into two groups: non-metastatic (M0) and metastatic (M1). Trends in stage distribution, treatment and relative survival rates were evaluated according to histology. RESULTS:

Among all 35,760 patients, the percentage of an unknown tumour stage decreased from 34% to 10% during the study period, whereas the percentage of patients with metastatic disease increased from 21% to 34%. Among surgically treated patients 32% underwent a resection in a high-volume hospital in 2005 which increased to 92% in 2014. Use of neoadjuvant chemoradiotherapy increased in non-metastatic oesophageal adenocarcinoma (OAC) and squamous cell carcinoma (OSCC) patients from respectively 4% and 2% in 2000-2004 to 43% and 26% in 2010-2014. Five-year relative survival increased from 8% to 22% for all patients; from 12% to 36% for non-metastatic OAC and from 9% to 27% for non-metastatic OSCC over 26 years. Median overall survival of metastatic patients improved from 18 to 22 weeks.

CONCLUSION:

In the Netherlands, survival for oesophageal cancer patients improved significantly, especially in the period 2005-2014 which might be the result of better treatment related to the centralisation of surgery and introduction of neoadjuvant chemoradiotherapy.

Impactfactor: 7.191

Lower Leg Chronic Exertional Compartment Syndrome in Patients 50 Years of Age and Older

de Bruijn JA, van Zantvoort APM, Winkes MB, van der Cruijsen-Raaijmakers M, Hoogeveen AR, **Teijink JAW**, Scheltinga MRM

Orthop J Sports Med. 2018 Mar 2 6(3):2325967118757179. eCollection 2018 Mar

Background:

Lower leg chronic exertional compartment syndrome (CECS) is usually diagnosed in young and athletic individuals. The presence of CECS in older patients has received little attention in the literature, and patient characteristics are unknown.

Purpose:

To determine the prevalence of CECS in older patients (=50 years) and to assess whether older patients with CECS differ clinically from younger patients with CECS.

Study Design: Cohort study; Level of evidence, 3.

Methods:

All individuals with exercise-induced lower leg pain who visited a referral center for CECS between January 2001 and December 2013 were eligible for analysis. Patients were included if history, physical examination, and dynamic intracompartmental pressure measurement indicated CECS. Characteristics of patients 50 years of age or older were compared with characteristics of patients younger than 50.

Results:

A total of 698 patients with CECS were included: 98 patients were aged 50 years or older and 600 patients were younger than 50 years. Older individuals more often reported a history of lower leg events or comorbidities (=50 years, 45% vs <50 years, 25%; P < .01) and unilateral symptoms (=50 years, 45% vs <50 years, 22%; P < .01). Most older patients (62%) did not participate in sport or only walked or hiked, whereas the same was true of only 7% of the younger population. Pain (=50 years, 94%; <50 years, 96%) and tightness (=50 years, 57%; <50 years, 62%) were the predominant symptoms of CECS in both groups. Type of CECS differed significantly (P < .01); the anterior muscle

compartment was involved more frequently in older patients (=50 years, 82% vs <50 years, 59%) and deep flexor muscle CECS was more often diagnosed in younger patients (=50 years, 26% vs <50 years, 53%). Conclusion:

In the present population, 1 in 7 patients diagnosed with lower leg CECS was 50 years of age or older. These individuals were less active and had more comorbidities than patients younger than 50 years. Older individuals predominantly have anterior CECS. Clinicians should consider CECS in older individuals with exercise-induced lower leg pain, particularly if it is unilateral.

Impactfactor: 0.935

Major influence of postoperative complications on costs of cytoreductive surgery and HIPEC in patients with colorectal peritoneal metastases

Simkens GA, Rovers KP, van Oudheusden TR, Nienhuijs SW, Rutten HJ, de Hingh IH

Medicine (Baltimore). 2018 Mar 97(10):e0042.

Complications after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) result in impaired short- and long-term outcomes. However, financial consequences of complications after CRS and HIPEC in a European health care setting are unknown. This study aims to assess the consequences of complications on hospital costs after CRS and HIPEC.In this prospective observational cohort study, patients with colorectal peritoneal metastases treated with CRS and HIPEC were included. Financial information was collected according to the Dutch manual for costs analyses. Costs were compared between patients without complications (NC), minor complications (MC), or severe complications (SC), according to the Clavien-Dindo classification.One hundred and sixty-one patients were included, of whom 42% experienced NC, 27% MC and 31% SC. Mean hospital costs were &OV0556;9.406?±?2.235 in NC patients, &OV0556;12.471?±?3.893 in MC patients, and &OV0556;29.409?±?22.340 in SC patients. The 31% of patients with severe complications accounted for 56% of all hospital costs. Hospital admission costs in SC patients were 320% higher compared to NC patients. Costs of complications were estimated to be 43% of all admission costs.Severe postoperative complications have major influence on costs after CRS and HIPEC and result in a threefold increase of hospital costs in affected patients. This finding stresses the need for adequate risk assessment of developing severe complications after CRS and HIPEC.

Impactfactor: 1.804

Manipulating spatial distance in virtual reality: Effects on treadmill walking performance in patients with intermittent claudication

Cuperus AA., Keizer A., Evers AW., **Van den Houten MM**, **Teijink JA**, Van der Ham IJ

Computers in Human Behavior 2018;79:211-216

Research indicates that the manipulation of spatial distance between objects in a previously observed environment may go unnoticed when the categorical information of these objects, such as their order, matches that of memory for the environment. Using a repeated measures design, we investigated whether manipulations of spatial distance in virtual reality (VR) can influence treadmill exercise performance (i.e., walking distance) in patients with intermittent claudication; a cramping pain or discomfort in the legs, which occurs during exercise. Participants (N = 19) carried out four treadmill exercise sessions; one without VR and three with a VR environment to move through while walking. They were instructed to walk until the pain forced them to stop. All VR sessions contained the same environment, but in the second and third session it was 'stretched' and 'compressed'. Walking distance was not influenced by the mere addition of VR. However, both VR manipulations led to greater walking distance than the VR baseline session and participants walked furthest when presented with the stretched environment. The results indicate that the manipulation of spatial distance in VR can be of clinical relevance; a finding that may be applied in the development of future medical applications.

Impactfactor: 3.536

Matched Short-Term Results of SADI Versus GBP After Sleeve Gastrectomy

Ceha CM, **van Wezenbeek MR, Versteegden DP, Smulders J, Nienhuijs SW**

Obes Surg. 2018 Dec;28(12):3809-3814. doi: 10.1007/s11695-018-3415-5

BACKGROUND:

The gastric bypass (GBP) is the most popular revisional technique after sleeve gastrectomy (SG). However, the results after revision are not always satisfactory in terms of additional weight loss and complications. The single anastomosis duodenoileal bypass (SADI) could be a valuable alternative.

OBJECTIVE:

This study is a retrospective matched-control study reviewing short-term results in terms of weight loss and comorbidities reduction of both SADI and GBP as a revisional procedure after primary sleeve gastrectomy. Complications and vitamin deficiencies will be evaluated as well.

METHODS:

Patients with a SADI procedure after a primary sleeve gastrectomy (SG) with a minimum follow-up of 1 year were included. Their results were retrospectively reviewed and matched with a cohort of GBP patient on age, BMI, and gender. Comparison was on comorbidities, weight loss, complications, and blood markers.

RESULTS:
A total of 64 patients were included, 32 SADI procedures and 32 matched gastric bypasses with no significant differences on baseline. No differences were found in terms of (additional) total weight loss. The operating time of the SADI was significantly longer (p?=?0.007). No clinically relevant differences were found concerning comorbidities or blood markers. In the SADI group, more defecation problems were reported and fewer vitamin deficiencies were encountered.
CONCLUSION:
Based on a small group and short-term results, the SADI could be regarded as a safe alternative to a GBP following SG with a similar amount of additional weight loss and fewer post-operative early complications. Longer follow-up and larger studies are needed to determine its full potential.

Impactfactor: 3.895

Mesh Versus Patch Repair for Epigastric and Umbilical Hernia (MORPHEUS Trial); One-Year Results of a Randomized Controlled Trial

Ponten JE, Leenders BJ, Leclercq WK, Lettinga T, Heemskerk J, Konsten JL, **Castelijns PS**, **Nienhuijs SW**
World J Surg. 2018 May;42(5):1312-1320

DESIGN:
This trial is a randomized controlled, patient-blinded, multicentre, superiority trial.
METHODS:
All patients =18 years with a single, symptomatic and primary umbilical or epigastric hernia (<2 fingers) qualified for participation in the study. Flat polypropylene mesh repair was compared to patch repair (PROCEED® Ventral Patch) (PVP). The objective of this trial was to identify a superior method for umbilical and epigastric hernia repair in terms of complication rates.
RESULTS:
A total of 352 patients were randomized in this trial; 348 patients received the intervention (n = 177 PVP vs. n = 171 mesh). No peri-operative complications occurred. PVP placement was significantly faster compared to mesh placement (30 min, SD 11 vs. 35 min, SD 11) and was scored as an easier procedure. At 1-month follow-up, 76 patients suffered any kind of complication. There was no significant difference in the proportion of complications (24.9% for PVP and 18.7% for mesh, p = 0.195). A significant difference was seen in re-operation rate within 1 month, significantly less early re-operations in the mesh group (0.0 vs. 2.8%, p = 0.027). After 1-year follow-up, no significant differences are seen in recurrence rates (n = 13, 7.8% PVP vs. n = 5, 3.3% mesh, p = 0.08).
CONCLUSIONS:
Both mesh and PVP had a comparable amount of reported complications. There was a significantly higher incidence of early re-operations due to early complications in the PVP group. No differences were seen in infection rates and the need for antibiotic treatment. No significant difference was seen in the recurrence rates.

Impactfactor: 2.766

Metachronous Peritoneal Metastases After Adjuvant Chemotherapy are Associated with Poor Outcome After Cytoreduction and HIPEC

Sluiter NR, **Rovers KP**, Salhi Y, Vlek SL, Coupé VM, Verheul HM, Kazemier G, **de Hingh IH**, Tuynman JB
Ann Surg Oncol. 2018 Aug;25(8):2347-2356

INTRODUCTION:
Cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) improve the survival of colorectal cancer (CRC) patients with peritoneal metastases. Patient selection is key since this treatment is associated with high morbidity. Patients with peritoneal recurrence within 1 year after previous adjuvant chemotherapy are thought to benefit less from HIPEC treatment; however, no published data are available to assist in clinical decision making. This study assessed whether peritoneal recurrence within 1 year after adjuvant chemotherapy was associated with survival after HIPEC treatment.
METHODS:
Peritoneal recurrence within 1 year after adjuvant chemotherapy, as well as other potentially prognostic clinical and pathological variables, were tested in univariate and multivariate analysis for correlation with primary outcomes, i.e. overall survival (OS) and disease-free survival (DFS). Two prospectively collected databases from the VU University Medical Center Amsterdam and Catherina Hospital Eindhoven containing 345 CRC patients treated with the intent of HIPEC were utilized.
RESULTS:
High Peritoneal Cancer Index (PCI) scores were associated with worse DFS [hazard ratio (HR) 1.04, 95% confidence interval (CI) 1.00-1.08, p?=?0.040] and OS (HR 1.11, 95% CI 1.07-1.15, p?<?0.001) in multivariate analysis. Furthermore, patients with peritoneal recurrence within 1 year following adjuvant chemotherapy had worse DFS (HR 2.13, 95% CI 1.26-3.61, p?=?0.005) and OS (HR 2.76, 95% CI 1.45-5.27, p?=?0.002) than patients who did not receive adjuvant chemotherapy or patients with peritoneal recurrence after 1 year.
CONCLUSION:
Peritoneal recurrence within 1 year after previous adjuvant chemotherapy, as well as high PCI scores, are associated

with poor survival after cytoreduction and HIPEC. These factors should be considered in order to avoid high-morbidity treatment in patients who might not benefit from such treatment.

Impactfactor: 3.857

Minimally invasive esophagectomy: a propensity score-matched analysis of semiprone versus prone position

Seesing MFJ, Goense L, Ruurda JP, **Luyer MDP**, **Nieuwenhuijzen GAP**, van Hillegersberg R

Surg Endosc. 2018 Jun;32(6):2758-2765. Epub 2017 Dec 5

BACKGROUND:

The preferred surgical approach for esophageal cancer is a minimally invasive transthoracic esophagectomy with a two-field lymph node dissection. The thoracoscopic phase may be performed either in prone- or in left lateral decubitus (LLD) position. Prone positioning has been associated with better pulmonary outcomes compared to LLD positioning; however, conversion to a classic thoracotomy is more difficult. The semiprone position has been proposed as an alternative approach.

METHODS:

A retrospective review of a prospectively maintained database (2008-2014) was performed to compare postoperative complications, surgical radicality, and lymph node yield between patients who underwent three-stage minimally invasive transthoracic esophagectomy in either the prone or semiprone position. Comparative analyses were conducted before and after propensity score matching.

RESULTS:

One hundred and twenty-one patients were included. In total, 82 patients underwent minimally invasive esophagectomy (MIE) in semiprone position and 39 patients in prone position. After propensity score matching, both groups consisted of 39 patients. The operative time in the semiprone group was longer (368 vs. 225 min, P?<?0.001) and in this group the lymph node yield was significantly higher (16 (range 6-80) vs. 13 (range 3-33), P?=?0.019). There were no statistically significant differences regarding radical resections, postoperative complications, and hospital stay.

CONCLUSION:

The use of semiprone positioning in MIE is safe, feasible, and at least comparable to MIE in prone position in terms of oncological clearance and postoperative complications.

Impactfactor: 3.117

Minimally invasive surgery techniques in pelvic exenteration: a systematic and meta-analysis review

PelvEx Collaborative: **Rutten HJ, Burger JW**

Surg Endosc. 2018 Dec;32(12):4707-4715

BACKGROUND:

Pelvic exenteration is potentially curative for locally advanced and recurrent pelvic cancers. Evolving technology has facilitated the use of minimally invasive surgical (MIS) techniques in selected cases. We aimed to compare outcomes between open and MIS pelvic exenteration.

METHODS:

A review of comparative studies was performed. Firstly, we evaluated the differences in surgical techniques with respect to operative time, blood loss, and margin status. Secondly, we assessed differences in 30-day morbidity and mortality rates, and length of hospital stay.

RESULTS:

Four studies that directly compared open and MIS exenteration were included. Analysis was performed on 170 patients; 78.1% (n?=?133) had open pelvic exenteration, while 21.8% (n?=?37) had a MIS exenteration. The median age for open exenteration was 57.7 years versus 63 years for MIS exenteration. Even though the operative time for MIS exenteration was 83 min longer (p?<?0.001), it was associated with a median of 1,750mls less blood loss. The morbidity rate for MIS exenterative group was 56.7% (n?=?21/37) versus 88.5% (n?=?85/96) in the open exenteration group, with pooled analysis observing a 1.17 relative risk increase in 30-day morbidity (p?=?0.172) in the open exenteration group. In addition, the MIS cohort had a 6-day shorter length of hospital stay (p?=?0.04).

CONCLUSION:

MIS exenteration can be performed in highly selective cases, where there is favourable patient anatomy and tumour characteristics. When feasible, it is associated with reduced intra-operative blood loss, shorter length of hospital stay, and reduced morbidity.

Impactfactor: 3.117

Minimally invasive versus open pancreatoduodenectomy (LEOPARD-2): study protocol for a randomized controlled trial

de Rooij T, van Hilst J, Bosscha K, Dijkgraaf MG, Gerhards MF, Groot Koerkamp B, Hagendoorn J, **de Hingh IH**, Karsten TM, Lips DJ, **Luyer MD**, Molenaar IQ, van Santvoort HC, Tran TCK, Busch OR, Festen S, Besselink MG Dutch Pancreatic Cancer Group.

Trials. 2018 Jan 3 19(1):1

BACKGROUND:
Data from observational studies suggest that minimally invasive pancreatoduodenectomy (MIPD) is superior to open pancreatoduodenectomy regarding intraoperative blood loss, postoperative morbidity, and length of hospital stay, without increasing total costs. However, several case-matched studies failed to demonstrate superiority of MIPD, and large registry studies from the USA even suggested increased mortality for MIPDs performed in low-volume (<10 MIPDs annually) centers. Randomized controlled multicenter trials are lacking but clearly required. We hypothesize that time to functional recovery is shorter after MIPD compared with open pancreatoduodenectomy, even in an enhanced recovery setting.
METHODS/DESIGN:
LEOPARD-2 is a randomized controlled, parallel-group, patient-blinded, multicenter, phase 2/3, superiority trial in centers that completed the Dutch Pancreatic Cancer Group LAELAPS-2 training program for laparoscopic pancreatoduodenectomy or LAELAPS-3 training program for robot-assisted pancreatoduodenectomy and have performed?=?20 MIPDs. A total of 136 patients with symptomatic benign, premalignant, or malignant disease will be randomly assigned to undergo minimally invasive or open pancreatoduodenectomy in an enhanced recovery setting. After the first 40 patients (phase 2), the data safety monitoring board will assess safety outcomes (not blinded for treatment allocation) and decide on continuation to phase 3. Patients from phase 2 will then be included in phase 3. The primary outcome measure is time (days) to functional recovery. All patients will be blinded for the surgical approach, at least until postoperative day 5, but preferably until functional recovery has been attained. Secondary outcome measures are operative and postoperative outcomes, including clinically relevant complications, mortality, quality of life, and costs.
DISCUSSION:
The LEOPARD-2 trial is designed to assess whether MIPD reduces time to functional recovery, as compared with open pancreatoduodenectomy in an enhanced recovery setting.

Impactfactor: 2.067

Models of Care for Survivors of Childhood Cancer From Across the Globe: Advancing Survivorship Care in the Next Decade

Tonorezos ES, Barnea D, Cohn RJ, Cypriano MS, Fresneau BC, Haupt R, Hjorth L, Ishida Y, Kruseova J, Kuehni CE, Kurkure PA, Langer T, Nathan PC Skeen JE, Skinner R, Tacyildiz N, van den Heuvel-Eibrink MM, Winther JF, Hudson MM, Oeffinger KC, Dutch Snapshot Research Group**: Brinkman DJ, Rutten HJ, Simkens GA**
J Clin Oncol. 2018 Jul 20;36(21):2223-2230

With improvements in cancer treatment and supportive care, a growing population of survivors of childhood cancer at risk for significant and potentially life-threatening late effects has been identified. To provide a current snapshot of the models of care from countries with varying levels of resources and health care systems, stakeholders in childhood cancer survivorship clinical care and research were identified from 18 countries across five continents. Stakeholders responded to a survey and provided a brief narrative regarding the current state of survivorship care. Findings indicate that among pediatric-age survivors of childhood cancer (allowing for differences in age cutoffs across countries), resources are generally available, and a large proportion of survivors are seen by a physician familiar with late effects in most countries. After survivors transition to adulthood, only a minority are seen by a physician familiar with late effects. Despite the need to improve communication between pediatric oncology and primary care, only a few countries have existing national efforts to educate primary care physicians, although many more reported that educational programs are in development. These data highlight common challenges and potential solutions for the lifelong care of survivors of childhood cancer. Combining risk-based and patient-oriented solutions for this population is likely to benefit both providers and patients.

Impactfactor: 26.303

Mycotic innominate artery aneurysm repair using a bovine pericardial bifurcation prosthesis

Hoff AHT**, Akca F, Cuypers PWM,** Ter Woorst JF
J Card Surg. 2018 Mar 33(3):146-148. Epub 2018 Mar 11

We report the use of a bovine pericardial bifurcation prosthesis to repair a mycotic innominate artery aneurysm.

Impactfactor: 1.179

Nationwide comprehensive gastro-intestinal cancer cohorts: the 3P initiative

Coebergh van den Braak RRJ, van Rijssen LB, van Kleef JJ, Vink GR, Berbee M, van Berge Henegouwen MI, Bloemendal HJ, Bruno MJ, Burgmans MC, Busch ORC, Coene PPLO, Coupé VMH, Dekker JWT, van Eijck CHJ, Elferink MAG, Erdkamp FLG, van Grevenstein WMU, de Groot JWB, van Grieken NCT, **de Hingh IHJT**, Hulshof MCCM, Ijzermans, **Nieuwenhuijzen GAP**, et al
Acta Oncol. 2018 Feb 57(2):195-202. Epub 2017 Jul 19

BACKGROUND:
The increasing sub-classification of cancer patients due to more detailed molecular classification of tumors, and limitations of current trial designs, require innovative research designs. We present the design, governance and

current standing of three comprehensive nationwide cohorts including pancreatic, esophageal/gastric, and colorectal cancer patients (NCT02070146). Multidisciplinary collection of clinical data, tumor tissue, blood samples, and patient-reported outcome (PRO) measures with a nationwide coverage, provides the infrastructure for future and novel trial designs and facilitates research to improve outcomes of gastrointestinal cancer patients.
MATERIAL AND METHODS:
All patients aged =18 years with pancreatic, esophageal/gastric or colorectal cancer are eligible. Patients provide informed consent for: (1) reuse of clinical data; (2) biobanking of primary tumor tissue; (3) collection of blood samples; (4) to be informed about relevant newly identified genomic aberrations; (5) collection of longitudinal PROs; and (6) to receive information on new interventional studies and possible participation in cohort multiple randomized controlled trials (cmRCT) in the future.
RESULTS:
In 2015, clinical data of 21,758 newly diagnosed patients were collected in the Netherlands Cancer Registry. Additional clinical data on the surgical procedures were registered in surgical audits for 13,845 patients. Within the first two years, tumor tissue and blood samples were obtained from 1507 patients; during this period, 1180 patients were included in the PRO registry. Response rate for PROs was 90%. The consent rate to receive information on new interventional studies and possible participation in cmRCTs in the future was >85%. The number of hospitals participating in the cohorts is steadily increasing.
CONCLUSION:
A comprehensive nationwide multidisciplinary gastrointestinal cancer cohort is feasible and surpasses the limitations of classical study designs. With this initiative, novel and innovative studies can be performed in an efficient, safe, and comprehensive setting.

Impactfactor 3.473

Neoadjuvant (Chemo)radiotherapy With Total Mesorectal Excision Only Is Not Sufficient to Prevent Lateral Local Recurrence in Enlarged Nodes: Results of the Multicenter Lateral Node Study of Patients With Low cT3/4 Rectal Cancer

Ogura A, Konishi T, Cunningham C, Garcia-Aguilar J, Iversen H, Toda S, Lee IK, Lee HX, Uehara K, Lee P, Putter H, van de Velde CJH, Beets GL, **Rutten HJT**, **Kusters M**; Lateral Node Study Consortium

J Clin Oncol. 2018 Nov 7.[Epub ahead of print]

PURPOSE:
Improvements in magnetic resonance imaging (MRI), total mesorectal excision (TME) surgery, and the use of (chemo)radiotherapy ([C]RT) have improved local control of rectal cancer; however, we have been unable to eradicate local recurrence (LR). Even in the face of TME and negative resection margins (R0), a significant proportion of patients with enlarged lateral lymph nodes (LLNs) suffer from lateral LR (LLR). Japanese studies suggest that the addition of an LLN dissection (LLND) could reduce LLR. This multicenter pooled analysis aims to ascertain whether LLNs actually pose a problem and whether LLND results in fewer LLRs.
PATIENTS AND METHODS:
Data from 1,216 consecutive patients with cT3/T4 rectal cancers up to 8 cm from the anal verge who underwent surgery in a 5-year period were collected. LLND was performed in 142 patients (12%). MRIs were re-evaluated with a standardized protocol to assess LLN features.
RESULTS:
On pretreatment MRI, 703 patients (58%) had visible LLN, and 192 (16%) had a short axis of at least 7 mm. One hundred eight patients developed LR (5-year LR rate, 10.0%), of which 59 (54%) were LLRs (5-year LLR rate, 5.5%). After multivariable analyses, LLNs with a short axis of at least 7 mm resulted in a significantly higher risk of LLR (hazard ratio, 2.060; P = .045) compared with LLNs of less than 7 mm. In patients with LLNs at least 7 mm, (C)RT plus TME plus LLND resulted in a 5-year LLR of 5.7%, which was significantly lower than that in patients who underwent (C)RT plus TME (5-year LLR, 19.5%; P = .042).
CONCLUSION:
LLR is still a significant problem after (C)RT plus TME in LLNs with a short axis at least 7 mm on pretreatment MRI. The addition of LLND results in a significantly lower LLR rate.

Impactfactor: 26.303

Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial

Noordman BJ, Wijnhoven BPL, Lagarde SM, Boonstra JJ, Coene PPLO, Dekker JWT, Doukas M, van der Gaast A, Heisterkamp J, Kouwenhoven EA, **Nieuwenhuijzen GAP**, Pierie JEN, Rosman C, van Sandick JW, van der Sangen MJC, Sosef MN, Spaander MCW, Valkema R, van der Zaag ES, Steyerberg EW, van Lanschot JJB SANO-study group.: Creemers GJ, Schoon EJ, Wyndaele D

BMC Cancer. 2018 Feb 6 18(1):142

BACKGROUND:
Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard treatment for locally advanced oesophageal cancer. With this treatment, 29% of patients have a pathologically complete response in the resection specimen.

This provides the rationale for investigating an active surveillance approach. The aim of this study is to assess the (cost-)effectiveness of active surveillance vs. standard oesophagectomy after nCRT for oesophageal cancer.
METHODS:
This is a phase-III multi-centre, stepped-wedge cluster randomised controlled trial. A total of 300 patients with clinically complete response (cCR, i.e. no local or disseminated disease proven by histology) after nCRT will be randomised to show non-inferiority of active surveillance to standard oesophagectomy (non-inferiority margin 15%, intra-correlation coefficient 0.02, power 80%, 2-sided a 0.05, 12% drop-out). Patients will undergo a first clinical response evaluation (CRE-I) 4-6 weeks after nCRT, consisting of endoscopy with bite-on-bite biopsies of the primary tumour site and other suspected lesions. Clinically complete responders will undergo a second CRE (CRE-II), 6-8 weeks after CRE-I. CRE-II will include 18F-FDG-PET-CT, followed by endoscopy with bite-on-bite biopsies and ultra-endosonography plus fine needle aspiration of suspected lymph nodes and/or PET- positive lesions. Patients with cCR at CRE-II will be assigned to oesophagectomy (first phase) or active surveillance (second phase of the study). The duration of the first phase is determined randomly over the 12 centres, i.e., stepped-wedge cluster design. Patients in the active surveillance arm will undergo diagnostic evaluations similar to CRE-II at 6/9/12/16/20/24/30/36/48 and 60 months after nCRT. In this arm, oesophagectomy will be offered only to patients in whom locoregional regrowth is highly suspected or proven, without distant dissemination. The main study parameter is overall survival; secondary endpoints include percentage of patients who do not undergo surgery, quality of life, clinical irresectability (cT4b) rate, radical resection rate, postoperative complications, progression-free survival, distant dissemination rate, and cost-effectiveness. We hypothesise that active surveillance leads to non-inferior survival, improved quality of life and a reduction in costs, compared to standard oesophagectomy.
DISCUSSION:
If active surveillance and surgery as needed after nCRT leads to non-inferior survival compared to standard oesophagectomy, this organ-sparing approach can be implemented as a standard of care.

Impactfactor: *3.288*

Neuropathy by folic acid supplementation in a patient with anaemia and an untreated cobalamin deficiency: a case report

Smelt HJ, Pouwels S, **Said M, Smulders JF**

Clin Obes. 2018 Aug;8(4):300-304

The rising rates of bariatric surgery (BS) are accompanied by neurological complications related to nutrient deficiencies. One of the risk factors for neurological complications in BS patients is poor vitamin and mineral supplementation. Prevention, diagnosis and treatment of these disorders are necessary parts of lifelong care after BS. Particularly important for optimal functioning of the nervous system are vitamin B1 , B6 , B12 (cobalamin), E, copper and possibly vitamin B11 (folic acid). In this case report, we narrate about a patient with anaemia and multiple vitamin and mineral deficiencies after Roux-en-Y gastric bypass (RYGB) with an alimentary limb of 150?cm and a biliopancreatic limb of 100?cm. RYGB is associated with an increased risk of vitamin deficiencies, especially a vitamin B12 deficiency. The patient in this case report developed psychiatric-neurological symptoms due to folic acid supplementation in an untreated cobalamin deficiency. Second, we tried to elucidate the vitamin physiology to understand specific mechanisms after BS.

Impactfactor: --

Night Splinting for Idiopathic Trigger Digits

Drijkoningen T, **van Berckel M**, Becker SJE, Ring DC, Mudgal CS

Hand (N Y). 2018 Sep;13(5):558-562. Epub 2017 Aug 20

BACKGROUND:
This study assessed nighttime splinting for 6 weeks as treatment for recent onset idiopathic trigger fingers.
METHODS:
Patients over 18 years with a Quinnell grade 1 or 2, idiopathic trigger finger or thumb causing symptoms for less than 3 months were eligible for a custom-made hand-based orthoplast night orthotic. Improvement of symptoms and/or resolution of triggering were recorded. Patients also completed the short version of the Disabilities of the Arm, Shoulder and Hand and a numerical rating scale for pain at the initial visit, after 6 to 8 weeks, and after 3 months.
RESULTS:
Thirty-four patients wore a night orthotic for at least 6 weeks. At final evaluation, there was a substantial reduction in disability and pain. Symptoms of triggering resolved completely in 18 patients (55%). Sixteen patients did not resolve their triggering after splinting and therefore underwent a steroid injection.
CONCLUSION:
Night splinting is a noninvasive treatment option for idiopathic trigger fingers/thumb with symptoms for less than 3 months.

Impactfactor: --

Nutritional interventions to improve recovery from postoperative ileus

Smeets BJ, Luyer MD

Curr Opin Clin Nutr Metab Care. 2018 Sep;21(5):394-398

PURPOSE OF REVIEW:
Postoperative ileus (POI) is an important contributor to postoperative morbidity. However, postoperative outcomes have improved by enhanced recovery after surgery (ERAS) programs. Enteral nutrition is an essential part of ERAS and many studies suggest a therapeutic effect of nutrition on POI.
RECENT FINDINGS:
Early postoperative enteral nutrition has been shown to reduce various complications, including POI, although studies are heterogeneous. Experimental studies suggest that composition and timing of the enteral feed is important for the potential beneficial effects: lipid-enriched nutrition given just before, during, and directly after surgery was most effective in reducing POI in an experimental setting. In a clinical study in patients undergoing advanced rectal cancer surgery, direct start of enteral tube feeding reduced POI. Conversely, perioperative lipid-enriched enteral nutrition did not reduce POI in patients undergoing colorectal surgery with an ERAS protocol.
SUMMARY:
POI is common and remains an important determinant of postoperative recovery following colorectal surgery. Nutrition is a potential therapeutic means to reduce POI. Timing and composition of the enteral feed have been shown to be essential for the beneficial effects of enteral nutrition in an experimental setup. However perioperative lipid-enriched nutrition does not reduce POI in patients undergoing colorectal surgery with an ERAS protocol.
Impactfactor: 4.534

Oncologic outcome and recurrence rate following anastomotic leakage after curative resection for colorectal cancer

Ramphal W, Boeding JRE, Gobardhan PD, **Rutten HJ**, de Winter LJ, Crolla RM, Schreinemakers JM

Surg Oncol. 2018 Dec;27(4):730-736

INTRODUCTION:
Anastomotic leakage is one of the most severe early complications after colorectal surgery, and it is associated with a high reoperation rate-, and increased in short-term morbidity and mortality rates. It remains unclear whether anastomotic leakage is associated with poor oncologic outcomes. The aim of this study was to determine the impacts of anastomotic leakage on long-term oncologic outcomes, disease-free survival and overall mortality in patients who underwent curative surgery for colorectal cancer.
METHODS:
This single-centre, retrospective, observational cohort study included patients who underwent curative surgery for colorectal cancer between 2005 and 2015 and who had a primary anastomosis. Survival- and multivariate cox regression analyses were performed to adjust for confounding.
RESULTS:
A total of 1984 patients had a primary anastomosis after surgery. The overall incidence of anastomotic leakage was 7.5%; 19 patients were excluded because they were lost to follow-up. Of the remaining 1965 patients, 41 (2.1%) developed local recurrence associated with anastomotic leakage [adjusted hazard ratio (HR)?=?2.25; 95% confidence interval (CI) 1.14-5.29; P?=?0.03]. Distant recurrence developed in 291(14.8%) patients with no association with anastomotic leakage [adjusted HR?=?1.30 (95% CI: 0.85-1.97) P?=?0.23]. Anastomotic leakage was associated with increased long-term mortality [adjusted HR?=?1.69 (95% CI 1.32-2.18) P?<?0.01]. Five year disease-free survival was significantly decreased in patients with anastomotic leakage, (log rank test P?<?0.01).
CONCLUSION:
Anastomotic leakage was significantly associated with increased rates of local recurrence, disease free-survival and overall mortality. Associations of anastomotic leakage with distant recurrence was not found.
Impactfactor: 2.558

Oncologic treatment strategies and relative survival of patients with stage I-III rectal cancer - A EURECCA international comparison between the Netherlands, Belgium, Denmark, Sweden, England, Ireland, Spain, and Lithuania

Breugom AJ, Bastiaannet E, Boelens PG, Van Eycken E, Iversen LH, Martling A, Johansson R, Evans T, Lawton S, O'Brien KM, Ortiz H, Janciauskiene R, Dekkers OM, **Rutten HJ**, Liefers GJ, Lemmens VE, van de Velde CJ

Eur J Surg Oncol. 2018 Sep;44(9):1338-1343

INTRODUCTION:
The aim of this EURECCA international comparison is to compare oncologic treatment strategies and relative survival of patients with stage I-III rectal cancer between European countries.
MATERIAL AND METHODS:
Population-based national cohort data from the Netherlands (NL), Belgium (BE), Denmark (DK), Sweden (SE), England (ENG), Ireland (IE), Spain (ES), and single-centre data from Lithuania (LT) were obtained. All operated patients with (y)pTNM stage I-III rectal cancer diagnosed between 2004 and 2009 were included. Oncologic treatment strategies and relative survival were calculated and compared between neighbouring countries.

RESULTS:
We included 57,120 patients. Treatment strategies differed between NL and BE ($p < 0.001$), DK and SE ($p < 0.001$), and ENG and IE ($p < 0.001$). More preoperative radiotherapy as single treatment before surgery was administered in NL compared with BE (59.7% vs. 13.1%), in SE compared with DK (55.1% vs. 10.4%), and in ENG compared with IE (15.2% vs. 9.6%). Less postoperative chemotherapy was given in NL (9.6% vs. 39.1%), in SE (7.9% vs. 14.1%), and in IE (12.6% vs. 18.5%) compared with their neighbouring country. In ES, 55.1% of patients received preoperative chemoradiation and 62.3% postoperative chemotherapy. There were no significant differences in relative survival between neighbouring countries.
CONCLUSION:
Large differences in oncologic treatment strategies for patients with (y)pTNM I-III rectal cancer were observed across European countries. No clear relation between oncologic treatment strategies and relative survival was observed. Further research into selection criteria for specific treatments could eventually lead to individualised and optimal treatment for patients with non-metastasised rectal cancer.

Impactfactor: 3.688

Optimal management of localized rectal cancer in older patients

Bujko K, Glynne-Jones R, Papamichael D, **Rutten HJ**

J Geriatr Oncol. 2018 Nov;9(6):696-704

In advising the optimal management for older patients, health care professionals try to balance the risks from frailty, vulnerability, and comorbidity against the patient's ultimate prognosis, potential functional outcomes and quality of life (QOL). At the same time it is important to involve the patient and incorporate their preferences. But how can we present and balance the potential downside of radical radiotherapy and risks of unsalvageable recurrence against the potential risks of postoperative morbidity and mortality associated with radical surgery? There are currently no nationally approved and evidence-based guidelines available to ensure consistency in discussions with older adults or frail and vulnerable patients. In this overview we hope to provide an insightful discussion of the relevant issues and options currently available.

Impactfactor: 3.359

Outcomes After Minimally-invasive Versus Open Pancreatoduodenectomy: A Pan-European Propensity Score Matched Study

Klompmaker S, van Hilst J, Wellner UF, Busch OR, Coratti A, D'Hondt M, Dokmak S, Festen S, Kerem M, Khatkov I, Lips DJ, Lombardo C, **Luyer M**, Manzoni A, Molenaar IQ, Rosso E, Saint-Marc O, Vansteenkiste F, Wittel UA, Bonsing B, Groot Koerkamp B, Abu Hilal M, et al

Ann Surg. 2018 Jun 1. [Epub ahead of print]

OBJECTIVE:
To assess short-term outcomes after minimally invasive (laparoscopic, robot-assisted, and hybrid) pancreatoduodenectomy (MIPD) versus open pancreatoduodenectomy (OPD) among European centers.
BACKGROUND:
Current evidence on MIPD is based on national registries or single expert centers. International, matched studies comparing outcomes for MIPD and OPD are lacking.
METHODS:
Retrospective propensity score matched study comparing MIPD in 14 centers (7 countries) performing =10 MIPDs annually (2012-2017) versus OPD in 53?German/Dutch surgical registry centers performing =10 OPDs annually (2014-2017). Primary outcome was 30-day major morbidity (Clavien-Dindo =3).
RESULTS:
Of 4220 patients, 729/730 MIPDs (412 laparoscopic, 184 robot-assisted, and 130 hybrid) were matched to 729 OPDs. Median annual case-volume was 19 MIPDs (interquartile range, IQR 13-22), including the first MIPDs performed in 10/14 centers, and 31 OPDs (IQR 21-38). Major morbidity (28% vs 30%, $P = 0.526$), mortality (4.0% vs 3.3%, $P = 0.576$), percutaneous drainage (12% vs 12%, $P = 0.809$), reoperation (11% vs 13%, $P = 0.329$), and hospital stay (mean 17 vs 17 days, $P > 0.99$) were comparable between MIPD and OPD. Grade-B/C postoperative pancreatic fistula (POPF) (23% vs 13%, $P < 0.001$) occurred more frequently after MIPD. Single-row pancreatojejunostomy was associated with POPF in MIPD (odds ratio, OR 2.95, $P < 0.001$), but not in OPD. Laparoscopic, robot-assisted, and hybrid MIPD had comparable major morbidity (27% vs 27% vs 35%), POPF (24% vs 19% vs 25%), and mortality (2.9% vs 5.2% vs 5.4%), with a fewer conversions in robot-assisted- versus laparoscopic MIPD (5% vs 26%, $P < 0.001$).
CONCLUSIONS:
In the early experience of 14 European centers performing =10 MIPDs annually, no differences were found in major morbidity, mortality, and hospital stay between MIPD and OPD. The high rates of POPF and conversion, and the lack of superior outcomes (ie, hospital stay, morbidity) could indicate that more experience and higher annual MIPD volumes are needed

Impactfactor: 1.536

Overall survival before and after centralization of gastric cancer surgery in the Netherlands

van Putten M, Nelen SD, Lemmens VE, Stoot JH, Hartgrink HH, Gisbertz SS, Spillenaar Bilgen EJ, Heisterkamp J, Verhoeven RH, **Nieuwenhuijzen GA**

Br J Surg. 2018 Dec;105(13):1807-1815

BACKGROUND:

Centralization of surgery has been shown to improve outcomes for oesophageal and pancreatic cancer, and has been implemented for gastric cancer since 2012 in the Netherlands. This study evaluated the impact of centralizing gastric cancer surgery on outcomes for all patients with gastric cancer.

METHODS:

Patients diagnosed with non-cardia gastric adenocarcinoma in the intervals 2009-2011 and 2013-2015 were selected from the Netherlands Cancer Registry. Clinicopathological data, treatment characteristics and mortality were assessed for the periods before (2009-2011) and after (2013-2015) centralization. Cox regression analyses were used to assess differences in overall survival between these intervals.

RESULTS:

A total of 7204 patients were included. Resection rates increased slightly from 37·6 per cent before to 39·6 per cent after centralization (P?= 0·023). Before centralization, 50·1 per cent of surgically treated patients underwent gastrectomy in hospitals that performed fewer than ten procedures annually, compared with 9·2 per cent after centralization. Patients who had gastrectomy in the second interval were younger and more often underwent total gastrectomy (29·3 per cent before versus 41·2 per cent after centralization). Thirty-day postoperative mortality rates dropped from 6·5 to 4·1 per cent (P?= 0·004), and 90-day mortality rates decreased from 10·6 to 7·2 per cent (P?= 0·002). Two-year overall survival rates increased from 55·4 to 58·5 per cent among patients who had gastrectomy (P?= 0·031) and from 27·1 to 29·6 per cent for all patients (P?= 0·003). Improvements remained after adjustment for case mix; however, adjustment for hospital volume attenuated this association for surgically treated patients.

CONCLUSION:

Centralization of gastric cancer surgery was associated with reduced postoperative mortality and improved survival.

Impactfactor: 5.433

Overstenting the hypogastric artery during endovascular aneurysm repair with and without prior coil embolization: AÂ comparative analysis from the ENGAGE Registry

Stokmans RA, Broos PPHL, van Sambeek MRHM, Teijink JAW, Cuypers PWM

J Vasc Surg. 2018 Jan;67(1):134-141. Epub 2017 Jun 27

BACKGROUND: Endovascular aneurysm repair of aortoiliac or iliac aneurysms is often performed with stent graft coverage of the origin of the hypogastric artery (HA) to ensure adequate distal seal. It is considered common practice to perform adjunctive coiling of the HA to prevent a type II endoleak. Our objective was to question the necessity of pre-emptive coiling by comparing the outcomes of HA coverage with and without prior coil embolization.

METHODS: Data from the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE), which prospectively enrolled 1263 endovascular aneurysm repair patients between March 2009 and April 2011 from multiple centers worldwide, were used for this study. We identified patients in whom the Endurant stent graft (Medtronic Vascular, Santa Rosa, Calif) covered one or both HAs and grouped them into cases in which prior HA embolization-coils or plugs-was performed (CE) and cases in which HA embolization was not performed (NE). The occurrence of covered HA-related endoleak and secondary interventions were compared between groups.

RESULTS: In 197 patients, 225 HAs were covered. Ninety-one HAs were covered after coil embolization (CE group), and 134 HAs were covered without prior coil embolization (NE group). Both groups were similar at baseline and had comparable length of follow-up to last image (665.2 ± 321.7 days for CE patients; 641.6 ± 327.6 days for NE patients; P = .464). Importantly, both groups showed equivalent iliac morphology concerning common iliac artery proximal, mid, and distal dimensions and tortuosity, making them suitable for comparative analysis. During follow-up, HA-related endoleaks were sparse and occurred equally often in both groups (CE 5.5% vs NE 3.0%; P = .346). Secondary intervention to resolve an HA-related endoleak was performed twice in the CE group and three times in the NE group. Late non-HA-related endoleaks occurred more often in the CE group compared with the NE group, (25.0% vs 15.0%; P = .080). Secondary interventions for other reasons than HA-related endoleaks occurred in 7.5% of NE cases and 15.4% of CE cases (P = .057), mostly for occlusions in the ipsilateral iliac limb. During follow-up, 19 NE patients and 9 CE patients died, which is not significantly different (P = .225), and no deaths were related directly or indirectly to HA coverage. Also, no reports of gluteal necrosis and bowel ischemia were made.

CONCLUSIONS: This study shows that HA coverage with the Endurant endograft without prior coil embolization does not increase the incidence of endoleak or related secondary interventions. These findings together with the already available evidence suggest that omission of coil embolization may be a more resource-effective strategy whenever HA coverage is required.

Impactfactor: 2.758

Perioperative lipid-enriched enteral nutrition versus standard care in patients undergoing elective colorectal surgery (SANICS II): a multicentre double-blind randomised controlled trial

Peters EG, Smeets BJJ, Nors J, Back CM, Funder JA, Sommer T, Laurberg S, Løve US, Leclercq WKG, Slooter GD, de Vries Reilingh TS, Wegdam JA, **Nieuwenhuijzen GAP**, Hiligsmann M, Buise MP, Buurman WA, de Jonge WJ, **Rutten HJT**, **Luyer MDP**

Lancet Gastroenterol Hepatol. 2018 Apr 3(4):242-251. Epub 2018 Feb 14

BACKGROUND:
Postoperative ileus and anastomotic leakage severely impair recovery after colorectal resection. We investigated the effect of perioperative lipid-enriched enteral nutrition versus standard care on the risk of postoperative ileus, anastomotic leakage, and other clinical outcomes.
METHODS:
We did an international, multicentre, double-blind, randomised, controlled trial of patients (=18 years) undergoing elective colorectal surgery with primary anastomosis at six clinical centres in the Netherlands and Denmark. Patients were randomly assigned (1:1), stratified by location (colonic and rectal) and type of surgery (laparoscopic and open), via online randomisation software, with block sizes of six, to receive either continuous lipid-enriched enteral tube feeding from 3 h before until 6 h after surgery (intervention) or no perioperative nutrition (control). Surgeons, patients, and researchers were masked to treatment allocation for the entire study period. The primary outcome was postoperative ileus. Secondary outcomes included anastomotic leakage, pneumonia, preoperative gastric volumes, time to functional recovery, length of hospital stay, the need for additional interventions, intensive care unit admission, postoperative inflammatory response, and surgical complications. Analyses were by intention to treat.
FINDINGS:
Between July 28, 2014, and February 20, 2017, 280 patients were randomly assigned, 15 of whom were excluded after random allocation because they fulfilled one or more exclusion criteria. 265 patients received perioperative nutrition (n=132) or standard care (n=133) and were included in the analyses. A postoperative ileus occurred in 37 (28%) patients in the intervention group versus 29 (22%) in the control group (risk ratio [RR] 1·09, 95% CI 0·95-1·25; p=0·24). Anastomotic leakage occurred in 12 (9%) patients in the intervention group versus 11 (8%) in the control group (RR 1·01, 95% CI 0·94-1·09; p=0·81). Pneumonia occurred in ten (8%) patients in the intervention group versus three (2%) in the control group (RR 1·06, 95% CI 1·00-1·12; p=0·051). All other secondary outcomes were similar between groups (all p>0·05).
INTERPRETATION:
Perioperative lipid-enriched enteral nutrition in patients undergoing elective colorectal surgery has no advantage over standard care in terms of postoperative complications.

Impactfactor: --

Perioperative Outcomes of Primary Bariatric Surgery in North-Western Europe: a Pooled Multinational Registry Analysis

Poelemeijer YQ, Liem RS, Våge V, Mala T, Sundbom M, Ottosson J, **Nienhuijs SW**

Obes Surg. 2018 Dec;28(12):3916-3922

INTRODUCTION: The global prevalence of obesity has increased in recent decades, and bariatric surgery has become a part of the treatment algorithm of obesity. National high-quality registries enable large-scale evaluations of the use and outcome of bariatric surgery and may allow for improved knowledge. The main objective was to evaluate the rate and type of complications after primary bariatric surgery in three North-Western European countries using nationwide registries.
MATERIALS AND METHODS: Data from three registries for bariatric surgery were used (January 2015-December 2016). All registries have nationwide coverage with data on patient characteristics, obesity-related diseases, surgical technique, complications, grading of complications, reinterventions, readmissions, and mortality. Eligibility criteria for bariatric surgery were similar and included body mass index of =?40.0 or =?35.0 kg/m2, with one or more obesity-associated diseases.
RESULTS: A total of 35,858 procedures (32,177 primary) were registered. The most common procedure was gastric bypass in the Netherlands (78.9%) and Sweden (67.0%), and sleeve gastrectomy in Norway (58.2%). A total of 904 (2.8%) patients developed major complications after primary surgery and 12 patients (0.04%) died within 30 days. Total number of complications between the registries were comparable (p?=?0.939). However, significant differences were seen for Clavien-Dindo Classification grades IIIb and IV (p?<?0.001). Pooled readmission rates were 4.3% (n?=?1386).
DISCUSSION: Bariatric surgery is safely performed in the three evaluated countries. Standardization of registries and consensus of variables are essential for international comparison and may contribute to improved quality of treatment across nations.

Impactfactor: *3.895*

Permissive weight bearing in trauma patients with fracture of the lower extremities: prospective multicenter comparative cohort study

Kalmet PHS, Meys G, V Horn YY, Evers SMAA, Seelen HAM, Hustinx P, Janzing H, **Vd Veen A**, Jaspars C, Sintenie JB, Blokhuis TJ, Poeze M, Brink PRG

BMC Surg. 2018 Feb 2 18(1):8

BACKGROUND:
The standard aftercare treatment in surgically treated trauma patients with fractures around or in a joint, known as (peri)- or intra-articular fractures of the lower extremities, is either non-weight bearing or partial weight bearing. We have developed an early permissive weight bearing post-surgery rehabilitation protocol in surgically treated patients with fractures of the lower extremities. In this proposal we want to compare our early permissive weight bearing protocol to the existing current non-weight bearing guidelines in a prospective comparative cohort study.
METHODS/DESIGN:
The study is a prospective multicenter comparative cohort study in which two rehabilitation aftercare treatments will be contrasted, i.e. permissive weight bearing and non-weight bearing according to the AO-guideline. The study population consists of patients with a surgically treated fracture of the pelvis/acetabulum or a surgically treated (peri)- or intra-articular fracture of the lower extremities. The inclusion period is 12 months. The duration of follow up is 6 months, with measurements taken at baseline, 2,6,12 and 26 weeks post-surgery.
PRIMARY OUTCOME MEASURE:
ADL with Lower Extremity Functional Scale. Outcome variables for compliance, as measured with an insole pressure measurement system, encompass peak load and step duration.
DISCUSSION:
This study will investigate the (cost-) effectiveness of a permissive weight bearing aftercare protocol. The results will provide evidence whether a permissive weight bearing protocol is more effective than the current non-weight bearing protocol.

Impactfactor: 1.692

Personalized management of elderly patients with rectal cancer: Expert recommendations of the European Society of Surgical Oncology, European Society of Coloproctology, International Society of Geriatric Oncology, and American College of Surgeons Commission on Cancer

Montroni I, Ugolini G, Saur NM, Spinelli A, Rostoft S, Millan M, Wolthuis A, Daniels IR, Hompes R, Penna M, Fürst A, Papamichael D, Desai AM, Cascinu S, Gèrard JP, Myint A, Lemmens VE, Berho M, Lawler M, De Liguori Carino N, Potenti F, Nanni O, Altini M 23, Beets G, **Rutten H**, Winchester D, Wexner SD, Audisio RA

Eur J Surg Oncol. 2018 Nov;44(11):1685-1702

With an expanding elderly population and median rectal cancer detection age of 70 years, the prevalence of rectal cancer in elderly patients is increasing. Management is based on evidence from younger patients, resulting in substandard treatments and poor outcomes. Modern management of rectal cancer in the elderly demands patient-centered treatment, assessing frailty rather than chronological age. The heterogeneity of this group, combined with the limited available data, impedes drafting evidence-based guidelines. Therefore, a multidisciplinary task force convened experts from the European Society of Surgical Oncology, European Society of Coloproctology, International Society of Geriatric Oncology and the American College Surgeons Commission on Cancer, with the goal of identifying the best practice to promote personalized rectal cancer care in older patients. A crucial element for personalized care was recognized as the routine screening for frailty and geriatrician involvement and personalized care for frail patients. Careful patient selection and improved surgical and perioperative techniques are responsible for a substantial improvement in rectal cancer outcomes. Therefore, properly selected patients should be considered for surgical resection. Local excision can be utilized when balancing oncologic outcomes, frailty and life expectancy. Watch and wait protocols, in expert hands, are valuable for selected patients and adjuncts can be added to improve complete response rates. Functional recovery and patient-reported outcomes are as important as oncologic-specific outcomes in this age group. The above recommendations and others were made based on the best-available evidence to guide the personalized treatment of elderly patients with rectal cancer.

Impactfactor: 3.688

Predicting breast and axillary response after neoadjuvant treatment for breast cancer: The role of histology vs receptor status

Vugts G, Van den Heuvel F, Maaskant-Braat AJ, Voogd AC, Van Warmerdam LJ, **Nieuwenhuijzen GA,** van der Sangen MJ

Breast J. 2018 Nov;24(6):894-901

PURPOSE:
Neoadjuvant systemic treatment (NST) is increasingly administered in breast cancer patients. This study was conducted to identify predictors for tumor response in the breast and axilla.

METHODS:
All female patients with nonmetastatic, noninflammatory breast cancer receiving NST between 2003-2013 at the Catharina Cancer Institute in Eindhoven, The Netherlands, were included.
RESULTS:
The majority of 216 of the 337 patients receiving NST (65%) presented with a cT2 tumor. In 159 patients (47%), the axilla was clinically node positive. A pathologic complete response (pCR) in the breast was achieved in 83 patients (24.6%), and a pCR in the axilla in 65 node-positive patients (40.9%). The triple-negative (OR 4.29, 95% CI 2.15-8.55) and hormone receptor (HR)-negative/HER2-positive tumors (OR 3.73, 95% CI 1.59-8.75) were associated with in-breast pCR. Patients with invasive lobular carcinoma (ILC) were less likely to experience in-breast pCR (OR 0.10, 95% CI 0.01-0.73) than those with invasive ductal cancer. Axillary pCR was found in 65 clinically node-positive patients (41%). Axillary pCR was more likely to occur in HR-positive/HER2-positive (OR 6.24, 95% CI 1.86-20.90) and HR-negative/HER2-positive tumors (OR 6.41, 95% CI 1.95-21.06), compared to HER2-negative disease. In-breast pCR was strongly associated with axillary pCR (OR 10.89, 95% CI 4.20-28.22).
CONCLUSION:
Response to NST in the breast and axilla is largely determined by receptor status, with high pCR rates occurring in HER2-positive and triple-negative tumors. For axillary pCR, in-breast pCR and HER2-positive disease are the most important predictive factors.

Impactfactor: 2.424

Predicting suitability of intramedullary fixation for displaced midshaft clavicle fractures

Hulsmans MHJ, van Heijl M, Frima H, van der Meijden OAJ, van den Berg HR, **van der Veen AH**, Gunning AC, Houwert RM, Verleisdonk EJMM

Eur J Trauma Emerg Surg. 2018 Aug;44(4):581-587. Epub 2017 Oct 9

PURPOSE:
Implant-related irritation is a technique-specific complication seen in a substantial number of patients treated with intramedullary nailing for clavicle fractures. The purpose of this study was to identify predictors for developing implant-related irritation in patients with displaced midshaft clavicle fractures treated with elastic stable intramedullary nailing.
METHODS:
A retrospective analysis of the surgical database in two level 2 trauma centers was performed. Patients who underwent intramedullary nailing for displaced midshaft clavicle fractures between 2005 and 2012 in the first hospital were included. Age, gender, fracture comminution and fracture location were assessed as possible predictors for developing irritation using multivariate logistic regression analysis. These predictors were externally validated using data of patients treated in another hospital.
RESULTS:
Eighty-one patients were included in initial analysis. In the multivariate analysis, comminuted fractures in comparison to non-comminuted fractures (72 vs. 38%, p?=?0.027) and fracture location (p?<?0.001) were significantly associated with the development of implant-related irritation. In particular, lateral diaphyseal fractures caused irritation compared to fractures on the medial side of the cut-off point (88 vs. 26%). External validation of these predictors in 48 additional patients treated in another hospital showed a similar predictive value of the model and a good fit.
CONCLUSION:
Comminuted and lateral diaphyseal fractures were found to be statistically significant and independent predictors for developing implant-related irritation. We, therefore, believe that intramedullary nailing might not be suitable for these types of fractures. Future studies are needed to determine whether alternative surgical techniques or implants would be more suitable for these specific types of fractures.

Impactfactor: 1.704

Predictive value of abdominal CT in evaluating internal herniation after bariatric laparoscopic Roux-en-Y gastric bypass

Ederveen JC**, van Berckel MMG, Nienhuijs SW**, Weber RJP, Nederend J

Br J Surg. 2018 Nov 105(12):1623-1629. Epub 2018 Jun 4

BACKGROUND:
Internal herniation, a serious complication after bariatric surgery, is challenging to diagnose. The aim of this study was to determine the accuracy of abdominal CT in diagnosing internal herniation.
METHODS:
The study included consecutive patients who had undergone laparoscopic gastric bypass surgery between 1 January 2011 and 1 January 2015 at a bariatric centre of excellence. To select patients suspected of having internal herniation, reports of abdominal CT and reoperations up to 1 January 2017 were screened. CT was presumed negative for internal herniation if no follow-up CT or reoperation was performed within 90?days after the initial CT, or no internal herniation was found during reoperation. The accuracy of abdominal CT in diagnosing internal herniation was calculated using two-way contingency tables.

RESULTS:
A total of 1475 patients were included (84·7 per cent women, mean age 46·5?years, median initial BMI 41·8?kg/m2). CT and/or reoperation was performed in 192 patients (13·0 per cent) in whom internal herniation was suspected. Internal herniation was proven laparoscopically in 37 of these patients. The incidence of internal herniation was 2·5 per cent. An analysis by complaint included a total of 265 episodes, for which 247 CT scans were undertaken. CT was not used to investigate 18 episodes, but internal herniation was encountered in one-third of these during reoperation. Combining the follow-up and intraoperative findings, the accuracy of CT for internal herniation had a sensitivity of 83·8 (95 per cent c.i. 67·3 to 93·2) per cent, a specificity of 87·1 (81·7 to 91·2) per cent, a positive predictive value of 53·4 (40·0 to 66·5) per cent and a negative predictive value of 96·8 (92·9 to 98·7) per cent.
CONCLUSION:
Abdominal CT is an important tool in diagnosing internal herniation, with a high specificity and a high negative predictive value.

Impactfactor: 5.433

Preliminary results of a cohort study of induction chemotherapy-based treatment for locally recurrent rectal cancer

van Zoggel DMGI, Bosman SJ, Kusters M, Nieuwenhuijzen GAP, Cnossen JS**,** Creemers GJ, van Lijnschoten G, **Rutten HJT**

Br J Surg. 2018 Mar;105(4):447-452.Epub 2017 Nov 23

BACKGROUND:
A significant number of patients treated for locally recurrent rectal cancer have local or systemic failure, especially after incomplete surgical resection. Neoadjuvant treatment regimens in patients who have already undergone preoperative (chemo)radiotherapy for the primary tumour are limited. The objective of the present study was to evaluate the influence of a neoadjuvant regimen incorporating induction chemotherapy (ICT) in patients with locally recurrent rectal cancer who had preoperative (chemo)radiotherapy for the primary cancer or an earlier local recurrence.
METHODS:
Patients were treated with a sequential neoadjuvant regimen including three or four cycles of 5-fluorouracil and oxaliplatin-containing chemotherapy. When no progressive disease was found at evaluation, neoadjuvant treatment was continued with chemoradiation therapy (CRRT) using 30?Gy with concomitant capecitabine. If there was a response to ICT, the patient was advised to continue with systemic chemotherapy after CRRT as consolidation chemotherapy while waiting for resection. These patients were compared with patients who received CRRT alone in the same time interval.
RESULTS:
Of 58 patients who had ICT, 32 (55 per cent) had surgery with clear resection margins, of whom ten (17 per cent) exhibited a pathological complete response (pCR). The remaining 26 patients had 23 R1 and three R2 resections. In 71 patients who received CRRT, a similar rate of R0 (35 patients) and R1 (36) resection was found (P?=?0·506), but only three patients (4 per cent) had a pCR (P?=?0·015).
CONCLUSION:
The incorporation of ICT in neoadjuvant regimens for locally recurrent rectal cancer is a promising strategy.

Impactfactor: 5.433

Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer

Schaap DP, Ogura A, Nederend J, Maas M, Cnossen JS**,** Creemers GJ, van Lijnschoten I**, Nieuwenhuijzen GA, Rutten HJ, Kusters M**

Br J Surg. 2018 Dec;105(13):1844-1852

BACKGROUND:
Lateral nodal disease in rectal cancer remains a subject of debate and is treated differently in the East and the West. The predictive value of lateral lymph node and MRI-detected extramural vascular invasion (mrEMVI) features on oncological outcomes was assessed in this study.
METHODS:
In this retrospective cohort study, data on patients with cT3-4 rectal cancer within 8?cm from the anal verge were considered over a 5-year period (2009-2013). Lateral lymph node size, malignant features and mrEMVI features were evaluated and related to oncological outcomes.
RESULTS:
In total, 192 patients were studied, of whom 30 (15·6 per cent) underwent short-course radiotherapy and 145 (75·5 per cent) received chemoradiotherapy. A lateral lymph node short-axis size of 10?mm or more was associated with a significantly higher 5-year lateral/presacral local recurrence rate of 37 per cent, compared with 7·7 per cent in nodes smaller than 10?mm (P?=?0·041). Enlarged nodes did not result in a higher 5-year rate of distant metastasis (23 per cent versus 27·7 per cent in nodes smaller than 10?mm; P?=?0·563). However, mrEMVI positivity was related to more metastatic disease (5-year rate 43 versus 26·3 per cent in the mrEMVI-negative group; P?=?0·014), but not with increased lateral/presacral recurrence. mrEMVI occurred in 46·6 per cent of patients with nodes

smaller than 10?mm, compared with 29 per cent in patients with nodes of 10?mm or larger (P?=?0·267). CONCLUSION:

Although lateral nodal disease is more a local problem, mrEMVI mainly predicts distant recurrence. The results of this study showed an unacceptably high local recurrence rate in patients with a short axis of 10?mm or more, despite neoadjuvant (chemo)radiotherapy.

Impactfactor: 5.433

Propensity Score-Matched Analysis Comparing Minimally Invasive Ivor Lewis Versus Minimally Invasive Mckeown Esophagectomy

van Workum F, Slaman AE, van Berge Henegouwen MI, Gisbertz SS, Kouwenhoven EA, van Det MJ, van den Wildenberg FJH, Polat F, **Luyer MDP, Nieuwenhuijzen GAP**, Rosman C

Ann Surg. 2018 Aug 10. [Epub ahead of print]

INTRODUCTION:

Totally minimally invasive esophagectomy (TMIE) is increasingly used in treatment of patients with esophageal carcinoma. However, it is currently unknown if McKeown TMIE or Ivor Lewis TMIE should be preferred for patients in whom both procedures are oncologically feasible.

METHODS:

The study was performed in 4 high-volume Dutch esophageal cancer centers between November 2009 and April 2017. Prospectively collected data from consecutive patients with esophageal cancer localized in the distal esophagus or gastroesophageal junction undergoing McKeown TMIE or Ivor Lewis TMIE were included. Patients were propensity score matched for age, body mass index, sex, American Society of Anesthesiologists classification, Charlson Comorbidity Index, tumor type, tumor location, clinical stage, neoadjuvant treatment, and the hospital of surgery. The primary outcome parameter was anastomotic leakage requiring reintervention or reoperation. Secondary outcome parameters were operation characteristics, pathology results, complications, reinterventions, reoperations, length of stay, and mortality.

RESULTS:

Of all 787 included patients, 420 remained after matching. The incidence of anastomotic leakage requiring reintervention or reoperation was 23.3% after McKeown TMIE versus 12.4% after Ivor Lewis TMIE (P = 0.003). Ivor Lewis TMIE was significantly associated with a lower incidence of pulmonary complications (46.7% vs 31.9%), recurrent laryngeal nerve palsy (9.5% vs 0.5%), reoperations (18.6% vs 11.0%), 90-day mortality (7.1% vs 2.9%), shorter median intensive care unit length of stay (2 days vs 1 day) and shorter median hospital length of stay (12 vs 11 days) (all P < 0.05). R0 resection rate was similar between the groups. The median number of examined lymph nodes was 21 after McKeown TMIE and 25 after Ivor Lewis TMIE (P < 0.001).

CONCLUSIONS:

Ivor Lewis TMIE is associated with a lower incidence of anastomotic leakage, 90-day mortality and other postoperative morbidity compared to McKeown TMIE in patients in whom both procedures are oncologically feasible.

Impactfactor: 1.536

Quality of life after Nissen fundoplication in patients with gastroesophageal reflux disease

Castelijns PSS, Ponten JEH, Vd Poll MCG, Bouvy ND, **Smulders JF**

J Minim Access Surg. 2018 Jul-Sep;14(3):213-220

Introduction: Nissen fundoplication is the golden standard for surgical treatment of gastroesophageal reflux disease (GERD). Numerous studies report excellent short-term results. However, data regarding long-term quality of life are lacking. The aim of this study is to investigate the long-term quality of life after Nissen fundoplication in patients with GERD and to compare this with the short-term results.

Patients and Methods: We retrospectively analysed all patients who underwent laparoscopic Nissen fundoplication for GERD between January 2004 and January 2016. All patients received a validated GERD-Health-Related Quality of Life questionnaire by mail to assess post-operative quality of life. Maximum quality of life is represented by a score of 75. Secondary outcome measures were complications and recurrence rate.

Results: One hundred and seventy-five (77.1%) of the 227 operated patients returned the questionnaire. The median follow-up was 3.7 (0.1-10.3) years. Mean age was 51.6 (range 15-85) and 72 patients were male. We report an excellent quality of life with a median total score of 70 (range 2-75). Re-operation rate was 13.6% (23/169); the re-operation was due to recurrent reflux in 12 patients and due to persistent dysphagia in 11 patients. 91.3% of the re-operations were performed within the first 5 years after surgery. Mortality rate was zero.

Conclusion: We report a large series of single-centre, single-surgeon laparoscopic Nissen fundoplication. Despite the re-operation rate of 13.6%, we found excellent long-term symptomatic outcome. There was no difference between short- and long-term results.

Impactfactor: 1.137

Quantification of aortic stiffness and wall stress in healthy volunteers and abdominal aortic aneurysm patients using time-resolved 3D ultrasound: a comparison study

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Eur Heart J Cardiovasc Imaging. 2018 Mar 29. [Epub ahead of print]

Aims:

Using non-invasive 3D ultrasound, peak wall stress (PWS) and aortic stiffness can be evaluated, which may provide additional criteria in abdominal aortic aneurysm (AAA) risk assessment. In this study, these measures were determined in both young and age-matched individuals, and AAA patients while its relation to age, maximum diameter, and growth was assessed statistically.

Methods and results:

Time-resolved 3D-US data were acquired for 30 volunteers and 65 AAA patients. The aortic geometry was segmented, and tracked over the cardiac cycle using 3D speckle tracking to characterize the wall motion. Wall stress analysis was performed using finite element analysis. Model parameters were optimized until the model output matched the measured 3D displacements. A significant increase in aortic stiffness was measured between the age-matched volunteers [median 0.58, interquartile range (IQR) 0.48-0.71?kPa·m] and the small AAA patients (median 1.84, IQR 1.38-2.46?kPa·m; P < 0.001). In addition, an increase in aortic stiffness was evaluated between the small (30-39?mm) and large (=50?mm) AAAs (median 2.72, IQR 1.99-3.14?kPa·m; P?=?0.01). The 99th percentile wall stress showed a positive correlation with diameter (??=?0.73, P < 0.001), and significant differences between age-matched volunteers and AAA patients.

Conclusion:

The AAA pathology causes an early and significant increase in aortic stiffness of the abdominal aorta, even after correcting for the expected effect of ageing and differences in arterial pressure. Moreover, some AAAs revealed relatively high PWS, although the maximum diameter was below the threshold for surgical repair. Using the current method, these measures become available during follow-up, which could improve AAA rupture risk assessment.

Impactfactor: 8.336

Randomised controlled trial of transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND Study)

Barendse RM, Musters GD, de Graaf EJR, van den Broek FJC, Consten ECJ, Doornebosch PG, Hardwick JC, **de Hingh IHJT**, Hoff C, Jansen JM, van Milligen de Wit AWM, van der Schelling GP, Schoon EJ, Schwartz MP, Weusten BLAM, Dijkgraaf MG, Fockens P, Bemelman WA, Dekker E; TREND Study group

Gut. 2018 May;67(5):837-846. Epub 2017 Jun 28

OBJECTIVE:

Non-randomised studies suggest that endoscopic mucosal resection (EMR) is equally effective in removing large rectal adenomas as transanal endoscopic microsurgery (TEM), but EMR might be more cost-effective and safer. This trial compares the clinical outcome and cost-effectiveness of TEM and EMR for large rectal adenomas.

DESIGN:

Patients with rectal adenomas =3?cm, without malignant features, were randomised (1:1) to EMR or TEM, allowing endoscopic removal of residual adenoma at 3 months. Unexpected malignancies were excluded postrandomisation. Primary outcomes were recurrence within 24 months (aiming to demonstrate non-inferiority of EMR, upper limit 10%) and the number of recurrence-free days alive and out of hospital.

RESULTS:

Two hundred and four patients were treated in 18 university and community hospitals. Twenty-seven (13%) had unexpected cancer and were excluded from further analysis. Overall recurrence rates were 15% after EMR and 11% after TEM; statistical non-inferiority was not reached. The numbers of recurrence-free days alive and out of hospital were similar (EMR 609±209, TEM 652±188, p=0.16). Complications occurred in 18% (EMR) versus 26% (TEM) (p=0.23), with major complications occurring in 1% (EMR) versus 8% (TEM) (p=0.064). Quality-adjusted life years were equal in both groups. EMR was approximately €3000 cheaper and therefore more cost-effective.

CONCLUSION:

Under the statistical assumptions of this study, non-inferiority of EMR could not be demonstrated. However, EMR may have potential as the primary method of choice due to a tendency of lower complication rates and a better cost-effectiveness ratio. The high rate of unexpected cancers should be dealt with in further studies.

Impactfactor: 17.016

"Reflection-Before-Practice" Improves Self-Assessment and End-Performance in Laparoscopic Surgical Skills Training

Ganni S, Botden SMBI, **Schaap DP**, Verhoeven BH, Goossens RHM, Jakimowicz JJ

J Surg Educ. 2018 Mar - Apr;75(2):527-533

OBJECTIVE:

To establish whether a systematized approach to self-assessment in a laparoscopic surgical skills course improves accordance between expert- and self-assessment.

DESIGN:
A systematic training course in self-assessment using Competency Assessment Tool was introduced into the normal course of evaluation within a Laparoscopic Surgical Skills training course for the test group (n = 30). Differences between these and a control group (n = 30) who did not receive the additional training were assessed.
SETTING:
Catharina Hospital, Eindhoven, The Netherlands (n = 27), and GSL Medical College, Rajahmundry, India (n = 33).
PARTICIPANTS:
Sixty postgraduate year 2 and 3 surgical residents who attended the 2-day Laparoscopic Surgical Skills grade 1 level 1 curriculum were invited to participate.
RESULTS:
The test group (n = 30) showed better accordance between expert- and self-assessment (difference of 1.5, standard deviation [SD] = 0.2 versus 3.83, SD = 0.6, p = 0.009) as well as half the number (7 versus 14) of cases of overreporting. Furthermore, the test group also showed higher overall mean performance (mean = 38.1, SD = 0.7 versus mean = 31.8, SD = 1.0, p < 0.001) than the control group (n = 30). The systematic approach to self-assessment can be viewed as responsible for this and can be seen as "reflection-before-practice" within the framework of reflective practice as defined by Donald Schon.
CONCLUSION:
Our results suggest that "reflection-before-practice" in implementing self-assessment is an important step in the development of surgical skills, yielding both better understanding of one's strengths and weaknesses and also improving overall performance.

Impactfactor: *2.302*

Repeat Sentinel Lymph Node Biopsy for Ipsilateral Breast Tumor Recurrence: A Systematic Review of the Results and Impact on Prognosis

Poodt IGM, Vugts G, Schipper RJ, Nieuwenhuijzen GAP

Ann Surg Oncol. 2018 May 25(5):1329-1339

BACKGROUND:
During recent years, an increasing number of patients with ipsilateral breast tumor recurrence (IBTR) and previous axillary surgery have undergone repeat sentinel lymph node biopsy (rSLNB). The influence of axillary nodal status on prognosis for IBTR patients remains unclear. This study aimed to evaluate the technical success rate, follow-up assessment, and prognostic value of rSLNB for patients with IBTR.
METHODS:
A systematic search conducted in MEDLINE, Embase, and the Cochrane Library up to July 2017 included all studies on rSLNB in IBTR.
RESULTS:
A total of 34 articles describing 1761 patients were identified. A repeat sentinel lymph node (rSLN) was successfully harvested from 64.3% of the patients with IBTR, and the rate was significantly higher for the patients who had a previous SLNB than for those who had a previous axillary lymph node dissection (ALND) (75.7% vs. 46.1%; P < 0.0001). The rSLN was tumor-positive for 18.2% of the rSLNs, 40% of which were harvested in basins other than the ipsilateral axilla. The negative predictive value of the rSLNB was 96.5%. Overall survival, reported for 21.5% of the patients, was 95.2% after a mean follow-up period of 29.6 months.
CONCLUSION:
The prognostic impact of rSLN-positive versus rSLN-negative IBTR remains unclear. Further studies are needed to fill in the gap in the management of lymph nodes for patients with IBTR. However, based on the current evidence, rSLNB is feasible for 64% of patients, especially after previous SLNB. With a negative predictive value of 96.5%, rSLNB appears to be highly specific, with substantial advantages over ipsilateral ALND in IBTR.

Impactfactor: *3.857*

Reply to: "Letter to the Editor for the Manuscript the complex interplay of physical fitness protein intake and vitamin D supplementation after bariatric surgery"

Pouwels S, Smelt HJM, Celik A, Gupta A, **Smulders JF**

Obes Surg. 2018 Apr 28(4):1140-1141

Geen abstract beschikbaar

Impactfactor: *3.895*

Reply to: "Patients' Expectations Are Important for Success in Bariatric Surgery"

Pouwels S, Smelt HJM, **Smulders JF**

Obes Surg. 2018 Apr 28(4):1146

Geen abstract beschikbaar

Impactfactor: *3.895*

Review: Pathology and Its Clinical Relevance of Mucinous Appendiceal Neoplasms and Pseudomyxoma Peritonei

Legué LM, Creemers GJ, **de Hingh IHJT**, Lemmens VEPP, Huysentruyt CJ

Clin Colorectal Cancer. 2018 Dec 6. pii: S1533-0028(18)30467-5. [Epub ahead of print]

Until recently, many classifications existed for the terminology and histopathologic classification of appendiceal mucinous neoplasms, mucinous appendiceal adenocarcinomas, and pseudomyxoma peritonei (PMP). A major accomplishment was achieved by consensus-based histopathologic classifications on behalf of the Peritoneal Surface Oncology Group International regarding mucinous appendiceal tumours and PMP. As different classifications were used over the years and also owing to the rare nature of these tumors, many clinicians are not familiar with the terminology and the impact on patient management. Hence, an overview concerning mucinous appendiceal neoplasms, mucinous appendiceal adenocarcinomas, and PMP is provided to serve as an introduction into the basic morphology of these tumors with tentative recommendations for management.

Impactfactor: 3.861

[Risk of heart failure diminished thanks to stomach reduction in obesity] - Hartfalen afgenomen door maagverkleining bij obesitas

Botter B, Koolen E, **van Montfort G,** Bracke F, Bouwman A, Buise M

Ned Tijdschr Geneeskd. 2018;162:D1972

BACKGROUND: Obesity is a chronic disease and a risk factor for heart failure. In end-stage heart failure, heart transplantation may be the only available treatment option, but obesity is a contraindication for this treatment because of its unfavourable prognosis. Bariatric surgery and its subsequent weight loss may affect the indication for transplantation in patients with heart failure and morbid obesity.

CASE DESCRIPTION: A 46-year-old patient with morbid obesity and heart failure underwent gastric sleeve resection in preparation of a heart transplantation. Without it, he would not have been considered eligible for transplantation because of his obesity. The bariatric intervention was also intended to use weight loss as a way to reduce the symptoms of his heart failure and to make rehabilitation possible. One year after surgery, the condition of the patient had improved so much that heart transplantation was no longer necessary.

CONCLUSION: Bariatric surgery is safe for morbidly obese patients with severe heart failure and may sometimes even avoid heart transplantation.

impactfactor: 3.861

Risk of Regional Recurrence After Negative Repeat Sentinel Lymph Node Biopsy in Patients with Ipsilateral Breast Tumor Recurrence

Poodt IGM, **Vugts G**, Maaskant-Braat AJG, **Schipper RJ**, Voogd AC, **Nieuwenhuijzen GAP**

Sentinel Node and Recurrent Breast Cancer (SNARB) study group

Ann Surg Oncol. 2018 May 25(5):1312-1321. Epub 2018 Mar 1

BACKGROUND:

Repeat sentinel lymph node biopsy (rSLNB) has increasingly been used in patients with ipsilateral breast tumor recurrence (IBTR). The safety in terms of regional disease control after this procedure remains unclear. This study evaluates occurrence of regional recurrence as first event in patients with IBTR and negative rSLNB, treated without additional lymph node dissection.

PATIENTS AND METHODS:

Data were obtained from the Sentinel Node and Recurrent Breast Cancer (SNARB) study. In 201 patients, tumor-negative rSLNB was obtained without performing additional lymph node dissections.

RESULTS:

With median follow-up of 4.7 (range 0.9-12.7) years, regional recurrence occurred after median time of 3.0 (range 0.4-6.7) years in 4.5% (N = 9) of patients as first event after IBTR and rSLNB. In four of these nine patients, the site of recurrence was in concordance with the anatomical location of rSLNB. Two of the nine recurrences were reported in the ipsilateral axilla, resulting in an ipsilateral axillary regional recurrence rate of 1.0%. In the other seven patients, regional recurrence occurred in aberrant basins. Univariable analysis showed that triple-negative IBTR and lower amount of radioactive-labeled tracer (99mtechnetium) used during rSLNB were associated with developing regional recurrence as first event after negative rSLNB ($P < 0.05$).

CONCLUSIONS:

The risk of developing regional recurrence after negative rSLNB is low. The low relapse rate supports the safety of rSLNB as primary nodal staging tool in IBTR. The time has come for clinical guidelines to adopt rSLNB as axillary staging tool in patients with IBTR.

Impactfactor: 3.857

Routine versus on demand removal of the syndesmotic screw; a protocol for an international randomised controlled trial (RODEO-trial)

Dingemans SA, Birnie MFN, Sanders FRK, van den Bekerom MPJ, Backes M, van Beeck E, Bloemers FW, van Dijkman B, Flikweert E, Haverkamp D, Holtslag HR, Hoogendoorn JM, Joosse P, Parkkinen M, Roukema G, Sosef N, Twigt BA, van Veen RN, **van der Veen AH**, Vermeulen J, Winkelhagen J, van der Zwaard BC, et al.
BMC Musculoskelet Disord. 2018 Jan 31 19(1):35

BACKGROUND:
Syndesmotic injuries are common and their incidence is rising. In case of surgical fixation of the syndesmosis a metal syndesmotic screw is used most often. It is however unclear whether this screw needs to be removed routinely after the syndesmosis has healed. Traditionally the screw is removed after six to 12 weeks as it is thought to hamper ankle functional and to be a source of pain. Some studies however suggest this is only the case in a minority of patients. We therefore aim to investigate the effect of retaining the syndesmotic screw on functional outcome.
DESIGN:
This is a pragmatic international multicentre randomised controlled trial in patients with an acute syndesmotic injury for which a metallic syndesmotic screw was placed. Patients will be randomised to either routine removal of the syndesmotic screw or removal on demand. Primary outcome is functional recovery at 12 months measured with the Olerud-Molander Score. Secondary outcomes are quality of life, pain and costs. In total 194 patients will be needed to demonstrate non-inferiority between the two interventions at 80% power and a significance level of 0.025 including 15% loss to follow-up.
DISCUSSION:
If removal on demand of the syndesmotic screw is non-inferior to routine removal in terms of functional outcome, this will offer a strong argument to adopt this as standard practice of care. This means that patients will not have to undergo a secondary procedure, leading to less complications and subsequent lower costs.

Impactfactor: 1.998

Safety and effectiveness of SGM-101 a fluorescent antibody targeting carcinoembryonic antigen for intraoperative detection of colorectal cancer: a dose-escalation pilot study

Boogerd LSF, Hoogstins CES, **Schaap DP**, Kusters M, Handgraaf HJM, van der Valk MJM, Hilling DE, Holman FA, Peeters KCMJ, Mieog JSD, van de Velde CJH, Farina-Sarasqueta A, van **Lijnschoten I**, Framery B, Pèlegrin A, Gutowski M, **Nienhuijs SW**, **de Hingh IHJT, Nieuwenhuijzen GAP, Rutten HJT**, Cailler F, Burggraaf J, et al.
Lancet Gastroenterol Hepatol. 2018 Mar 3(3):181-191. Epub 2018 Jan 30

BACKGROUND:
Tumour-targeted fluorescence imaging has the potential to advance current practice of oncological surgery by selectively highlighting malignant tissue during surgery. Carcinoembryonic antigen (CEA) is overexpressed in 90% of colorectal cancers and is a promising target for colorectal cancer imaging. We aimed to assess the tolerability of SGM-101, a fluorescent anti-CEA monoclonal antibody, and to investigate the feasibility to detect colorectal cancer with intraoperative fluorescence imaging.
METHODS:
We did an open-label, pilot study in two medical centres in the Netherlands. In the dose-escalation cohort, we included patients (aged =18 years) with primary colorectal cancer with increased serum CEA concentrations (upper limit of normal of =3 ng/mL) since diagnosis, who were scheduled for open or laparoscopic tumour resection. In the expansion cohort, we included patients (aged =18 years) with recurrent or peritoneal metastases of colorectal cancer, with increasing serum concentrations of CEA since diagnosis, who were scheduled for open surgical resection. We did not mask patients, investigators, or anyone from the health-care team. We assigned patients using a 3 + 3 dose design to 5 mg, 7·5 mg, or 10 mg of SGM-101 in the dose-escalation cohort. In the expansion cohort, patients received a dose that was considered optimal at that moment of the study but not higher than the dose used in the dose-escalation cohort. SGM-101 was administered intravenously for 30 min to patients 2 or 4 days before surgery. Intraoperative imaging was done to identify near-infrared fluorescent lesions, which were resected and assessed for fluorescence. The primary outcome was tolerability and safety of SGM-101, assessed before administration and continued up to 12 h after dosing, on the day of surgery, the first postoperative day, and follow-up visits at the day of discharge and the first outpatient clinic visit. Secondary outcomes were effectiveness of SGM-101 for detection of colorectal cancer, assessed by tumour-to-background ratios (TBR); concordance between fluorescent signal and tumour status of resected tissue; and diagnostic accuracy in both cohorts. This trial is registered with the Nederlands Trial Register, number NTR5673, and ClinicalTrials.gov, number NCT02973672.
FINDINGS:
Between January, 2016, and February, 2017, 26 patients (nine in the dose-escalation cohort and 17 in the expansion cohort) were included in this study. SGM-101 did not cause any treatment-related adverse events, although three possibly related mild adverse events were reported in three (33%) of nine patients in the dose-escalation cohort and five were reported in three (18%) of 17 patients in the expansion cohort. Five moderate adverse events were reported in three (18%) patients in the expansion cohort, but they were deemed unrelated to SGM-101. No changes in vital signs, electrocardiogram, or laboratory results were found after administration of the maximum dose of 10 mg of SGM-101 in both cohorts. A dose of 10 mg, administered 4 days before surgery, showed the highest TBR

(mean TBR 6·10 [SD 0·42] in the dose-escalation cohort). In the expansion cohort, 19 (43%) of 43 lesions were detected using fluorescence imaging and were not clinically suspected before fluorescent detection, which changed the treatment strategy in six (35%) of 17 patients. Sensitivity was 98%, specificity was 62%, and accuracy of fluorescence intensity was 84% in the expansion cohort.

INTERPRETATION:

This study presents the first clinical use of CEA-targeted detection of colorectal cancer and shows that SGM-101 is safe and can influence clinical decision making during the surgical procedure for patients with colorectal cancer.

Impactfactor: --

Salvage Abdominoperineal Resection for Squamous Cell Anal Cancer: A 30-Year Single-Institution Experience

Hagemans JA, Blinde SE, Nuyttens JJ, Morshuis WG, Mureau MA, Rothbarth J, Verhoef C, **Burger JW**

Ann Surg Oncol. 2018 Jul;25(7):1970-1979

BACKGROUND:

Failure of chemoradiotherapy (CRT) for anal squamous cell carcinoma (SCC) results in persistent or recurrent anal SCC. Treatment with salvage abdominoperineal resection (APR) can potentially achieve cure. The aims of this study are to analyze oncological and surgical outcomes of our 30-year experience with salvage APR for anal SCC after failed CRT and identify prognostic factors for overall survival (OS).

METHODS:

All consecutive patients who underwent salvage APR between 1990 and 2016 for histologically confirmed persistent or recurrent anal SCC after failed CRT were retrospectively analyzed.

RESULTS:

Forty-seven patients underwent salvage APR for either persistent (n = 24) or recurrent SCC (n = 23). Median OS was 47 months [95% confidence interval (CI) 10.0-84.0 months] and 5-year survival was 41.6%, which did not differ significantly between persistent or recurrent disease (p = 0.551). Increased pathological tumor size (p < 0.001) and lymph node involvement (p = 0.014) were associated with impaired hazard for OS on multivariable analysis, and irradical resection only (p = 0.001) on univariable analysis. Twenty-one patients developed local recurrence after salvage APR, of whom 8 underwent repeat salvage surgery and 13 received palliative treatment. Median OS was 9 months (95% CI 7.2-10.8 months) after repeat salvage surgery and 4 months (95% CI 2.8-5.1 months) following palliative treatment (p = 0.055).

CONCLUSIONS:

Salvage APR for anal SCC after failed CRT resulted in adequate survival, with 5-year survival of 41.6%. Negative prognostic factors for survival were increased tumor size, lymph node involvement, and irradical resection. Patients with recurrent anal SCC after salvage APR had poor prognosis, irrespective of performance of repeat salvage surgery, which never resulted in cure.

Impactfactor: *3.857*

Salvage endoscopic resection in patients with esophageal adenocarcinoma after chemoradiotherapy

Noordzij IC, Curvers WL, Huysentruyt CJ**, Nieuwenhuijzen GA,** Creemers GJ, van der Sangen MJ, Schoon EJ

Endosc Int Open. 2018 Sep;6(9):E1126-E1129

Background and study aims For early esophageal adenocarcinoma, endoscopic resection is an accepted curative treatment with an excellent long-term prognosis. Case series from Japan have reported endoscopic resection of residual esophageal squamous cell carcinoma after chemoradiotherapy. This is the first report describing endoscopic resection of residual esophageal adenocarcinoma after chemoradiotherapy. Two patients with advanced esophageal adenocarcinoma had been treated with chemoradiotherapy because comorbidity precluded esophageal resection. When residual tumor was observed endoscopically, complete remission was achieved by salvage endoscopic therapy alone or in combination with argon plasma coagulation (APC). Both patients achieved long-term sustained remission and died of non-tumor-related causes.

Impactfactor: --

Session 3: Beyond the boundaries of Total Mesorectal Excision - where surgeons fear to tread

Patel A, Holm T, Wale A, **Rutten H**, Nicholls J, Hawkins M, Steele RJC, Marks J, Brown G

Colorectal Dis. 2018 May 20 Suppl 1:61-64. doi: 10.1111/codi.14082

Approximately 10-15% of patients present with an advanced rectal cancer that extends beyond the conventional total mesorectal excision (TME) planes. In such cases extending the surgery to ensure resection with clear margins (R0 resection) is essential in order to achieve long-term cure. Professor Holm describes the techniques of beyond-TME exenterative surgery, the methods of patient selection and outcomes.

Impactfactor: *2.778*

Session 3: Boosting primary and recurrent rectal cancer: how far can we push the radiotherapy envelope?

Balyasnikova S, Vuong T, Wale A, Chong I, **Rutten H**, Brown G

Colorectal Dis. 2018 May;20 Suppl 1:88-91

Neoadjuvant pelvic radiotherapy is widely used for patients with advanced rectal cancer. The trade-off between dose and response is well-established, yet little consensus remains on the precise methods of delivery and doses given in different scenarios. Professor Vuong reviews the evidence base and trial evidence on the escalation of radiotherapy dose and the methods of achieving this.

Impactfactor: 2.778

Session 3: Intra-operative radiotherapy - creating new surgical boundaries

Patel A, Chang G, Wale A, Chong I, **Rutten H**, Nicholls J, Hawkins M, Steele RJC, Marks J, Brown G

Colorectal Dis. 2018 May 20 Suppl 1:65-75

In patients with advanced and recurrent colorectal cancer, surgical resection with clear margins is the greatest challenge and is limited by known anatomical constraints. Preoperative or intra-operative assessment of the limits of surgical dissection may help to explore the possibility of improving resectability through either targeted external beam radiotherapy or intra-operative radiotherapy. Professor Chang reviews the evidence base and potential advantages and disadvantages of this approach, whilst the expert panel agree a consensus on the evidence for assessment and therapy of such patients.

Impactfactor: 2.778

Shift Towards Older Bariatric Patients

Versteegden DPA, Buise MP**, Nienhuijs SW**

Obes Surg. 2018 Feb 28(2):555-556.

Impactfactor: 3.895

Short-term complications in elderly patients undergoing CRS and HIPEC: A single center's initial experience

Oemrawsingh A, de Boer NL, Brandt-Kerkhof AR, Verhoef C, **Burger JW**, Madsen EV

Eur J Surg Oncol. 2018 Nov 2 [Epub ahead of print]

INTRODUCTION:

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a well-established curative treatment for patients with peritoneal carcinomatosis (PC) from colorectal cancer (CRC) and pseudomyxoma peritonei (PMP). The study's aim was to present a single center's initial experience with CRS and HIPEC and report the postoperative morbidity in elderly patients.

METHODS:

A retrospective observational study was conducted of all patients with peritoneally disseminated colorectal cancer or pseudomyxoma peritonei undergoing CRS and HIPEC between March 2014 and March 2017. Patient characteristics and the peri- and postoperative course were reviewed. Elderly patients were defined as those aged = 65 years. Postoperative complications were classified according to the Serious Adverse Event (SAE) grading system.

RESULTS:

122 patients undergoing CRS and HIPEC were split into two groups based on age (< 65 years versus?=?65 years) at the time of surgery. Both groups were comparable for ASA score, Peritoneal Cancer Index (PCI), procedure time and blood loss. Serious Adverse Event (SAE) grade?>?3 morbidity was 26.7% in the elderly group as opposed to 10.4% in the younger group (p?=?0.034). Both univariate and multivariate logistic regression analysis demonstrated that age was a significant risk factor (OR?=?3.2, 95% CI 1.1-9.4, p?=?0.033) for severe postoperative morbidity (SAE?>?3).

CONCLUSION:

This retrospective study showed advanced age to be a significant risk factor for SAE?>?3, after undergoing CRS and HIPEC. The initial institutional experience resembles previously published literature in terms of severe postoperative morbidity in elderly patients.

Impactfactor: 3.688

Should the Extended Lateral Approach Remain Part of Standard Treatment in Displaced Intra-articular Calcaneal Fractures?

Jansen SC, Bransen J, van Montfort G, Besselaar AT**, van der Veen AH**

J Foot Ankle Surg. 2018 Nov - Dec;57(6):1120-1124

The aim of this study was to evaluate the results of open reduction and internal fixation through the extended lateral approach (ELA) in displaced intra-articular calcaneal fractures and to determine whether this approach should remain part of standard therapy. This retrospective cohort study included 60 patients with 64 displaced intra-articular calcaneal fractures who underwent surgical treatment through the ELA. Outcome measures were the visual analog scale foot and ankle (VAS FA), the American Orthopedic Foot and Ankle Society (AOFAS) score, surgical site infections (SSIs), and reoperations. We determined the AOFAS score for 40 patients with 42 fractures, and 42 patients with 44 fractures completed the VAS FA questionnaire. The mean VAS FA score was 61.0 ± 23.4 and the median AOFAS score was 83 (range 33 to 100), with 55% good to excellent scores. We found 10.9% superficial SSIs successfully treated with antibiotics. In 4.7% of patients a deep SSI was diagnosed, wherefore premature implant

removal was necessary. Patients with an SSI did not have significantly lower VAS FA or AOFAS scores than did patients without an SSI (p = .318 and p = .766, respectively). Implant removal in absence of SSIs was necessary in 17 patients because of pain, and 3 patients needed secondary arthrodesis because of persistent pain. We concluded that the ELA proved to be a safe procedure, and moreover the most common complications did not influence the long-term outcomes of patients. However, recent literature demonstrates that less invasive techniques seem to exceed the ELA with respect to wound complications.

Impactfactor: 1.138

Snapshot Study on the Value of Omentoplasty in Abdominoperineal Resection with Primary Perineal Closure for Rectal Cancer

Blok RD, Musters GD, Borstlap WA, Buskens CJ, Bemelman WA, Tanis PJ; Collaborative Dutch Snapshot Research Group: **Brinkman DJ**, **Rutten HJ, Simkens GA**

Ann Surg Oncol. 2018 Mar;25(3):729-736

BAKGROUND:

Perineal wound complications are often encountered following abdominoperineal resection (APR). Filling of the pelvic space by omentoplasty (OP) might prevent these complications, but there is scant evidence to support its routine application.

OBJECTIVE:

The aim of this study was to evaluate the impact of OP on perineal wound complications.

METHODS:

All patients undergoing APR with primary perineal closure (PPC) for non-locally advanced rectal cancer in 71 Dutch centers in 2011 were selected from a cross-sectional snapshot study. Outcomes were compared between PPC with or without OP, which was based on variability in practice among surgeons.

RESULTS:

Of 639 patients who underwent APR for rectal cancer, 477 had a non-locally advanced tumor and PPC was performed. Of those, 172 (36%) underwent OP. Patients with OP statistically more often underwent an extralevator approach (32% vs. 14%). Median follow-up was 41 months (interquartile range 22-47). There were no significant differences with or without OP in terms of non-healing of the perineal wound at 30 days (47% vs. 48%), non-healing at the end of follow-up (9% vs. 5%), pelvic abscess (12% vs. 13%) or re-intervention for ileus (5% vs. 3%). Perineal hernia developed significantly more often after OP (13% vs. 7%), also by multivariable analysis (odds ratio 2.61, 95% confidence interval 1.271-5.364; p = 0.009).

CONCLUSIONS:

In contrast to previous assumptions, OP after APR with PPC appeared not to improve perineal wound healing and seemed to increase the occurrence of perineal hernia. These findings question the routine use of OP for primary filling of the pelvic space.

Impactfactor: 3.857

Supervised Exercise Therapy for Intermittent Claudication Is Increasingly Endorsed by Dutch Vascular Surgeons

Hageman D, Lauret GJ, Gommans LNM, Koelemay MJW, **van Sambeek MRHM**, Scheltinga MRM, **Teijink JAW**

Ann Vasc Surg. 2018 Feb 47:149-156.. Epub 2017 Sep 9

BACKGROUND: Although supervised exercise therapy (SET) is generally accepted as an effective noninvasive treatment for intermittent claudication (IC), Dutch vascular surgeons were initially somewhat hesitant as reported by a 2011 questionnaire study. Later on, a nationwide multidisciplinary network for SET was introduced in the Netherlands. The aim of this questionnaire study was to determine possible trends in conceptions among Dutch vascular surgeons regarding the prescription of SET.

METHODS: In the year of 2015, Dutch vascular surgeons, fellows, and senior residents were asked to complete a 26-item questionnaire including issues that were considered relevant for prescribing SET such as patient selection criteria and comorbidity. Outcome was compared to the 2011 survey.

RESULTS: Data of 124 respondents (82% males; mean age 46 years; 64% response rate) were analyzed. SET referral rate of new IC patients was not different over time (2015: 81% vs. 2011: 75%; P = 0.295). However, respondents were more willing to prescribe SET in IC patients with chronic obstructive pulmonary disease (2015: 86% vs. 2011: 69%; P = 0.002). Nevertheless, a smaller portion of respondents found that SET was also indicated for aortoiliac disease (2015: 63% vs. 2011: 76%; P = 0.049). Insufficient health insurance coverage and/or personal financial resources were the most important presumed barriers preventing patients from initiating SET (80% of respondents). Moreover, 94% of respondents judged that SET should be fully reimbursed by all Dutch basic health insurances.

CONCLUSIONS: The concept of SET for IC is nowadays generally embraced by the vast majority of Dutch vascular surgeons. SET may have gained in popularity in IC patients with cardiopulmonary comorbidity. However, SET remains underutilized for aortoiliac disease. Reimbursement is considered crucial for a successful SET implementation.

Impactfactor: 1.363

Supervised exercise therapy versus home-based exercise therapy versus walking advice for intermittent claudication

Hageman D, Fokkenrood HJ, Gommans LN, van den Houten MM, Teijink JA

Cochrane Database Syst Rev. 2018 Apr 6 4:CD005263. 10.1002/14651858.CD005263.pub4

BACKGROUND:

Although supervised exercise therapy (SET) provides significant symptomatic benefit for patients with intermittent claudication (IC), it remains an underutilized tool. Widespread implementation of SET is restricted by lack of facilities and funding. Structured home-based exercise therapy (HBET) with an observation component (e.g., exercise logbooks, pedometers) and just walking advice (WA) are alternatives to SET. This is the second update of a review first published in 2006.

OBJECTIVES:

The primary objective was to provide an accurate overview of studies evaluating effects of SET programs, HBET programs, and WA on maximal treadmill walking distance or time (MWD/T) for patients with IC. Secondary objectives were to evaluate effects of SET, HBET, and WA on pain-free treadmill walking distance or time (PFWD/T), quality of life, and self-reported functional impairment.

SEARCH METHODS:

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register (December 16, 2016) and the Cochrane Central Register of Controlled Trials (2016, Issue 11). We searched the reference lists of relevant studies identified through searches for other potential trials. We applied no restriction on language of publication.

SELECTION CRITERIA:

We included parallel-group randomized controlled trials comparing SET programs with HBET programs and WA in participants with IC. We excluded studies in which control groups did not receive exercise or walking advice (maintained normal physical activity). We also excluded studies comparing exercise with percutaneous transluminal angioplasty, bypass surgery, or drug therapy.

DATA COLLECTION AND ANALYSIS:

Three review authors (DH, HF, and LG) independently selected trials, extracted data, and assessed trials for risk of bias. Two other review authors (MvdH and JT) confirmed the suitability and methodological quality of trials. For all continuous outcomes, we extracted the number of participants, mean outcome, and standard deviation for each treatment group through the follow-up period, if available. We extracted Medical Outcomes Study Short Form 36 outcomes to assess quality of life, and Walking Impairment Questionnaire outcomes to assess self-reported functional impairment. As investigators used different scales to present results of walking distance and time, we standardized reported data to effect sizes to enable calculation of an overall standardized mean difference (SMD). We obtained summary estimates for all outcome measures using a random-effects model. We assessed the quality of evidence using the GRADE approach.

MAIN RESULTS:

For this update, we included seven additional studies, making a total of 21 included studies, which involved a total of 1400 participants: 635 received SET, 320 received HBET, and 445 received WA. In general, SET and HBET programs consisted of three exercise sessions per week. Follow-up ranged from six weeks to two years. Most trials used a treadmill walking test to investigate effects of exercise therapy on walking capacity. However, two trials assessed only quality of life, functional impairment, and/or walking behavior (i.e., daily steps measured by pedometer). The overall methodological quality of included trials was moderate to good. However, some trials were small with respect to numbers of participants, ranging from 20 to 304.SET groups showed clear improvement in MWD/T compared with HBET and WA groups, with overall SMDs at three months of 0.37 (95% confidence interval [CI] 0.12 to 0.62; P = 0.004; moderate-quality evidence) and 0.80 (95% CI 0.53 to 1.07; P < 0.00001; high-quality evidence), respectively. This translates to differences in increased MWD of approximately 120 and 210 meters in favor of SET groups. Data show improvements for up to six and 12 months, respectively. The HBET group did not show improvement in MWD/T compared with the WA group (SMD 0.30, 95% CI -0.45 to 1.05; P = 0.43; moderate-quality evidence).Compared with HBET, SET was more beneficial for PFWD/T but had no effect on quality of life parameters nor on self-reported functional impairment. Compared with WA, SET was more beneficial for PFWD/T and self-reported functional impairment, as well as for some quality of life parameters (e.g., physical functioning, pain, and physical component summary after 12 months), and HBET had no effect.Data show no obvious effects on mortality rates. Thirteen of the 1400 participants died, but no deaths were related to exercise therapy. Overall, adherence to SET was approximately 80%, which was similar to that reported with HBET. Only limited adherence data were available for WA groups.

AUTHORS' CONCLUSIONS:

Evidence of moderate and high quality shows that SET provides an important benefit for treadmill-measured walking distance (MWD and PFWD) compared with HBET and WA, respectively. Although its clinical relevance has not been definitively demonstrated, this benefit translates to increased MWD of 120 and 210 meters after three months in SET groups. These increased walking distances are likely to have a positive impact on the lives of patients with IC. Data provide no clear evidence of a difference between HBET and WA. Trials show no clear differences in quality of life parameters nor in self-reported functional impairment between SET and HBET. However, evidence is of low and very low quality, respectively. Investigators detected some improvements in quality of life favoring SET

over WA, but analyses were limited by small numbers of studies and participants. Future studies should focus on disease-specific quality of life and other functional outcomes, such as walking behavior and physical activity, as well as on long-term follow-up.

Update of Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. [Cochrane Database Syst Rev. 2013]

Impactfactor: 6.754

Symptoms of anxiety and depression among colorectal cancer survivors from the population-based longitudinal PROFILES Registry: Prevalence predictors and impact on quality of life

Mols F, Schoormans D, **de Hingh I**, Oerlemans S, Husson O

Cancer. 2018 Jun 15 124(12):2621-2628. Epub 2018 Apr 6

BACKGROUND:

The aims of this study were to prospectively assess symptoms of anxiety and depression among survivors of colorectal cancer (CRC), to compare these survivors with a normative population, and to identify subgroups at risk for experiencing symptoms of anxiety and/or depression across a 4-year time period. Also, the impact on health-related quality of life (HRQOL) was studied.

METHODS:

The population-based Eindhoven Cancer Registry was used to select patients diagnosed with CRC between 2000 and 2009. The Hospital Anxiety and Depression Scale and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (HRQOL) were completed by patients in 2010 (n?=?2625 [73% response rate]), 2011, 2012, and 2013 and by an age- and sex-matched normative sample (n?=?315) in 2011.

RESULTS:

Patients reported a significantly higher prevalence of depression (19.0% vs 12.8%) and anxiety (20.9% vs 11.8%) in comparison with the norm. Anxiety was stable, whereas depression scores changed over time, although this was not clinically relevant. A longer time since diagnosis was associated with fewer depressive symptoms over time, whereas older age and being male were associated with less anxiety and more depression. Being married was associated with less anxiety and depression, and a low education level and comorbid conditions were associated with more anxiety and depression. Higher levels of symptoms of depression and anxiety were associated with a lower global quality of life and lower physical, role, cognitive, emotional, and social functioning over time.

CONCLUSIONS:

Because of the increased prevalence of depression and anxiety among patients with CRC and their negative effect on HRQOL, screening and referral are of the utmost importance, especially among those who are single, have a low educational level, and have comorbid conditions, even years after diagnosis and treatment.

Impactfactor:6.537

Systematic review of transversus abdominis release in complex abdominal wall reconstruction

Wegdam JA, Thoolen JMM, **Nienhuijs SW**, de Bouvy N, de Vries Reilingh TS

Hernia. 2018 Dec 11. [Epub ahead of print]

BACKGROUND: Transversus abdominis release (TAR), as a type of posterior component separation, is a new myofascial release technique in complex ventral hernia repair. TAR preserves rectus muscle innervation, creates an immense retromuscular plane and allows bilaminar ingrowth of the mesh. The place of the TAR within the range of established anterior component separation techniques (CST) is unclear. Aim of this systematic literature review is to estimate the position of the TAR in the scope of ventral hernia repair techniques.

METHODS: MEDLINE, Embase, Pubmed and the Cochrane controlled trials register and Science citation index were searched using the following terms: 'posterior component separation', 'transversus abdominis release', 'ventral hernia repair', 'complex abdominal wall reconstruction'. To prevent duplication bias, only studies with a unique cohort of patients who underwent transversus abdominis release for complex abdominal wall reconstruction were eligible. Postoperative complications and recurrences had to be registered adequately. The rate of surgical site occurrences and recurrences of the TAR were compared with those after anterior CST, published earlier in two meta-analyses.

RESULTS: Five articles met our strict inclusion criteria, describing 646 TAR patients. Methodological quality per study was good. Mean hernia surface was 509 cm2 and 88% of the hernias were located in the midline. Preoperative risk stratification was distributed in low risk (10%), co-morbid (55%), potentially contaminated (32%) and infected (3%). Pooled calculations demonstrated a mean SSO rate of 15% after TAR (20-35% after anterior CST) and a mean 2-year hernia recurrence rate of 4% (13% after anterior CST). Mean hernia surface was 300 cm2 in anterior component separation studies.

CONCLUSION: This review demonstrates that the transversus abdominis release is a good alternative for anterior CST in terms of SSO and recurrence, especially in very large midline ventral hernias.

Impactfactor: 2.417

Textbook Outcome: an Ordered Composite Measure for Quality of Bariatric Surgery

Poelemeijer YQM, Marang-van de Mheen PJ, Wouters MWJM, **Nienhuijs SW**, Liem RSL

Obes Surg. 2018 Dec 19. [Epub ahead of print]

INTRODUCTION:

Textbook outcome (TO) studies have previously shown that a composite measure can provide additional information on the overall quality of surgical care. However, these were binominal outcomes which do not give individual hospitals the required information on how to improve their performance. The aim of this study is to create an ordered TO consisting of multiple outcome parameters for bariatric surgery to assess the extent of hospital variation.

METHODS:

Patients who underwent a primary bariatric procedure in the Netherlands were included for analyses. The outcomes were ordered as mortality, severe postoperative complications, readmission, mild complications and prolonged length of stay (LOS) within 30 days after primary surgery with TO defined as none of these outcomes occurring. Hospitals were identified with a significantly higher or lower observed/expected ratio than expected based on case-mix and the extent of hospital variation was expressed as the median and interquartile range (IQR).

RESULTS:

From a total of 27,360 patients on average, 88.7% reached TO (range 35.5-96.9%). Two hospitals had less than expected TO due to more prolonged LOS (57.6%) in one hospital and more mild complications in another (17.1%). Hospital variation was much smaller for TO (median OR 0.91 IQR [0.62-1.06]) than for an ordered TO (median POR 0.66 IQR [0.55-0.96]).

CONCLUSION:

Using the ordered TO for bariatric surgery, more hospital variation was captured thereby enabling individual hospitals to identify which outcomes and specific groups need improvement. This could attribute to the ongoing effort to improve the quality of the outcome of bariatric surgery.

Impactfactor: 3.895

The administration of adjuvant chemo(-immuno) therapy in the post ACOSOG-Z0011 era; a population based study

Poodt IGM, Rots ML, **Vugts G**, van Dalen T, Kuijer A, **Vriens BEPJ, Nieuwenhuijzen GAP, Schipper RJ**

Eur J Surg Oncol. 2018 Aug 44(8):1151-1156. Epub 2018 Mar 14

PURPOSE:

The ACOSOG-Z0011-study has resulted in a trend to a more conservative treatment of the axilla for selected sentinel-node-positive patients. However, axillary nodal involvement has always been an important factor for tumor staging and tailoring adjuvant chemotherapy plans. This study evaluates the impact of omitting completion axillary lymph node dissection (cALND) on the administration of adjuvant chemo (-immuno)therapy in Dutch clinical T1-2N0M0 (cT1-2N0M0) sentinel-node-positive breast cancer patients.

METHODS:

Data were obtained from the nationwide NABON breast cancer audit. Descriptive analyses were used to demonstrate trends in axillary surgery and adjuvant chemo (-immuno)therapy. Multivariable logistic regression analyses were used to identify factors associated with the prescription of chemo (-immuno)therapy.

RESULTS:

In this cohort of 4331 patients, the omission of a cALND increased from 34% to 92%, and the administration of chemo (-immuno)therapy decreased from 68% to 55%, between 2011 and 2015 ($P < 0.001$). Patients treated with cALND had an OR of 2.2 for receiving adjuvant chemo (-immuno)therapy compared with SLNB only patients. Lower age, a hormone receptor (HR) status other than HR-positive, HER2-negative, increasing tumor grade and stage, and a lymph node status = pN2 were independently associated with a higher probability of chemo (-immuno)therapy ($P < 0.05$).

CONCLUSIONS:

This study showed that Dutch cT1-2N0M0 sentinel node-positive breast cancer patients treated with cALND had a higher independent probability for receiving adjuvant chemo (-immuno)therapy compared with SLNB only patients, even when corrected for lymph node status and HR-status. Probably, the decisions to administer adjuvant chemo (-immuno)therapy were not only based on guidelines and tumor characteristics, but also on the preferences from physicians and patients.

Impactfactor: 3.688

The current practice of cytoreductive surgery and HIPEC for colorectal peritoneal metastases: Results of a worldwide web-based survey of the Peritoneal Surface Oncology Group International (PSOGI)

Bushati M, Rovers KP, Sommariva A, Sugarbaker PH, Morris DL, Yonemura Y, Quadros CA, Somashekhar SP, Ceelen W, Dubé P, Li Y, Verwaal VJ, Glehen O, Piso P, Spiliotis J, Teo MC, González-Moreno S, Cashin PH, Lehmann K, Deraco M, Moran B, **de Hingh IH**

Eur J Surg Oncol. 2018 Dec;44(12):1942-1948

BACKGROUND:
At present, selected patients with resectable colorectal peritoneal metastases (CRC-PM) are increasingly treated with a combination therapy of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). The aim of this study was to investigate the current worldwide practice.
METHODS:
HIPEC experts from 19 countries were invited through the Peritoneal Surface Oncology Group International (PSOGI) to complete an online survey concerning their personal expertise and current hospital and countrywide practice.
RESULTS:
It is estimated that currently more than 3800 patients with CRC-PM (synchronous and metachronous) are annually treated with CRS and HIPEC in 430 centers. Integration of CRS and HIPEC in national guidelines varies, resulting in large treatment disparities between countries. Amongst the experts, there was general agreement on issues related to indication, surgical technique and follow up but less on systemic chemotherapy or proactive strategies.
CONCLUSION:
This international survey demonstrates that CRS and HIPEC is now performed on a large scale for CRC-PM patients. Variation in treatment may result in heterogeneity in surgical and oncological outcomes, emphasising the necessity to reach consensus on several issues of this comprehensive procedure. Future initiatives directed at achieving an international consensus statement are needed.

Impactfactor: 3.688

The Dutch Audit of Carotid Interventions: Transparency in Quality of Carotid Endarterectomy in Symptomatic Patients in the Netherlands

Karthaus EG, Vahl A, Kuhrij LS, Elsman BH, Geelkerken RH, Wouters MW, Hamming JF, de Borst GJ; Dutch Society of Vascular Surgery; Steering Committee of the Dutch Audit for Carotid Interventions; Dutch Institute for Clinical Auditing: **Teijink JA, Sambeek MR**

Eur J Vasc Endovasc Surg. 2018 Oct;56(4):476-485

BACKGROUND:
The Dutch Audit for Carotid Interventions (DACI) registers all patients undergoing interventions for carotid artery stenosis in the Netherlands. This study describes the design of the DACI and results of patients with a symptomatic stenosis undergoing carotid endarterectomy (CEA). It aimed to evaluate variation between hospitals in process of care and (adjusted) outcomes, as well as predictors of major stroke/death after CEA.
METHODS:
All patients with a symptomatic stenosis, who underwent CEA and were registered in the DACI between 2014 and 2016 were included in this cohort. Descriptive analyses of patient characteristics, process of care, and outcomes were performed. Casemix adjusted hospital procedural outcomes as (30 day/in hospital) mortality, stroke/death, and major stroke/death, were compared with the national mean. A multivariable logistic regression model (backward elimination at $p > 0.10$) was used to identify predictors of major stroke/death.
RESULTS:
A total of 6459 patients, registered by 52 hospitals, were included. The majority (4,832, 75%) were treated <2 weeks after their first hospital consultation, varying from 40% to 93% between hospitals. Mortality, stroke/death, and major stroke/death were, respectively, 1.1%, 3.6%, and 1.8%. Adjusted major stroke/death rates for hospital comparison varied between 0 and 6.5%. Nine hospitals performed significantly better, none performed significantly worse. Predictors of major stroke/death were sex, age, pulmonary disease, presenting neurological symptoms, and peri-operative shunt.
CONCLUSION:
CEA in The Netherlands is associated with an overall low mortality and (major) stroke/death rate. Whereas the indicator time to intervention varied between hospitals, mortality and (major) stroke/death were not significantly distinctive enough to identify worse practices and therefore were unsuitable for hospital comparison in the Dutch setting. Additionally, predictors of major stroke/death at population level could be identified.

Impactfactor 3.877

The Effect of 6 and 12 months Duodenal-Jejunal Bypass Liner Treatment on Obesity and Type 2 Diabetes: a Crossover Cohort Study

van Rijn S*, Betzel B, de Jonge C, van Dijk DPJ, Janssen IM, Berends FJ, Bouvy ND, Greve JWM

Obes Surg. 2018 May;28(5):1255-1262

OBJECTIVE:
The aim of this research was to study the duodenal-jejunal bypass liner (DJBL) treatment for obesity and type 2 diabetes mellitus (T2DM) in patients after dietary treatment in a cross-over design.
BACKGROUND:
DJBL treatment has been proven effective for treatment of obesity and T2DM. However, data on safety and efficacy of a 12-month DJBL treatment is limited.
METHODS:
In 2014, our research group reported on a multicenter randomized clinical trial. Patients were randomized to DJBL

or dietary treatment (control group). Twenty-eight patients crossed over after their dietary treatment and received up to 12 months of DJBL treatment. Patient visits were conducted at baseline, during DJBL treatment (1 week, 1-6, 9, 12 months) and 6 months after removal of the liner. Patients underwent a standard physical examination, blood sampling, assessment of adverse events, nutritional and diabetes counseling, and a standardized meal tolerance test.

RESULTS:

Of the 28 patients included in this study, 24 patients completed 6 months of treatment. Eighteen patients were extended to 12 months of DJBL treatment; 13 patients completed this treatment period. After 6 months of DJBL treatment, a significant increase in excess weight loss (EWL) and decrease in weight, BMI, HbA1c, fasting glucose, cholesterol, HDL and LDL improved significantly. After 12 months of DJBL treatment, these parameters stabilized.

CONCLUSIONS:

The DJBL is an effective, minimally invasive treatment option. Even after successful treatment with dietary restrictions, the DJBL is still capable of significantly reducing weight and improving cardiovascular and type 2 diabetes mellitus parameters in obese patients.

Impactfactor 3.895

**Ten tijde van publicatie ook verbonden aan: Department of General Surgery, Maastricht University Medical Center, Maastricht*

The Effect of Myopenia on the Inflammatory Response Early after Colorectal Surgery

Smeets BJJ, Brinkman DJ, Horsten ECJ, Langius JAE, **Rutten HJT**, de Jonge WJ, **Luyer MDP**

Nutr Cancer. 2018 Apr 70(3):460-466

BACKGROUND:

Myopenia (low skeletal muscle mass) is associated with an increased risk of complications following colorectal surgery, however, the underlying mechanism is poorly understood. This study investigates the effect of myopenia on the early postoperative systemic inflammatory response.

MATERIALS AND METHODS:

In 78 patients undergoing colorectal surgery, the presence of myopenia was preoperatively assessed using computed tomography images of the third lumbar vertebra. Interleukin-8 (IL-8) and soluble tumor necrosis factor receptor-1 (TNFRSF1A) were measured in plasma before and 4 h after start of surgery as part of a randomized controlled trial investigating the effect of perioperative gum chewing on the inflammatory response. Multivariable linear regression analysis was performed to assess the effect of myopenia on inflammatory markers while correcting for possible confounders.

RESULTS:

Four hours after start of surgery, IL-8 was higher in patients with myopenia than in patients without myopenia (352 ± 268 vs. 239 ± 211 pg/ml, P = 0.048), while TNFRSF1A was similar between groups. After adjusting for sex and the intervention with perioperative gum chewing, myopenia remained associated with higher postoperative IL-8 concentrations (P = 0.047).

CONCLUSION:

Myopenia may affect IL-8 early after colorectal surgery. However, more studies are needed to validate these findings.

Impactfactor: 2.261

The evolving management of small bowel adenocarcinoma

de Bree E, **Rovers KP**, Stamatiou D, Souglakos J, Michelakis D, **de Hingh IH**

Acta Oncol. 2018 Jun 57(6):712-722. doi: Epub 2018 Jan 30

BACKGROUND:

Small bowel adenocarcinoma (SBA) is rare despite the fact that the small bowel represents the longest part and has the largest surface of all alimentary tract sections. Its incidence is 50-fold lower than that of colorectal carcinoma. It is often diagnosed at an advanced stage due to atypical and late symptoms, its low index of suspicion, difficult endoscopic access and poor detection by radiological imaging, resulting in impaired outcome. Due to its rarity and being molecularly a unique intestinal cancer, data regarding its optimal management are relatively sparse.

MATERIAL AND METHODS:

A PubMed search was performed to identify relevant manuscripts that were recently published. Emerging data regarding the pathogenesis, the diagnosis and the treatment of SBA that resulted from recent research are discussed in this comprehensive review.

RESULTS:

Genomic analysis has demonstrated that SBA is a molecularly unique intestinal cancer. Double balloon enteroscopy and capsule endoscopy are novel techniques which may result in earlier diagnosis and consequently in improvement of the generally poor prognosis. For clinically localized disease, the quality of surgery has recently been defined, with removal of at least 8-10 lymph nodes correlating with improved prognosis. Moreover, adjuvant chemotherapy seems to improve outcome of stage III disease. The combination of a fluoropyrimidine and oxaliplatin appears to be the most effective systemic chemotherapy for disseminated disease. Genomic profiling

can identify potentially targetable genomic alterations in a significant proportion of SBA patients. The role of administration of targeted agents or immune checkpoint inhibitors is still unknown and subject of ongoing clinical trials. In the common case of peritoneal metastases, recent studies have shown that cytoreductive surgery and intraoperative hyperthermic intraperitoneal chemotherapy may be an attractive treatment option in selected patients.

CONCLUSIONS:

SBA is a rare and unique malignancy, whose diagnostic approach and treatment are evolving, resulting in improved outcome.

Impactfactor: 3.473

The impact of radiological retroperitoneal lymphadenopathy on survival after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases

van der Werf LR, Wassenaar E, de Niet A, Lalezari F, **Braam HJ**, van Ramshorst B, Nederend J, **de Hingh IHJT**, Kok NFM, Aalbers AGJ

Eur J Surg Oncol. 2018 Nov 1. pii: S0748-7983(18)31986-3. [Epub ahead of print]

OBJECTIVES:

To investigate the impact of retroperitoneal lymphadenopathy (RPLP) on pre-operative CT scan on overall survival (OS) and disease-free survival (DFS) after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) for peritoneal metastases (PM) of colorectal cancer.

BACKGROUND:

In patients with PM enlarged retroperitoneal lymph nodes (RPLP) are usually considered extra-regional lymph node metastases and therefore these patients may be excluded from CRS-HIPEC. This is a clinical dilemma since it is often hard to obtain histology from these nodes.

METHODS:

In this multicenter, retrospective study all consecutive patients with colorectal PM treated with CRS-HIPEC between 2004 and 2013 were included. The preoperative CT-scan was re-analyzed for the presence of RPLP based on the radiological appearance of enlarged lymph nodes. Outcomes were OS and DFS. Kaplan-Meier methods and Cox regression modeling were used to analyze the impact of RPLP on OS and DFS.

RESULTS:

In 25 of 401 patients (6.1%) RPLP was observed on the preoperative CT-scan. Patient, tumor and surgical characteristics did not statistically significantly differ between groups with and without RPLP. After a median follow-up of 46 months, the one-, three- and five-year survival was 80%, 59%, 38% and 90%, 50%, 36% in the group with and without RPLP respectively. Median OS (47 vs. 35 months, logrank: p?=?0.70) and median DFS (14 vs. 15 months, logrank: p?=?0.81) did not statistically significantly differ between groups. In multivariable analysis, RPLP did not significantly influence survival.

CONCLUSION:

Enlarged retroperitoneal lymph nodes on a pre-operative CT-scan should not automatically exclude patients from CRS-HIPEC.

Impactfactor: 3.688

The Influence of Age on Complications and Overall Survival After Ivor Lewis Totally Minimally Invasive Esophagectomy

Baranov NS, van Workum F, van der Maas J, Kouwenhoven E, van Det M, van den Wildenberg FJH, Polat F, **Nieuwenhuijzen GAP, Luyer MDP**, Rosman C

J Gastrointest Surg. 2018 Dec 18. [Epub ahead of print]

BACKGROUND:

The number of elderly patients suffering from esophageal cancer is increasing, due to an increasing incidence of esophageal cancer and increasing life expectancy. However, the effect of age on morbidity, mortality, and survival after Ivor Lewis total minimally invasive esophagectomy (TMIE) is not well known.

METHODS:

A prospectively documented database from December 2010 to June 2017 was analyzed, including all patients who underwent Ivor Lewis TMIE for esophageal cancer in three Dutch high-volume esophageal cancer centers. Patients younger than 75 years (younger group) were compared to patients aged 75 years or older (elderly group). Baseline patient characteristics and perioperative data were included. Surgical complications were graded using the Clavien-Dindo scale. The primary outcome was postoperative complications Clavien-Dindo =?3. Secondary outcome parameters were postoperative complications, in-hospital mortality, 30- and 90-day mortality and survival.

RESULTS:

Four hundred and forty-six patients were included, 357 in the younger and 89 in the elderly group. No significant differences were recorded regarding baseline patient characteristics. There was no significant difference in complications graded Clavien-Dindo =?3 and overall complications, short-term mortality, and survival. Delirium occurred in 27.0% in the elderly and 11.8% in the younger group (p?<?0.001). After correction for baseline

comorbidity this difference remained significant (p?=?0.001). Median hospital length of stay was 13 days in the elderly and 11 days in the younger group (p?=?0.010).

CONCLUSIONS:

Ivor Lewis TMIE can be safely performed in selected elderly patients without increasing postoperative morbidity and mortality.

Impactfactor: 2.813

The liver-first approach for locally advanced rectal cancer and synchronous liver metastases

Nierop PM, Verseveld M, Galjart B, Rothbarth J, Nuyttens JJ, van Meerten E, **Burger JW**, Grünhagen DJ, Verhoef C

Eur J Surg Oncol. 2018 Dec 10. [Epub ahead of print]

BACKGROUND:

Patients with locally advanced rectal cancer (LARC) and synchronous liver metastases (sRLM) can be treated according to the liver-first approach. This study aimed to evaluate prognostic factors for completing treatment and in how many patients extensive lower pelvic surgery might have been omitted.

METHODS:

Retrospective analysis of all patients with LARC and sRLM treated at the Erasmus MC Cancer Institute according to the liver-first between 2003 and 2016.

RESULTS:

In total 129 consecutive patients were included. In 90 patients (70%) the liver-first was completed. Ten patients had a (near) complete response (ypT0-1N0) of their primary tumour. In 36 out of 39 patients not completing the liver-first protocol palliative rectum resection was withheld. Optimal cut-offs for CEA level (53.15?µg/L), size (3.85?cm) and number (4) of RLMs were identified. A preoperative CEA level above 53.15?µg/L was an independent predictor for non-completion of the liver-first protocol (p?=?0.005).

CONCLUSION:

Ten patients had a (near) complete response of their primary tumour and, in retrospect, rectum sparing therapies could have been considered. Together with 36 patient in whom palliative rectum resection was not necessary this entails that nearly 40% patients with LARC and sRLM might be spared major pelvic surgery if the liver-first approach is applied. A predictor (CEA) was found for non-completion of the liver-first protocol. The majority of patients underwent resection of both primary tumour and hepatic metastasis with curative intent. These findings together entail that the liver-first approach may be considered in patients with LARC and sRLM.

Impactfactor: 3.688

The long-term effects of early oral feeding following minimal invasive esophagectomy

Berkelmans GHK, **Fransen L**, Weijs TJ, Lubbers M, **Nieuwenhuijzen GAP**, Ruurda JP, Kouwenhoven EA, van Det MJ, Rosman C, van Hillegersberg R, **Luyer MDP**

Dis Esophagus. 2018 Jan 1 31(1):1-8

A nil-by-mouth regime with enteral nutrition via an artificial route is frequently applied following esophagectomy. However, early initiation of oral feeding could potentially improve recovery and has shown to be beneficial in many types of abdominal surgery. Although short-term nutritional safety of oral intake after an esophagectomy has been documented, long-term effects of this feeding regimen are unknown. In this cohort study, data from patients undergoing minimal invasive Ivor-Lewis esophagectomy between 04-2012 and 09-2015 in three centers in Netherlands were collected. Patients in the oral feeding group were retrieved from a previous prospective study and compared with a cohort of patients with early enteral jejunostomy feeding but delayed oral intake. Body mass index (BMI) measurements, complications, and nutritional re-interventions (re- or start of artificial feeding, start of total parenteral nutrition) were gathered over the course of one year after surgery. One year after surgery the median BMI was 22.8 kg/m2 and weight loss was 7.0 kg (9.5%) in 114 patients. Patients in the early oral feeding group lost more weight during the first postoperative month (P = 0.004). However, in the months thereafter this difference was not observed anymore. In the early oral feeding group, 28 patients (56%) required a nutritional re-intervention, compared to 46 patients (72%) in the delayed oral feeding group (P = 0.078). During admission, more re-interventions were performed in the delayed oral feeding group (17 vs. 46 patients P < 0.001). Esophagectomy reduces BMI in the first year after surgery regardless of the feeding regimen. Direct start of oral intake following esophagectomy has no impact on early nutritional re-interventions and long-term weight loss.

Impactfactor 2.702

The occurrence and characteristics of endoscopically unexpected malignant degeneration in large rectal adenomas

Bronzwaer MES, Musters GD, Barendse RM, Koens L, de Graaf EJR, Doornebosch PG, Schwartz MP, Consten ECJ, Schoon EJ, **de Hingh IHJT**, Tanis PJ, Dekker E, Fockens P TREND study group

Gastrointest Endosc. 2018 Mar 87(3):862-871.e1. Epub 2017 Oct 10

BACKGROUND AND AIMS:
Large non-pedunculated rectal polyps are most commonly resected by endoscopic mucosal resection (EMR) or transanal endoscopic microsurgery (TEM). Despite pre-procedural diagnostics, unexpected rectal cancer is incidentally encountered within the resected specimen. This study aimed to compare the diagnostic assessment and procedural characteristics of lesions with and without unexpected submucosal invasion.
METHODS:
A post-hoc analysis of a multicenter randomized trial (TREND study) was performed in which patients with a non-pedunculated rectal polyp of =3 cm without endoscopic suspicion of invasive growth were randomized between EMR and TEM.
RESULTS:
Unexpected rectal cancer was detected in 13% (27/203) of patients; 15 after EMR and 12 after TEM. Most consisted of low-risk T1 cancers (78%, n = 18). There were no differences in the diagnostic assessment between lesions with and without unexpected submucosal invasion. Diagnostic biopsies revealed similar rates of high-grade dysplasia (28% [7/25] vs 18% [26/144]). When compared with EMR of adenomas, EMR procedures of unexpected cancers had a lower success rate of submucosal lifting (60% vs 93%, P < .001), were more often assessed as endoscopically incomplete (33% vs 10%, P = .01), and were more frequently terminated prematurely (60% vs 8%, P = .001).
CONCLUSIONS:
Diagnostic assessment of large non-pedunculated rectal polyps revealed similar characteristics between unexpected cancers and adenomas. Unexpected cancers during EMR were non-lifting in 40%, endoscopically assessed as incomplete in 33%, and terminated prematurely in 60%. In treatment-naive patients, these factors should raise suspicion of malignancy and need discussion in a multidisciplinary team meeting for decision on further treatment strategies.

Impactfactor *7.204*

The RAQET Study: the Effect of Eating a Popsicle Directly After Bariatric Surgery on the Quality of Patient Recovery; a Randomised Controlled Trial

Pouwels S, Stepaniak PS, Buise MP, Bouwman RA, **Nienhuijs SW**

Indian J Surg. 2018 Jun;80(3):245-251

Quality of recovery could be influenced positively if there is less postoperative sore throat (POST). Eating a popsicle might attenuate this sore throat. Especially for bariatric surgery, early recovery is important. Adding popsicles to the postoperative protocol could be beneficial. Our hypothesis is that offering a popsicle in the recovery room to patients after bariatric surgery will decrease POST and will increase quality of postoperative recovery. Patients undergoing elective bariatric surgery, between the 23 February 2015 and 3 April, were randomised to either the popsicle group or control group. Primary endpoint was the incidence of POST and secondly if a reduction in POST influences quality of recovery at the first day postoperative measured with the Bariatric Quality Of Recovery (BQoR) questionnaire. One hundred and thirty-three patients were assessed for eligibility. For the final analysis, 44 patients in the intervention and 65 in the control group were available. Eating a popsicle after bariatric surgery had no significant effect on the incidence of POST. Significant effects (in favour of the popsicle group) were seen in muscle pain score (p = 0.047) and sore mouth score (p = 0.012). Popsicle intragroup analysis revealed that eating the whole popsicle (compared to partially eating the popsicle) has positive effects on nausea (p = 0.059), feeling cold (p = 0.008), and mean total comfort score (p = 0.011). Of the patients who became nauseous and/or had to vomit because of the popsicle, n = 4 had more severe pain (p = 0.04) and the mean pain score was higher (p = 0.09). The present study demonstrates that offering a popsicle early during recovery after bariatric surgery is feasible without adverse effects, although eating popsicle did not reduce postoperative sore throat. There are possible beneficial effects, such as reduced muscle pains and less sore mouth, that may enhance the quality of recovery. More research is necessary to further substantiate the effect of eating popsicles on the quality of recovery in this patient population.

Impactfactor *0.509*

The rationale for and long-term outcome of incomplete axillary staging in elderly women with primary breast cancer

Poodt IG, Schipper RJ, Vugts G, Woensdregt K, van der Sangen M, Voogd AC, **Nieuwenhuijzen GA**

Eur J Surg Oncol. 2018 Nov;44(11):1714-1719

BACKGROUND:
The proportion of elderly women diagnosed with breast cancer is rising. Standard treatment, including axillary staging, is often not given to these patients. This study aimed to investigate reasons to omit any surgical axillary staging or to refrain from completion axillary lymph node dissection (cALND) after positive-sentinel lymph node biopsy (SLNB); so-called "incomplete staging". Furthermore, the impact of incomplete staging on regional control and survival in patients aged 75 or older was evaluated.
METHODS:
A retrospective cohort study was conducted including all primary breast cancer patients aged 75 or older, diagnosed between 2001 and 2008, and documented by the Netherlands Cancer Registry (NCR). Patients with incomplete

staging were compared to patients with complete axillary staging. Survival analyses were used to determine the risk of local, regional and distant recurrence and overall survival.
RESULTS:
In total, 1467 of 2116 (69%) patients were considered eligible, of whom 258 (17.2%) had incomplete axillary staging. For 93 patients, diagnosed in 6 of the 10 hospitals in the NCR-area, examination of clinical records revealed that age, comorbidities and patient preferences were the main reason for omitting complete axillary staging. The 10-year axillary recurrence rate in these 93 patients was 5.2% (95% CI, 0.03-10.1). Of the 77 patients who had died, 64 (83%) died of non-breast-cancer-related causes. No significant difference in overall survival was observed between patients with or without complete axillary staging.
CONCLUSION:
This study demonstrates that the omission of complete axillary staging is common in selected elderly breast cancer patients with =2 comorbidities, with no apparent impact on regional control and 10-year overall survival.

Impactfactor 3.688

The safety and efficiency of a fast-track protocol for sleeve gastrectomy: a team approach

Vreeswijk SJ, van Rutte PW, Nienhuijs SW, Bouwman RA, **Smulders JF**, Buise MP

Minerva Anestesiol. 2018 Aug;84(8):898-906

BACKGROUND:
Increasing numbers of morbid obese patients has led to increased numbers of bariatric procedures. Fast-track protocols are being developed to enhance the available resources, while maintaining a safe procedure. Reported results on safety merely apply to a mixed bariatric population. The objective was to evaluate safety and efficiency of the fast-track principles in patients undergoing sleeve gastrectomy.
METHODS:
Retrospective observational study including patients undergoing primary sleeve gastrectomy at the Obesity Centre of the Catharina Hospital Eindhoven, the Netherlands. Conventional perioperative care (CC) (2008-2011) versus a fast-track protocol (FT) (2011-2013), using short-acting anesthetic agents, a multi-modal pain protocol to reduce opioids, and early mobilization. The main parameters for safety were intraoperative, early and late postoperative complications. Procedure time and hospital stay were used to evaluate efficiency.
RESULTS:
This study included 805 patients, 494 patients were subjected to the conventional care and 318 patients to fast-track protocol. A reduction of median operation time from 60 (CC) to 40 minutes (FT) (P<0.001) and a reduction in median length of hospital stay from three to two days (P=0.001), with a significant reduction in early postoperative complications (9.9% [CC] vs. 5% [FT], P=0.016) was achieved. The amount of late complications was comparable for both groups (5.1% [CC] vs. 4.4% [FT] [P=0.738]).
CONCLUSIONS:
Implementation of a fast-track protocol for sleeve gastrectomy is safe and efficient. It effectively reduces operation time and length of hospital stay, while improving postoperative outcome. This pleads for standard implementation of the fast-track protocol in sleeve gastrectomy.

Impactfactor 1.784

Three Year Patency and Recurrence Rates of Revision Using Distal Inflow with a Venous Interposition Graft for High Flow Brachial Artery Based Arteriovenous Fistula

Gerrickens MW, Vaes RH, Govaert B, van Loon M, Tordoir JH, van Hoek F, **Teijink JA**, Scheltinga MR

Eur J Vasc Endovasc Surg. 2018 Jun;55(6):874-881

OBJECTIVES:
Upper arm arteriovenous fistulas (AVF) occasionally develop high flow. Revision using distal inflow (RUDI) effectively reduces flow of high flow accesses (HFA) in the short-term and is also popularised for treatment of haemodialysis access induced distal ischaemia (HAIDI). The long-term efficacy is unknown. The study's aim was to report on 3 year RUDI patency and recurrence rates for HFA with and without HAIDI.
MATERIAL AND METHODS:
This was a retrospective cohort study of patients with a HFA with or without HAIDI undergoing RUDI using greater saphenous vein (GSV) interposition between March 2011 and October 2017 at three facilities. AVFs were termed HFA if flow volumes exceeded 2 L/min on two consecutive measurements using dilution techniques. HAIDI was diagnosed as recommended. Following RUDI, follow up was not different from standard care in AVF patients. Data on post-operative flows and re-interventions were extracted from electronic patient files. Loss to follow up was avoided. Rates of patency and HFA recurrence were analysed.
RESULTS:
During the observation period, 21 patients were studied (7 females, 54 years ± 3). Fourteen had uncomplicated HFA whereas seven had additional HAIDI. Immediately post-operatively, flows decreased threefold (3120 mL/min ± 171 vs. 1170 mL/min ± 87, p < .001). Overall 3 year primary patency was 48% ± 12 (HFA, 55% ± 15 vs. HAIDI/HFA, 29% ± 17, p = .042). Secondary patency was identical in both groups (overall, 84% ± 9). Interventions were percutaneous transluminal angioplasty (n = 12, 9 patients), thrombectomy (n = 7, 3 patients), and revision with new interposition

grafts (n = 3). After 3 years, 51% ± 12 were free of high flow (HFA, 32% ± 13 vs. HAIDI/HFA, 100%, p = .018). High immediate post-operative access flow predicted recurrence (OR 1.004 [1.000-1.007], p = .044). Patients with recurrence were 12 years younger than those without (p = .055).

CONCLUSION:

RUDI with GSV interposition for HFA offers acceptable patency rates after 3 years although re-interventions are often required. High immediate post-operative flows and young age are associated with recurrent high flow.

Impactfactor 3.877

Time interval between neoadjuvant chemoradiotherapy and surgery for oesophageal or junctional cancer: A nationwide study

van der Werf LR, Dikken JL, van der Willik EM, van Berge Henegouwen MI, **Nieuwenhuijzen GAP**, Wijnhoven BPL
Dutch Upper Gastrointestinal Cancer Audit (DUCA) group

Eur J Cancer. 2018 Mar 91:76-85. Epub 2018 Jan 30

INTRODUCTION:

The optimal time between end of neoadjuvant chemoradiotherapy (nCRT) and oesophagectomy is unknown. The aim of this study was to assess the association between this interval and pathologic complete response rate (pCR), morbidity and 30-day/in-hospital mortality.

METHODS:

Patients with oesophageal cancer treated with nCRT and surgery between 2011 and 2016 were selected from a national database: the Dutch Upper Gastrointestinal Cancer Audit (DUCA). The interval between end of nCRT and surgery was divided into six periods: 0-5 weeks (n = 157;A), 6-7 weeks (n = 878;B), 8-9 weeks (n = 972;C), 10-12 weeks (n = 720;D), 13-14 weeks (n = 195;E) and 15 or more weeks (n = 180;F). The association between these interval groups and outcomes was investigated using univariable and multivariable analysis with group C (8-9 weeks) as reference.

RESULTS:

In total, 3102 patients were included. The pCR rate for the groups A to F was 31%, 28%, 26%, 31%, 40% and 37%, respectively. A longer interval was associated with a higher probability of pCR (=10 weeks for adenocarcinoma: odds ratio [95% confidence interval]: 1.35 [1.00-1.83], 1.95 [1.24-3.07], 1.64 [0.99-2.71] and =13 weeks for squamous cell carcinoma: 2.86 [1.23-6.65], 2.67 [1.29-5.55]. Patients operated =10 weeks after nCRT had the same probability for intraoperative/postoperative complications. Patients from groups D and F had a higher 30-day/in-hospital mortality (1.80 [1.08-3.00], 3.19 [1.66-6.14]).

CONCLUSION:

An interval of =10 weeks for adenocarcinoma and =13 weeks for squamous cell carcinoma between nCRT and oesophagectomy was associated with a higher probability of having a pCR. Longer intervals were not associated with intraoperative/postoperative complications. The 30-day/in-hospital mortality was higher in patients with extended intervals (10-12 and =15 weeks); however, this might have been due to residual confounding.

Impactfactor 7.191

Timing of postoperative chemotherapy in patients undergoing perioperative chemotherapy and gastrectomy for gastric cancer

Brenkman HJ, van Putten M, Visser E, Verhoeven RH, **Nieuwenhuijzen GA**, Slingerland M, van Hillegersberg R, Lemmens VE, Ruurda JP

Surg Oncol. 2018 Sep;27(3):421-427

BACKGROUND:

For patients who qualify for perioperative chemotherapy and gastrectomy for gastric cancer, the optimal timing of the postoperative chemotherapy (PC) seems equivocal. The aim of this study was to evaluate the influence of timing of PC on overall survival (OS) in patients receiving perioperative chemotherapy.

METHODS:

Patients undergoing perioperative chemotherapy and gastrectomy with curative intent (2010-2014) were extracted from the nationwide population-based Netherlands Cancer Registry. Timing of PC was analyzed as a linear and categorical variable (<6 weeks, 6-8 weeks, and >8 weeks). Risk factors for a late start of PC (=6 weeks), and the association between timing of PC and OS were assessed by multivariable regression analyses.

RESULTS:

Among 1066 patients who underwent perioperative chemotherapy and gastrectomy, 463 (43%) patients started PC. PC was administered within 6 weeks in 208 (45%) patients, within 6-8 weeks in 155 (33%) patients, and after 8 weeks in 100 (22%) patients. A total of 419 (91%) and 351 (76%) patients finished all cycles of preoperative and PC, respectively. A late start of PC was associated with a longer hospital stay (+1 hospital day: OR 1.15, 95% CI [1.08-1.23], p < 0.001). Timing of PC was not associated with OS (6-8 weeks vs. <6 weeks, HR 1.14, 95% CI [0.79-1.65], p?=?0.471; >8 weeks vs. <6 weeks, HR 1.04, 95% CI [0.79-1.65], p?=?0.872).

CONCLUSION:

Timing of postoperative chemotherapy does not influence survival in patients receiving perioperative

chemotherapy for gastric cancer. The results suggest that the early postoperative period may be safely used for recovery and optimizing patients for the start of PC.

Impactfactor 2.558

Total pelvic exenteration for locally advanced and locally recurrent rectal cancer in the elderly

Hagemans JA, Rothbarth J, Kirkels WJ, Boormans JL, van Meerten E, Nuyttens JJ, Madsen EV, Verhoef C, **Burger JW**

Eur J Surg Oncol. 2018 Oct;44(10):1548-1554

BACKGROUND:
Total pelvic exenteration (TPE) is a radical approach for locally advanced rectal cancer (LARC) and locally recurrent rectal cancer (LRRC) in case of tumour invasion into the urogenitary tract. The aim of this study is to assess surgical and oncological outcomes of TPE for LARC and LRRC in elderly patients compared to younger patients.
METHODS:
All patients who underwent TPE for LARC and LRRC between January 1990 and March 2017 were retrospectively analyzed. Patients aged <70 years were classified as younger and =70 years as elderly patients.
RESULTS:
In total 126 patients underwent TPE, of whom 88 younger and 38 elderly patients. Elderly patients had a significantly higher number of ASA > II patients (p = 0.01). Indication for surgery LARC (n = 73) and LRRC (n = 53) did not differ significantly. The 30-day mortality rate was significantly higher (p = 0.01) in elderly (13%) compared to younger patients (3%). Elderly patients experienced more anastomotic leakage (p = 0.02). Median overall survival (OS) was 75 months [95%CI 37.1; 112.9] for elderly and 45 months [95%CI 22.4; 67.8] for younger patients (p = 0.77). The 5-year OS rate was 44% in both groups. Median disease specific survival (DSS) was 78 months [95%CI 69.1; 86.9] for elderly and 60 months [95%CI 36.6; 83.4] for younger patients (p = 0.34). The 5-year DSS rate was 57% and 49%, respectively.
CONCLUSION:
TPE is an invasive treatment for rectal cancer with high 30-day mortality in elderly patients. Oncological outcomes are similar in elderly and younger patients. Therefore, TPE should not be withheld because of high age only, but careful patient selection is needed.

Impactfactor 3.688

Transanal total mesorectal excision (TaTME) versus laparoscopic TME for MRI-defined low rectal cancer: a propensity score-matched analysis of oncological outcomes

Roodbeen SX, Penna M, Mackenzie H, **Kusters M**, Slater A, Jones OM, Lindsey I, Guy RJ, Cunningham C, Hompes R

Surg Endosc. 2018 Oct 22. [Epub ahead of print]

BACKGROUND:
While a shift to minimally invasive techniques in rectal cancer surgery has occurred, non-inferiority of laparoscopy in terms of oncological outcomes has not been definitely demonstrated. Transanal total mesorectal excision (TaTME) has been pioneered to potentially overcome difficulties experienced when operating with a pure abdominal approach deep down in the pelvis. This study aimed to compare short-term oncological results of TaTME versus laparoscopic TME (lapTME), based on a strict anatomical definition for low rectal cancer on MRI.
METHODS:
From June 2013, all consecutive TaTME cases were included and compared to lapTME in a single institution. Propensity score-matching was performed for nine relevant factors. Primary outcome was resection margin involvement (R1), secondary outcomes included intra- and post-operative outcomes.
RESULTS:
After matching, forty-one patients were included in each group; no significant differences were observed in patient and tumor characteristics. The resection margin was involved in 5 cases (12.2%) in the laparoscopic group, versus 2 (4.9%) TaTME cases (P?=?0.432). The TME specimen quality was complete in 84.0% of the laparoscopic cases and in 92.7% of the TaTME cases (P?=?0.266). Median distance to the circumferential resection margin (CRM) was 5 mm in lapTME and 10 mm in TaTME (P?=?0.065). Significantly more conversions took place in the laparoscopic group, 9 (22.0%) compared to none in the TaTME group (P?<?0.001). Other clinical outcomes did not show any significant differences between the two groups.
CONCLUSION:
This is the first study to compare results of TaTME with lapTME in a highly selected patient group with MRI-defined low rectal tumors. A significant decrease in R1 rate could not be demonstrated, although conversion rate was significantly lower in this TaTME cohort.

Impactfactor 3.117

Treatment and Outcome of Synchronous Colorectal Carcinomas: A Nationwide Study

Bos ACRK, Matthijsen RA, van Erning FN, van Oijen MGH, **Rutten HJT**, Lemmens VEPP

Ann Surg Oncol. 2018 Feb 25(2):414-421. Epub 2017 Nov 20

BACKGROUND: Synchronous colorectal carcinomas (CRC) occur in 1-8% of patients diagnosed with CRC. This study evaluated treatment patterns and patient outcomes in synchronous CRCs compared with solitary CRC patients.
METHODS: All patients diagnosed with primary CRC between 2008 and 2013, who underwent elective surgery, were selected from the Netherlands Cancer Registry. Using multivariable regressions, the effects of synchronous CRC were assessed for both short-term outcomes (prolonged postoperative hospital admission, anastomotic leakage, postoperative 30-day mortality, administration of neoadjuvant or adjuvant treatment), and 5-year relative survival (RS).
RESULTS: Of 41,060 CRC patients, 1969 patients (5%) had synchronous CRC. Patients with synchronous CRC were older (mean age 71 ± 10.6 vs. 69 ± 11.4 years), more often male (61 vs. 54%), and diagnosed with more advanced tumour stage (stage III-IV 54 vs. 49%) compared with solitary CRC (all $p < 0.0001$). In 50% of the synchronous CRCs, an extended surgery was conducted (n = 934). Synchronous CRCs with at least one stage II-III rectal tumour less likely received neoadjuvant (chemo)radiation [78 vs. 86%; adjusted OR 0.6 (0.48-0.84)], and synchronous CRCs with at least one stage III colon tumour less likely received adjuvant chemotherapy [49 vs. 63%; adjusted OR 0.7 (0.55-0.89)]. Synchronous CRCs were independently associated with decreased survival [RS 77 vs. 71%; adjusted RER 1.1 (1.01-1.23)].
CONCLUSIONS: The incidence of synchronous CRCs in the Dutch population is 5%. Synchronous CRCs were associated with decreased survival compared with solitary CRC. The results emphasize the importance of identifying synchronous tumours, preferably before surgery to provide optimal treatment.

Impactfactor 3.857

Treatment and survival of rectal cancer patients over the age of 80 years: a EURECCA international comparison

Claassen YH, Vermeer NC, Iversen LH, van Eycken E, Guren MG, Mroczkowski P, Martling A, Codina Cazador A, Johansson R, Vandendael T, Wibe A, Moller B, Lippert H, **Rutten HJ**, Portielje JE, Liefers GJ, Holman FA, van de Velde CJ, Bastiaannet E

Br J Cancer. 2018 Aug;119(4):517-522

BACKGROUND:
The optimal treatment strategy for older rectal cancer patients remains unclear. The current study aimed to compare treatment and survival of rectal cancer patients aged 80+.
METHODS:
Patients of =80 years diagnosed with rectal cancer between 2001 and 2010 were included. Population-based cohorts from Belgium (BE), Denmark (DK), the Netherlands (NL), Norway (NO) and Sweden (SE) were compared side by side for neighbouring countries on treatment strategy and 5-year relative survival (RS), adjusted for sex and age. Analyses were performed separately for stage I-III patients and stage IV patients.
RESULTS:
Overall, 19?634 rectal cancer patients were included. For stage I-III patients, 5-year RS varied from 61.7% in BE to 72.3% in SE. Proportion of preoperative radiotherapy ranged between 7.9% in NO and 28.9% in SE. For stage IV patients, 5-year RS differed from 2.8% in NL to 5.6% in BE. Rate of patients undergoing surgery varied from 22.2% in DK to 40.8% in NO.
CONCLUSIONS:
Substantial variation was observed in the 5-year relative survival between European countries for rectal cancer patients aged 80+, next to a wide variation in treatment, especially in the use of preoperative radiotherapy in stage I-III patients and in the rate of patients undergoing surgery in stage IV patients.

Impactfactor 5.922

Trends on Axillary Surgery in Nondistant Metastatic Breast Cancer Patients Treated Between 2011 and 2015: A Dutch Population-based Study in the ACOSOG-Z0011 and AMAROS Era

Poodt IG, Spronk PE, **Vugts G**, van Dalen T, Peeters MT, Rots ML, Kuijer A, **Nieuwenhuijzen GA, Schipper RJ**

Ann Surg. 2018 Dec;268(6):1084-1090

OBJECTIVES:
To evaluate patterns of care in axillary surgery for Dutch clinical T1-4N0M0 (cT1-4N0M0) breast cancer patients and to assess the effect of the American College for Surgeons Oncology Group (ACOSOG)-Z0011 and After Mapping of the Axilla: Radiotherapy Or Surgery (AMAROS) trial on axillary surgery patterns in Dutch cT1-2N0M0 sentinel node positive breast cancer patients.
BACKGROUND:
Since publication of the ACOSOG-Z0011 and AMAROS trial, omitting a completion axillary lymph node dissection (cALND) in sentinel node positive breast cancer patients is proposed in selected patients.
METHODS:
Data were obtained from the nationwide Nationaal Borstkanker Overleg Nederland breast cancer audit. Descriptive analyses were used to demonstrate trends in axillary surgery. Multivariable logistic regression analyses were used to identify factors associated with the omission of cALND in cT1-2N0M0 sentinel node-positive breast cancer patients.

RESULTS:
Between 2011 and 2015 in cT1-4N0M0 breast cancer patients, the use of sentinel lymph node biopsy as definitive axillary staging increased from 72% to 93%, and (c)ALND as definitive axillary staging decreased from 24% to 6% (P < 0.001). The use of cALND decreased from 75% to 17% in cT1-2N0 sentinel node-positive patients (P < 0.001). Earlier year of diagnosis, lower age, primary mastectomy, invasive lobular subtype, increasing tumor grade, and treatment in a nonteaching hospital were associated with a lower probability of omitting cALND (P < 0.001).
CONCLUSIONS:
This study shows a trend towards less extensive axillary surgery in Dutch cT1-T4N0M0 breast cancer patients; illustrated by an overall increase of sentinel lymph node biopsy and decrease in cALND. Despite this trend, particularly noticed in cT1-2N0 sentinel node-positive patients after publication of the ACOSOG-Z0011 and AMAROS trial, variations in patterns of care in axillary surgery are still present.

Impactfactor 1.536

Two versus five days of antibiotics after appendectomy for complex acute appendicitis (APPIC): study protocol for a randomized controlled trial

van den Boom AL, de Wijkerslooth EM, van Rosmalen J, Beverdam FH, Boerma EG, Boermeester MA, Bosmans JW, Burghgraef TA, Consten EC, Dawson I, Dekker JW, Emous M, van Geloven AA, Go PM, Heijnen LA, Huisman SA, Jean Pierre D, de Jonge J, Kloeze JH, Koopmanschap MA, Langeveld HR, **Luyer MD**, Melles DC, Mouton JW, van der Ploeg APT, Poelmann FB, **Ponten JE**, van Rossem CC, Schreurs WH, Shapiro J, Steenvoorde P, Toorenvliet BR, Verhelst J, Versteegh HP, Wijnen RM, Wijnhoven BP

Trials. 2018 May 2;19(1):263

BACKGROUND:
Acute appendicitis is one of the most common indications for emergency surgery. In patients with a complex appendicitis, prolonged antibiotic prophylaxis is recommended after appendectomy. There is no consensus regarding the optimum duration of antibiotics. Guidelines propose 3 to 7 days of treatment, but shorter courses may be as effective in the prevention of infectious complications. At the same time, the global issue of increasing antimicrobial resistance urges for optimization of antibiotic strategies. The aim of this study is to determine whether a short course (48 h) of postoperative antibiotics is non-inferior to current standard practice of 5 days.
METHODS:
Patients of 8 years and older undergoing appendectomy for acute complex appendicitis - defined as a gangrenous and/or perforated appendicitis or appendicitis in presence of an abscess - are eligible for inclusion. Immunocompromised or pregnant patients are excluded, as well as patients with a contraindication to the study antibiotics. In total, 1066 patients will be randomly allocated in a 1:1 ratio to the experimental treatment arm (48 h of postoperative intravenously administered (IV) antibiotics) or the control arm (5 days of postoperative IV antibiotics). After discharge from the hospital, patients participate in a productivity-cost-questionnaire at 4 weeks and a standardized telephone follow-up at 90 days after appendectomy. The primary outcome is a composite endpoint of infectious complications, including intra-abdominal abscess (IAA) and surgical site infection (SSI), and mortality within 90 days after appendectomy. Secondary outcomes include IAA, SSI, restart of antibiotics, length of hospital stay (LOS), reoperation, percutaneous drainage, readmission rate, and cost-effectiveness. The non-inferiority margin for the difference in the primary endpoint rate is set at 7.5% (one-sided test at ? 0.025). Both per-protocol and intention-to-treat analyses will be performed.
DISCUSSION:
This trial will provide evidence on whether 48 h of postoperative antibiotics is non-inferior to a standard course of 5 days of antibiotics. If non-inferiority is established, longer intravenous administration following appendectomy for complex appendicitis can be abandoned, and guidelines need to be adjusted accordingly.

Impactfactor 2.067

Unknown primary carcinoma in the Netherlands: decrease in incidence and survival times remain poor between 2000 and 2012

Schroten-Loef C, Verhoeven RH, **de Hingh IH**, van de Wouw AJ, van Laarhoven HW, Lemmens VE

Eur J Cancer. 2018 Sep;101:77-86

BACKGROUND/AIM:
Unknown primary tumour (UPT) is the term applied to metastatic cancer, the origin of which remains unidentified. Since cancer treatment is primarily based on the tumour site of origin, treatment of UPT patients is challenging. The number of reports on incidence, treatment and survival of UPT is limited. We hereby report data on patients (2000-2012) with UPT in the Netherlands.
METHODS:
The age-standardised rate (ASR) of 'other and unspecified' malignancies in the Netherlands was compared with other European countries. Patients diagnosed with UPT between 2000 and 2012 were selected from the Netherlands Cancer Registry (NCR) to calculate incidence rates. Patient characteristics, treatment and survival rates were assessed.

RESULTS:
The ASR of 'other and unspecified' malignancies in the Netherlands did not differ from the European average ASRs (2008-2012). A total of 29,784 patients with an unknown primary tumour were selected from the NCR (2000-2012). The incidence decreased from 14 per 100,000 person years (European standardised rate) in 2000 to 7.0 in 2012. The most common metastatic sites were liver, lymph nodes, bone and lung (42%, 22%, 16% and 14%, respectively), and approximately two-thirds of patients were diagnosed with metastases at a single site. One-third of the patients were treated; these were mainly younger patients. The overall median survival for all patients was 1.7 months. The median survival of untreated patients was 1.0 month and of treated patients 6.3 months.
CONCLUSION:
The incidence of UPT between 2000 and 2012 is decreasing in the Netherlands, and one-third of these patients received treatment. Survival after diagnosis is limited to months rather than years.

Impactfactor 7.191

User Preferences for Mobile Health Interventions: A Survey among Intermittent Claudication Patients and Their Physical Therapists

van den Houten MML, Spruijt S, Fokkenrood HJP, Scheltinga MRM, **Teijink JAW**

Ann Vasc Surg. 2018 Jan 46:249-256. Epub 2017 Sep 8

BACKGROUND:
Smartphone apps provide novel ways for triggering lifestyle change by coupling objective measurements of health behavior with tailored feedback. Little is known about end-user preferences regarding the content of mobile health (mHealth) interventions. The aim of this study was to assess smartphone use and preferences regarding app content among intermittent claudication patients and their treating physical therapists.
METHODS:
A cross-sectional survey was sent via an internal email system to 1,514 physical therapists specialized in treating patients with intermittent claudication. They were asked to complete one questionnaire themselves and administer a second to their intermittent claudication patients currently under treatment. Data on participant characteristics and smartphone use were collected from all respondents. The preferred app components were obtained from participants owning a smartphone. Binary logistic regression analysis was used to explore the adjusted association between age and attained educational level, and smartphone use.
RESULTS:
The response rate of therapists was 40.8% (617/1,514), and a total of 488 patients completed the survey. After excluding incomplete forms, a total of 615 physical therapist forms and 483 patient forms were analyzed. Overall, 40.6% of patients and 95% of therapists owned a smartphone. Higher educational level was associated with smartphone ownership (adjusted odds ratio = 2.46, 95% confidence interval (CI) = 1.41-4.27, P = 0.001). Compared to patients aged =75 years, lower age was associated with higher odds of owning a smartphone (adjusted odds ratios for patients aged =54 years = 21.27, 95% CI = 6.82-66.30, P < 0.001; aged 55-64 years = 4.76, 95% CI = 2.52-9.00, P < 0.001; and aged 65-74 years = 2.58, 95% CI = 1.54-4.33, P < 0.001). The most preferred app components for intermittent claudication patients in possession of a smartphone included monitoring treadmill-measured walking distances (71%), global positioning system tracking of walks (50%), and daily physical activity monitoring (49%). Physical therapists were most interested in global positioning system tracking of walks (89%), daily physical activity monitoring (82%), keeping track of treadmill-measured walking distance (79%), help with smoking cessation (65%).
CONCLUSIONS:
Smartphone ownership is associated with younger age and a higher educational level in patients with intermittent claudication. This study provides a framework of end-user preferences regarding desired features to guide the development of an app to potentiate health outcomes of intermittent claudication treatment.

Impactfactor 1.363

Variation in hospital mortality after pancreatoduodenectomy is related to failure to rescue rather than major complications: a nationwide audit

van Rijssen LB, Zwart MJ, van Dieren S, de Rooij T, Bonsing BA, Bosscha K, van Dam RM, van Eijck CH, Gerhards MF, Gerritsen JJ, van der Harst E, **de Hingh IH**, de Jong KP, Kazemier G, Klaase J, van der Kolk BM, van Laarhoven CJ, **Luyer MD**, Molenaar IQ, Patijn GA, Rupert CG, Scheepers JJ, et al

HPB (Oxford). 2018 Aug;20(8):759-767. Epub 2018 Mar 21

BACKGROUND:
In the mandatory nationwide Dutch Pancreatic Cancer Audit, rates of major complications and Failure to Rescue (FTR) after pancreatoduodenectomy between low- and high-mortality hospitals are compared, and independent predictors for FTR investigated.
METHODS:
Patients undergoing pancreatoduodenectomy in 2014 and 2015 in The Netherlands were included. Hospitals were divided into quartiles based on mortality rates. The rate of major complications (Clavien-Dindo =3) and death after

a major complication (FTR) were compared between these quartiles. Independent predictors for FTR were identified by multivariable logistic regression analysis.

RESULTS:

Out of 1.342 patients, 391 (29%) developed a major complication and in-hospital mortality was 4.2%. FTR occurred in 56 (14.3%) patients. Mortality was 0.9% in the first hospital quartile (4 hospitals, 327 patients) and 8.1% in the fourth quartile (5 hospitals, 310 patients). The rate of major complications increased by 40% (25.7% vs 35.2%) between the first and fourth hospital quartile, whereas the FTR rate increased by 560% (3.6% vs 22.9%). Independent predictors of FTR were male sex (OR = 2.1, 95%CI 1.2-3.9), age >75 years (OR = 4.3, 1.8-10.2), BMI =30 (OR = 2.9, 1.3-6.6), histopathological diagnosis of periampullary cancer (OR = 2.0, 1.1-3.7), and hospital volume <30 (OR = 3.9, 1.6-9.6).

CONCLUSIONS:

Variations in mortality between hospitals after pancreatoduodenectomy were explained mainly by differences in FTR, rather than the incidence of major complications.

Impactfactor *3.131*

What to do with the rectal stump during sphincter preserving rectal cancer resection with end colostomy: a collaborative snapshot study

Westerduin E, Aukema TS, van Geloven AA, Bemelman WA, Tanis PJ; Dutch Snapshot Research Group: **Brinkman DJ**, **Rutten HJ**, **Simkens GA**

Colorectal Dis. 2018 Aug;20(8):696-703

AIM:

Low Hartmann's resection (LHR) and intersphincteric abdominoperineal excision (iAPR) are both feasible options in the treatment of rectal cancer when restoration of bowel continuity is not desired. The aim of this study was to compare the incidence of pelvic abscess and associated need for re-intervention and readmission after LHR and iAPR.

METHOD:

From a snapshot research project in which all rectal cancer resections from 71 Dutch hospitals in 2011 were evaluated, patients who underwent LHR or iAPR were selected.

RESULTS:

A total of 185 patients were included: 139 LHR and 46 iAPR. No differences in baseline characteristics were found except for more multivisceral resections in the iAPR group (22% vs 10%; P = 0.041). Pelvic abscesses were diagnosed in 17% of the LHR group after a median of 21 days (interquartile range 10-151 days), compared to 11% in the iAPR group (P = 0.352) after a median of 90 days (interquartile range 44-269 days; P = 0.102). All 28 patients with a pelvic abscess underwent at least one re-intervention. Four patients (9%) in the iAPR group and nine (7%) after LHR were readmitted because of a pelvic abscess over a median 39 months of follow-up.

CONCLUSION:

This cross-sectional multicentre study suggests that cross-stapling and intersphincteric resection of the rectal stump, during non-restorative rectal cancer resection, are associated with an equal risk of pelvic abscess formation and have a similar need for re-intervention and readmission.

Impactfactor *2.778*

Cardiothoracale Chirurgie

Clinical research: remote magnetic navigation vs. manually controlled catheter ablation of right ventricular outflow tract arrhythmias: a retrospective study

Shauer A, De Vries LJ, **Akca F**, Palazzolo J, Shurrab M, Lashevsky I, Tiong I, Singh SM, Newman D, Szili-Torok T, Crystal E

Europace. 2018 May 1;20(suppl_2):ii28-ii32

Aims:

Remote magnetic navigation (RMN) is an alternative to manual catheter control (MCC) radiofrequency ablation of right ventricular outflow tract (RVOT) arrhythmias. The data to support RMN approach is limited. We aimed to investigate the clinical and procedural outcomes in a cohort of patients undergoing RVOT premature ventricular complex/ventricular tachycardia (PVCs/VT) ablation procedures using RMN vs. MCC.

Methods and results:

Data was collected from two centres. Eighty-nine consecutive RVOT PVCs/VT ablation procedures were performed in 75 patients; RMN: 42 procedures and MCC: 47 procedures. CARTOXPTM or CARTO3 (Biosense Webster) was used for endocardial mapping in 19/42 (45%) in RMN group and 28/47 (60%) in MCC group; EnSiteTM NavXTM (St. Jude Medical) was used in the rest of the cohort. Stereotaxis platform (Stereotaxis Inc., St. Louis, MO, USA) was used for RMN approach. Procedural time was 113?±?53?min in the RMN group and 115?±?69?min in MCC (P?=?0.90). Total fluoroscopic time was 10.9?±?5.8 vs. 20.5?±?13.8 (P?<?0.05) and total ablation energy application time 7.0?±?4.7 vs 11.9?±?16 (P?=?0.67) accordingly. There were two complications in RMN group and five in MCC (P?=?0.43). Acute procedural success rate was 80% in RMN vs. 74% in MCC group (P?=?0.46). After a median follow-up of 25?months (interquartile range 13-34), the success rate remained 55% in the RMN group and 53% in MCC (P?=?0.96).

Conclusion:

Right ventricular outflow tract arrhythmia ablations were performed using half of fluoroscopic times with Stereotaxis platform RMN compared to manual approach. Acute and chronic success rates as well as complication rates were not significantly different.

Impactfactor 5.231

Conduction disorders and impact on survival after sutureless aortic valve replacement compared to conventional stented bioprostheses

Lam KY, Akca F, Verberkmoes NJ, van Dijk C, Claessens A, Soliman Hamad MA, van Straten AHM

Eur J Cardiothorac Surg. 2018 Dec 15. [Epub ahead of print]

OBJECTIVES:

Sutureless and rapid-deployment aortic valve prostheses are frequently used for the treatment of aortic stenosis. However, postoperative left bundle branch block (LBBB) and permanent pacemaker (PPM) implantation have emerged as frequent complications. The aim of this study was to compare the incidence of new-onset LBBB and PPM implantation after sutureless aortic valve replacement (sAVR) with stented bioprostheses, and the impact on postoperative survival.

METHODS:

Patients undergoing isolated surgical aortic valve replacement (AVR) or concomitant AVR with coronary artery bypass surgery between January 2010 and July 2017 were included in the study. Two groups were defined: sAVR and conventional AVR (cAVR). The findings of preoperative electrocardiograms were compared with postoperative electrocardiogram findings for both groups. The incidence of new-onset LBBB and the requirement for PPM implantation were recorded. The effect of these conduction disorders on late survival was analysed.

RESULTS:

A total of 987 patients were analysed, consisting of 132 sAVR and 855 cAVR patients. The sAVR group had an increased incidence of new-onset LBBB compared to the cAVR group (16.7% vs 2.3%, P?<?0.001). A significantly higher rate of postoperative PPM implantation was found for sAVR patients compared to cAVR (6.8% vs 1.6%, P?=?0.001). The multivariate Cox analysis revealed that neither postoperative new-onset LBBB nor PPM implantation was associated with increased mortality (hazard ratio 1.73, 95% confidence interval 0.74-4.03, P?=?0.204).

CONCLUSIONS:

sAVR is associated with an increased risk of new-onset LBBB and PPM requirement compared to cAVR. In this population, postoperative conduction disorders did not affect the mid-term survival.

Impactfactor 3.504

Epicardial Left Atrial Appendage Exclusion Reduces Blood Pressure in Patients With Atrial Fibrillation and Hypertension

Turagam MK, Vuddanda V, **Verberkmoes N**, Ohtsuka T, **Akca F**, Atkins D, Bommana S, Emmert MY, Gopinathannair R, Dunnington G, Rasekh A, Cheng J, Salzberg S, Natale A, Cox J, Lakkireddy DR

J Am Coll Cardiol. 2018 Sep 18;72(12):1346-1353

BACKGROUND:

Percutaneous left atrial appendage exclusion (LAAE) has evolved as an alternative strategy for stroke prevention in

atrial fibrillation (AF). Recent observational data have suggested that epicardial LAAE can have substantial impact on arrhythmia burden and hemodynamic profile.
OBJECTIVES:
The authors aimed to study the impact of epicardial versus endocardial LAAE on systemic blood pressure in hypertensive AF patients.
METHODS:
This was a prospective, nonrandomized study comparing 247 patients who underwent epicardial LAAE with 124 patients with endocardial exclusion. Clinical outcomes were measured at 3 months and 1 year. Primary outcome was improvement in systolic blood pressure (SBP) between both groups compared with baseline. Secondary outcome included changes in diastolic pressures (DBP), serum electrolytes, and creatinine.
RESULTS:
There was no significant difference in baseline SBP between epicardial and endocardial groups. SBP was significantly lower in the epicardial group both at 3 months (122 ± 11.8 mm Hg vs. 129.7 ± 8.2 mm Hg; p < 0.001) and 1 year (123 ± 11.6 mm Hg vs. 132.2 ± 8.8 mm Hg; p < 0.001) compared with the endocardial group. An adjusted multivariate linear mixed effects model demonstrated that epicardial LAAE significantly decreased SBP by 7.4 mm Hg at 3 months and by 8.9 mm Hg at 1 year (p < 0.0001). There was a trend toward lower DBP with epicardial LAAE at 3 months by 1.3 mm Hg (p = 0.2) and at 1 year by 1.8 mm Hg (p = 0.09). There was no significant difference in serum electrolytes and creatinine between both groups.
CONCLUSIONS:
In hypertensive AF patients, epicardial LAAE significantly decreases SBP both at 3 and 12 months compared with endocardial exclusion.

Impactfactor *16.834*

Health insurance outcome-based purchasing: The case of hospital contracting for cardiac interventions in the Netherlands

D. van Veghel, D. N. Schulz, **A. H. M. van Straten**, T. A. Simmers, A. Lenssen, L. Kuijten-Slegers, F. van Eenennaam, **M. A. Soliman Hamad**, B. A. de Mol & L. R. C. Dekker

INTERNATIONAL JOURNAL OF HEALTHCARE MANAGEMENT, 2018;11(4):371-8

Innovative forms of value-based purchasing contracts, based on outcome instead of volume, are imperative to face the imminent cost crisis in health care. The objective of this study was to design and implement a model for an outcome-based purchasing contract between a hospital and a health insurance company. The model was implemented in 2015. A study cohort (n = 14,944) from patients with coronary artery disease or atrial fibrillation treated in 2014 was compared to a historical reference cohort from patients treated between 2010 and 2013. The outcome measures and the model are based on Porter's value-based healthcare principles. Improvements in outcomes were observed, leading to a financial incentive to be spent on further quality improvement. Implementation of this model is a first step towards enabling inclusion of patient-relevant outcomes in purchasing for healthcare. It aligns the focus of health insurance companies and hospitals on patient value.

Impactfactor --

Impact of Sex on the Outcome of Isolated Aortic Valve Replacement and the Role of Different Preoperative Profiles

Ter Woorst JF, Hoff AHT, van Straten AHM, Houterman S, **Soliman-Hamad MA**

J Cardiothorac Vasc Anesth. 2018 Aug 24. pii: S1053-0770(18)30842-5. [Epub ahead of print]

OBJECTIVE:
The aim of this study was to compare the patient profiles and outcomes of men and women undergoing isolated aortic valve replacement.
DESIGN:
Patient data were analyzed retrospectively.
SETTING:
This single-center study was performed at Catharina Hospital in Eindhoven, the Netherlands.
PARTICIPANTS:
The study comprised 2,362 patients, of whom 1,040 (44%) were women and 1,322 were men (56%).
INTERVENTIONS:
Isolated aortic valve replacement was performed between January 1998 and December 2016.
MEASUREMENTS AND MAIN RESULTS:
The mean follow-up was 8.3 ± 5.1 years. Women were relatively older (69.9 years v 64.6 years; p < 0.001); more of them were underweight, obese, and diabetic; and they had lower hemoglobin values and worse renal function than did men. However, fewer women than men experienced chronic obstructive pulmonary disease, aortic regurgitation, left ventricular dysfunction, and endocarditis. Early mortality did not differ significantly between men and women (p?=?0.238). Overall survival was worse in women (p < 0.001). After correction for potential risk factors, female sex was not associated with worse survival. During the study period, the mean age of patients undergoing

aortic valve replacement increased. In addition, the mean age at the time of death increased, following the trend of national statistics.
CONCLUSIONS:
Although women undergoing aortic valve replacement have relatively more risk factors than do men, early mortality in women is not significantly higher than in men. Overall survival is worse in women than in men; however, after adjustment for preoperative risk factors, there is no difference in overall survival between women and men.

Impactfactor *1.574*

Intimal sarcoma of the left atrium

Pieraets MW, Hamad Soliman MA, van Straten BHM

J Card Surg. 2018 Apr 33(4):179-180. Epub 2018 Mar 23

Geen abstract beschikbaar

Impactfactor *1.179*

Mycotic innominate artery aneurysm repair using a bovine pericardial bifurcation prosthesis

Hoff AHT, Akca F, Cuypers PWM, **Ter Woorst JF**

J Card Surg. 2018 Mar 33(3):146-148. Epub 2018 Mar 11

We report the use of a bovine pericardial bifurcation prosthesis to repair a mycotic innominate artery aneurysm.

Impactfactor *1.179*

Significantly Elevated C-Reactive Protein Levels After Epicardial Clipping of the Left Atrial Appendage

Verberkmoes NJ, Akca F, Vandevenne AS, **Jacobs L, Soliman Hamad MA, van Straten AHM**

Innovations (Phila). 2018 Mar/Apr;13(2):125-131

OBJECTIVE:
Besides mechanical and anatomical changes of the left atrium, epicardial closure of the left atrial appendage has also possible homeostatic effects. The aim of this study was to assess whether epicardial clipping of the left atrial appendage has different biochemical effects compared with complete removal of the left atrial appendage.
METHODS:
Eighty-two patients were included and underwent a totally thoracoscopic AF ablation procedure. As part of the procedure, the left atrial appendage was excluded with an epicardial clip (n = 57) or the left atrial appendage was fully amputated with an endoscopic vascular stapler (n = 25). From all patients' preprocedural and postprocedural blood pressure, electrolytes and inflammatory parameters were collected.
RESULTS:
The mean age and left atrial volume index were comparable between the epicardial clip and stapler group (64 ± 8 years vs. 60 ± 9 years, P = non-significant; 44 ± 15 mL/m vs. 40 ± 13 mL/m, P = non-significant). Patients receiving left atrial appendage clipping had significantly elevated C-reactive protein levels compared with patients who had left atrial appendage stapling at the second, third, and fourth postoperative day (225 ± 84 mg/L vs. 149 ± 76 mg/L, P = 0.002, 244 ± 78 vs. 167 ± 76, P = 0.004, 190 ± 74 vs. 105 ± 48, P < 0.001, respectively). Patients had a significant decrease in sodium levels, systolic, and diastolic blood pressure at 24 and 72 hours after left atrial appendage closure. However, this was comparable for both the left atrial appendage clipping and stapling group.
CONCLUSIONS:
Increased activation of the inflammatory response was observed after left atrial appendage clipping compared with left atrial appendage stapling. Furthermore, a significant decrease in blood pressure was observed after surgical removal of the left atrial appendage. Whether the inflammatory response affects the outcome of arrhythmia surgery needs to be further evaluated.

Impactfactor --

The Hemodynamic Effects of Different Pacing Modalities After Cardiopulmonary Bypass in Patients With Reduced Left Ventricular Function

Gielgens RCW, Herold IHF, **van Straten AHM**, van Gelder BM, Bracke FA, Korsten HHM, **Soliman Hamad MA**, Bouwman RA

J Cardiothorac Vasc Anesth. 2018 Feb 32(1):259-266. . Epub 2017 Jul 8

OBJECTIVES:
Patients with decreased left ventricular function undergoing cardiac surgery have a greater chance of difficult weaning from cardiopulmonary bypass and a poorer clinical outcome. Directly after weaning, interventricular dyssynchrony, paradoxical septal motion, and even temporary bundle-branch block might be observed. In this study, the authors measured arterial dP/dtmax, mean arterial pressure (MAP), and cardiac index using transpulmonary thermodilution, pulse contour analysis, and femoral artery catheter and compared the effects between right ventricular (A-RV) and biventricular (A-BiV) pacing on these parameters.
DESIGN:
Prospective study.

SETTING:
Single-center study.
PARTICIPANTS:
The study comprised 17 patients with a normal or prolonged QRS duration and a left ventricular ejection fraction =35% who underwent coronary artery bypass grafting with or without valve replacement.
INTERVENTIONS:
Temporary pacing wires were placed on the right atrium and both ventricles. Different pacing modalities were used in a standardized order.
MEASUREMENTS AND MAIN RESULTS:
A-BiV pacing compared with A-RV pacing demonstrated higher arterial dP/dtmax values (846 ± 646 mmHg/s v 800 ± 587 mmHg/s, p = 0.023) and higher MAP values (77 ± 19 mmHg v 71 ± 18 mmHg, p = 0.036).
CONCLUSION:
In patients with preoperative decreased left ventricular function undergoing coronary artery bypass grafting, A-BiV pacing improve the arterial dP/dtmax and MAP in patients with both normal and prolonged QRS duration compared with standard A-RV pacing. In addition, arterial dP/dtmax and MAP can be used to evaluate the effect of intraoperative pacing. In contrast to previous studies using more invasive techniques, transpulmonary thermodilution is easy to apply in the perioperative clinical setting.

Impactfactor 1.574

The influence of oxygen delivery during cardiopulmonary bypass on the incidence of delirium in CABG patients; a retrospective study

Leenders J, Overdevest E, **van Straten B**, Golab H

Perfusion. 2018 Nov;33(8):656-662.

INTRODUCTION:
Postoperative delirium is the most common neurological complication of cardiac surgery. Hypoxia has been shown to increase the risk of postoperative delirium. The possibility to continuously monitor oxygen delivery (DO2) during cardiopulmonary bypass (CPB) offers an adequate approximation of the oxygen status in a patient. This study investigates the role of oxygen delivery during cardiopulmonary bypass in the incidence of postoperative delirium.
METHODS:
Three hundred and fifty-seven adult patients who underwent normothermic coronary artery bypass grafting (CABG) surgery were included in this retrospective study. The nadir indexed DO2 (DO2i) value on bypass, the total time under the critical DO2i level and the area under the curve (AUC) for critical DO2i were determined. Delirium was identified by the postoperative administration of haloperidol.
RESULTS:
The mean nadir DO2i significantly differed, comparing the group of patients with postoperative delirium to the group without. Multivariate analysis only identified age, pre-existing cognitive impairment, preoperative kidney dysfunction and cross-clamp time as independent risk factors for delirium. The results also indicated that patients of older age were more sensitive to a declined DO2i.
CONCLUSION:
A low DO2i during cardiopulmonary bypass is significantly associated with the incidence of postoperative delirium in CABG patients. However, the role of DO2 as an independent predictor of delirium could not be proven.

Impactfactor 1.147

Thoracoscopic Left Atrial Appendage Clipping: A Multicenter Cohort Analysis

van Laar C, **Verberkmoes NJ**, van Es HW, Lewalter T, Dunnington G, Stark S, Longoria J, Hofman FH, Pierce CM, Kotecha D, van Putte BP

JACC Clin Electrophysiol. 2018 Jul;4(7):893-901

OBJECTIVES:
This study sought to document the closure rate, safety, and stroke rate after thoracoscopic left atrial appendage (LAA) clipping.
BACKGROUND:
The LAA is the main source of stroke in patients with atrial fibrillation, and thoracoscopic clipping may provide a durable and safe closure technique.
METHODS:
The investigators studied consecutive patients undergoing clipping as part of a thoracoscopic maze procedure in 4 referral centers (the Netherlands and the United States) from 2012 to 2016. Completeness of LAA closure was assessed by either computed tomography (n = 100) or transesophageal echocardiography (n = 122). The primary outcome was complete LAA closure (absence of residual LAA flow and pouch <10 mm). The secondary outcomes were 30-day complications; the composite of ischemic stroke, hemorrhagic stroke, or transient ischemic attack; and all-cause mortality.
RESULTS:
A total of 222 patients were included, with a mean age of 66 ± 9 years, and 68.5% were male. The mean CHA2DS2-

VASc (congestive heart failure, hypertension, age =75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, sex category [female]) score was 2.3 ± 1.0. Complete LAA closure was achieved in 95.0% of patients. There were no intraoperative or clip-related complications, and the overall 30-day freedom from any complication rate was 96.4%. The freedom from cerebrovascular events after surgery was 99.1% after median follow-up of 20 months (interquartile range: 14 to 25 months; 369 patient-years of follow-up), and overall survival was 98.6%. The observed rate of cerebrovascular events after LAA clipping was low (0.5 per 100 patient-years).

CONCLUSIONS:

LAA clipping during thoracoscopic ablation is a feasible and safe technique for closure of the LAA in patients with atrial fibrillation. The lower than expected rate of cerebrovascular events after deployment was likely multifactorial, including not only LAA closure, but also the effect of oral anticoagulation and rhythm control.

Impactfactor --

Dermatologie

Comparison of long-term cosmetic outcomes for different treatments of superficial basal cell carcinoma.

Jansen MHE, Koekelkoren FHJ, Nelemans PJ, **Arits AHMM**, Roozeboom MH, Kelleners-Smeets NWJ, Mosterd K

J Am Acad Dermatol. 2018 Nov 79(5):961-964. doi: . Epub 2018 May 10

Geen abstract beschikbaar.

Impactfactor 6.898

CYLD mutations differentially affect splicing and mRNA decay in Brooke-Spiegler syndrome

Parren LJMT, Baron JM, Joussen S, Marquardt Y, Hanneken S, van Steensel MAM, **Steijlen PM**, van Geel M, Frank J

J Eur Acad Dermatol Venereol. 2018 Feb 25. [Epub ahead of print]

Geen abstract beschikbaar.

Impactfactor 4.287

Five-Year Results of a Randomized Controlled Trial Comparing Effectiveness of Photodynamic Therapy, Topical Imiquimod, and Topical 5-Fluorouracil in Patients with Superficial Basal Cell Carcinoma

Jansen MHE, **Mosterd K, Arits AHMM**, Roozeboom MH, Sommer A, Essers BAB, van Pelt HPA, Quaedvlieg PJF, **Steijlen PM**, Nelemans PJ, Kelleners-Smeets NWJ

J Invest Dermatol. 2018 Mar;138(3):527-533. Epub 2017 Oct 16

For the treatment of superficial basal cell carcinoma, a prospective, noninferiority, randomized controlled multicenter trial with 601 patients showed that 5% imiquimod cream was superior and 5-fluorouracil cream not inferior to methyl aminolevulinate photodynamic therapy (MAL-PDT) at 1 and 3 years after treatment. No definite conclusion could be drawn regarding the superiority of imiquimod over 5-fluorouracil. We now present the 5-year follow-up results according to the intention-to-treat analysis. Five years after treatment, the probability of tumor-free survival was 62.7% for methyl aminolevulinate photodynamic therapy (95% confidence interval [CI] = 55.3-69.2), 80.5% for imiquimod (95% CI = 74.0-85.6), and 70.0% for 5-fluorouracil (95% CI = 62.9-76.0). The hazard ratio for treatment failure of imiquimod and 5-fluorouracil were 0.48 (95% CI = 0.32-0.71, P < 0.001) and 0.74 (95% CI = 0.53-1.05, P = 0.09), respectively, when compared with methyl aminolevulinate photodynamic therapy. Compared with 5-fluorouracil, imiquimod showed a hazard ratio of 0.65 (95% CI 0.43-0.98, P = 0.04). In conclusion, 5 years after treatment, the results of this trial show that 5% imiquimod cream is superior to both methyl aminolevulinate photodynamic therapy and 5-fluorouracil cream in terms of efficacy for superficial basal cell carcinoma. We therefore consider 5% imiquimod cream as the first choice for noninvasive treatment in most primary superficial basal cell carcinomas.

Impactfactor 6.448

Genetic profiling of basal cell carcinomas detects postzygotic mosaicism in basal cell naevus syndrome.

Reinders MGHC, Cosgun B, Gijezen LMC, van Oosterhoud CN, Kelleners-Smeets NWJ, Vermander E, Vreeburg M, **Steijlen PM**, Mosterd K, van Geel M.

Br J Dermatol. 2018 Dec 5. [Epub ahead of print]

Basal cell naevus syndrome (BCNS) is associated with germline mutations in the PTCH1 gene. Postzygotic mosaicism can also cause BCNS. Here we describe two patients, one with multiple basal cell carcinomas (BCCs) and one with clinical BCNS, who had no PTCH1 mutation in DNA extracted from blood. In both patients, we performed genetic analysis on different BCCs, revealing the presence of a shared PTCH1 mutation in all tumours. Our findings show that in patients with symptoms of BCNS and initial absence of a PTCH1 mutation in blood, genetic profiling of BCCs can detect postzygotic mosaicism.

Impactfactor 6.129

Histological subtype of treatment failures after noninvasive therapy for superficial basal-cell carcinoma: an observational study

van Delft LCJ, Nelemans PJ, Jansen MHE, **Arits AHMM**, Roozeboom MH, Hamid MA, Mosterd K, Kelleners-Smeets NWJ

J Am Acad Dermatol. 2018 Dec 21. pii: S0190-9622(18)33100-1. [Epub ahead of print]

BACKGROUND:

There have been concerns that recurrences after noninvasive therapy for basal-cell carcinoma (BCC) transform into a 'more aggressive' histological subtype.

OBJECTIVE:

To evaluate the proportion of patients with a non-superficial treatment failure after noninvasive therapy for superficial BCC.

METHODS:

An observational study was performed using data from a single blind, non-inferiority, randomized controlled trial (March 2008-August 2010) with five year follow-up in patients with primary superficial BCC treated with

methylaminolevulinate-photodynamic therapy (MAL-PDT), 5-fluorouracil or imiquimod. Data were used from 166 adults with a histologically confirmed treatment failure.
RESULTS:
A non-superficial subtype was found in 64 of 166 treatment failures (38.6%). Proportions with a 'more aggressive' subtype than the primary tumor were 51.3% (38/74) for early and 28.3% (26/92) for later treatment failures (p=0.003). The proportion of 'more aggressive' early failures was significantly lower following imiquimod (26.3%) compared to MAL-PDT (54.8%, p=0.086) and 5-fluorouracil (66.7%, p=0.011).
LIMITATIONS:
There was limited information on the exact time of occurrence of treatment failures.
CONCLUSION:
'More aggressive' treatment failures after noninvasive therapy for superficial BCC occur most often within the first three months post-treatment probably indicating underdiagnosis of 'more aggressive' components in the primary tumor rather than transformation.

Impactfactor *6.898*

New mutations and an updated database for the patched-1 (PTCH1) gene

Reinders MG, van Hout AF, Cosgun B, Paulussen AD, Leter EM, **Steijlen PM**, Mosterd K, van Geel M, Gille JJ
Mol Genet Genomic Med. 2018 May 6(3):409-415. Epub 2018 Mar 25

BACKGROUND:
Basal cell nevus syndrome (BCNS) is an autosomal dominant disorder characterized by multiple basal cell carcinomas (BCCs), maxillary keratocysts, and cerebral calcifications. BCNS most commonly is caused by a germline mutation in the patched-1 (PTCH1) gene. PTCH1 mutations are also described in patients with holoprosencephaly.
METHODS:
We have established a locus-specific database for the PTCH1 gene using the Leiden Open Variation Database (LOVD). We included 117 new PTCH1 variations, in addition to 331 previously published unique PTCH1 mutations. These new mutations were found in 141 patients who had a positive PTCH1 mutation analysis in either the VU University Medical Centre (VUMC) or Maastricht University Medical Centre (MUMC) between 1995 and 2015.
RESULTS:
The database contains 331 previously published unique PTCH1 mutations and 117 new PTCH1 variations.
CONCLUSION:
We have established a locus-specific database for the PTCH1 gene using the Leiden Open Variation Database (LOVD). The database provides an open collection for both clinicians and researchers and is accessible online at http://www.lovd.nl/PTCH1.

Impactfactor *2.695*

Novel CLDN1 mutation in ichthyosis-hypotrichosis-sclerosing cholangitis syndrome without signs of liver disease

Nagtzaam IF, Peeters VPM, Vreeburg M, Wagner A, **Steijlen PM**, van Geel M, van Steensel MAM
Br J Dermatol. 2018 Mar;178(3):e202-e203. Epub 2018 Jan 23

Geen abstract beschikbaar

Impactfactor *6.129*

Patient preferences for the attributes of a noninvasive treatment for superficial basal cell carcinoma: a discrete choice experiment

Essers BAB, **Arits AH**, Hendriks MR, Mosterd K, Kelleners-Smeets NW
Br J Dermatol. 2018 Jan 178(1):e26-e27. Epub 2017 Nov 30

No abstract available.

Impactfactor *6.129*

The effect of Mindfulness-Based Stress Reduction on wound healing: a preliminary study

Meesters A, den Bosch-Meevissen YMCI, Weijzen CAH, Buurman WA, Losen M, Schepers J, **Thissen MRTM,** Alberts HJEM, Schalkwijk CG, Peters ML
J Behav Med. 2018 Jun;41(3):385-397. doi: 10.1007/s10865-017-9901-8. Epub 2017 Nov 20

Psychological factors have been shown to influence the process of wound healing. This study examined the effect of Mindfulness-Based Stress Reduction (MBSR) on the speed of wound healing. The local production of pro-inflammatory cytokines and growth factors was studied as potential underlying mechanism. Forty-nine adults were randomly allocated to a waiting-list control group (n = 26) or an 8-week MBSR group (n = 23). Pre- and post-intervention/waiting period assessment for both groups consisted of questionnaires. Standardized skin wounds were induced on the forearm using a suction blister method. Primary outcomes were skin permeability and reduction in wound size monitored once a day at day 3, 4, 5, 6, 7, and 10 after injury. Secondary outcomes were cytokines and growth factors and were measured in wound exudates obtained at 3, 6, and 22 h after wounding.

Although there was no overall condition effect on skin permeability or wound size, post hoc analyses indicated that larger increases in mindfulness were related to greater reductions in skin permeability 3 and 4 days after wound induction. In addition, MBSR was associated with lower levels of interleukin (IL)-8 and placental growth factor in the wound fluid 22 h after wound induction. These outcomes suggest that increasing mindfulness by MBSR might have beneficial effects on early stages of wound healing.

Impactfactor *2.880*

Vismodegib-resistant basal cell carcinomas in basal cell nevus syndrome: Clinical approach and genetic analysis

Sinx KA, Roemen GMJM, van Zutven V, Janssen R, Speel EM, **Steijlen PM**, van Geel M, **Mosterd K**

JAAD Case Rep. 2018 Apr 30;4(5):408-411

Geen abstract beschikbaar.

Impactfactor --

Dietetiek

Influence of Helicobacter pylori infection on gastrointestinal symptoms and complications in bariatric surgery patients: a review and meta-analysis

Smelt HJM, Smulders JF, Gilissen LPL, Said M, Ugale S, Pouwels S

Surg Obes Relat Dis. 2018 Oct;14(10):1645-1657

BACKGROUND: Numerous papers have discussed the importance of preoperative detection and eradication of Helicobacter pylori (HP) in bariatric patients.

OBJECTIVES: This systematic review specifically focuses on the influence of HP infection on clinical symptoms, complications, and abnormal endoscopic findings in postbariatric patients.

METHODS: A systematic search on the influence of HP infection on postoperative complications in bariatric surgery was conducted. The methodologic quality of the included studies was rated using the Newcastle-Ottawa rating scale. The agreement between the reviewers was assessed with Cohen's kappa. The included studies were assessed into 2 groups, studies with and without eradication therapy preoperatively.

RESULTS: A total of 21 studies were included with a methodologic quality ranging from poor to good. The agreement between the reviewers, assessed with the Cohen's kappa, was .70. Overall, tendency in the included studies was that HP infection was associated with an increased risk for developing marginal ulcers and postoperative complications. A meta-analysis on the incidence of marginal ulcers and overall postoperative complications was conducted and showed, respectively, an odds ratio of .508 (.031-8.346) and 2.863 (.262-31.268).

CONCLUSIONS: HP is frequently found in patients before and after bariatric and metabolic surgery. We assessed whether, according to the current literature, HP increases the risk for developing postoperative complications after surgery. This meta-analysis shows that a methodologically good study should be performed to clarify the role of HP in bariatric patients and the question of whether HP should be eradicated before surgery.

Impactfactor *3.900*

Lipoedema in patients after bariatric surgery: report of two cases and review of literature

Pouwels S, Huisman S, **Smelt HJM**, Said M, Smulders JF

Clin Obes. 2018 Apr 8(2):147-150. doi: Epub 2018 Jan 25

Lipoedema is a disorder of adipose tissue that is characterized by abnormal subcutaneous fat deposition, leading to swelling and enlargement of the lower limbs as well as the trunk. This entity is often misdiagnosed as lymphoedema or obesity and, therefore, may be overlooked and missed in patients scheduled for bariatric surgery. Patients with lipoedema who undergo bariatric surgery may have to continue to have extensive lower extremity and trunk adiposity despite adequate weight loss. In this report, we present two patients who had extensive trunk and lower extremity adiposity, one of them before and the other after the bariatric surgery.

Impactfactor *--*

Neuropathy by folic acid supplementation in a patient with anaemia and an untreated cobalamin deficiency: a case report

Smelt HJ, Pouwels S, Said M, Smulders JF

Clin Obes. 2018 Aug;8(4):300-304

The rising rates of bariatric surgery (BS) are accompanied by neurological complications related to nutrient deficiencies. One of the risk factors for neurological complications in BS patients is poor vitamin and mineral supplementation. Prevention, diagnosis and treatment of these disorders are necessary parts of lifelong care after BS. Particularly important for optimal functioning of the nervous system are vitamin B1 , B6 , B12 (cobalamin), E, copper and possibly vitamin B11 (folic acid). In this case report, we narrate about a patient with anaemia and multiple vitamin and mineral deficiencies after Roux-en-Y gastric bypass (RYGB) with an alimentary limb of 150?cm and a biliopancreatic limb of 100?cm. RYGB is associated with an increased risk of vitamin deficiencies, especially a vitamin B12 deficiency. The patient in this case report developed psychiatric-neurological symptoms due to folic acid supplementation in an untreated cobalamin deficiency. Second, we tried to elucidate the vitamin physiology to understand specific mechanisms after BS.

Impactfactor *--*

Reply to: "Letter to the Editor for the Manuscript the complex interplay of physical fitness protein intake and vitamin D supplementation after bariatric surgery"

Pouwels S, **Smelt HJM**, Celik A, Gupta A, Smulders JF

Obes Surg. 2018 Apr 28(4):1140-1141

Geen abstract beschikbaar

Impactfactor *3.895*

Reply to: "Patients' Expectations Are Important for Success in Bariatric Surgery"

Pouwels S, **Smelt HJM**, Smulders JF

Obes Surg. 2018 Apr 28(4):1146

Geen abstract beschikbaar

Impactfactor 3.895

ECC

The influence of oxygen delivery during cardiopulmonary bypass on the incidence of delirium in CABG patients; a retrospective study

Leenders J, **Overdevest E**, van Straten B, Golab H

Perfusion. 2018 Nov;33(8):656-662

INTRODUCTION:

Postoperative delirium is the most common neurological complication of cardiac surgery. Hypoxia has been shown to increase the risk of postoperative delirium. The possibility to continuously monitor oxygen delivery (DO2) during cardiopulmonary bypass (CPB) offers an adequate approximation of the oxygen status in a patient. This study investigates the role of oxygen delivery during cardiopulmonary bypass in the incidence of postoperative delirium.

METHODS:

Three hundred and fifty-seven adult patients who underwent normothermic coronary artery bypass grafting (CABG) surgery were included in this retrospective study. The nadir indexed DO2 (DO2i) value on bypass, the total time under the critical DO2i level and the area under the curve (AUC) for critical DO2i were determined. Delirium was identified by the postoperative administration of haloperidol.

RESULTS:

The mean nadir DO2i significantly differed, comparing the group of patients with postoperative delirium to the group without. Multivariate analysis only identified age, pre-existing cognitive impairment, preoperative kidney dysfunction and cross-clamp time as independent risk factors for delirium. The results also indicated that patients of older age were more sensitive to a declined DO2i.

CONCLUSION:

A low DO2i during cardiopulmonary bypass is significantly associated with the incidence of postoperative delirium in CABG patients. However, the role of DO2 as an independent predictor of delirium could not be proven.

Impactfactor 1.147

Geriatrie

Real-World Adverse Effects of Capecitabine Toxicity in an Elderly Population

van Beek MWH, Roukens M, Jacobs WCH, Timmer-Bonte JNH, Kramers C

Drugs Real World Outcomes. 2018 Jun 22. [Epub ahead of print]

BACKGROUND:
Few studies have assessed the safety and effectiveness of the numerous available chemotherapeutic therapies for geriatric oncology patients. Most safety studies are conducted in large trials, and there is some uncertainty surrounding whether the results would be the same in typical daily use.
OBJECTIVE:
This retrospective study aims to assess the adverse effects of real-world capecitabine use in elderly patients.
METHODS:
We reviewed the records of patients treated with capecitabine in an oncology department of a University Clinic in Nijmegen, The Netherlands. We scored adverse effects such as hand-foot syndrome and diarrhea, and dosage adjustments and the reasons for them. In total, 132 patients were included, 69 of whom were aged 70 years or below (mean age: 57 years), while 63 were aged older than 70 years (mean age: 74 years).
RESULTS:
Patients aged over 70 years experienced more serious adverse effects than younger patients. Grade 2 or 3 hand-foot syndrome toxicity was experienced by 20.2% of patients aged younger than 70 years and by 34.9% of patients older than 70 years (p?=?0.059). Grade 2, 3, or 4 diarrhea was experienced by 17.4% of the patients aged younger than 70 years but by 31.7% of the patients aged older than 70 years (p?=?0.044). Dosage was adjusted for 27/69 patients in the younger group and 52/63 patients in the older group (p?=?0.001).
CONCLUSION:
The difference in observed adverse effects cannot be the sole explanation for the high incidence of observed dose adjustments. A prospective follow-up study of elderly patients using capecitabine outside clinical trials is needed to evaluate the optimum balance between adverse effects and efficacy.

Impactfactor --

Tongue necrosis

Hems MA, Aarnoudse AL, Douwes-Draaijer P

Neth J Med. 2018 May;76(4):202-203

Geen abstract beschikbaar

Impactfactor *1.156*

Gynaecologie

Accuracy of postvoid residual volumes after vaginal delivery: a prospective equivalence study to compare an automatic scanning device with transurethral catheterization

Mulder FEM, van der Velde S, **Pol F**, Bos M, van Leeuwen JS, **Dietz V**, Hakvoort RA, Roovers JWR

Int Urogynecol J. 2018 Jun 27. [Epub ahead of print]

INTRODUCTION AND HYPOTHESIS:

Abnormal postvoid residual volumes (PVRV) after delivery are common in daily clinical practice. By using an automatic scanning device, unnecessary catheterizations can be prevented. The aim of this study was to determine the accuracy of PVRV after vaginal delivery measured by an automatic scanning device through a comparison with transurethral catheterization.

MATERIALS AND METHODS:

This prospective observational equivalence study was performed in patients who delivered vaginally between June 2012 and May 2017 in three teaching hospitals in The Netherlands. After the first spontaneous void after delivery, postvoid residual volume (PVRV) was measured with a portable automatic scanning device (BladderScan® BVI 9400). Directly afterward, it was measured by catheterization. Correlation between measurements was calculated using Spearman's correlation coefficient and agreement plot. The primary outcome was to validate the correlation between the BladderScan® compared with the gold standard of transurethral catheterization.

RESULTS:

Data of 407 patients was used for final analysis. Median PVRV as measured by BladderScan® was 380 ml (± 261-0-999 ml) and by catheterization was 375 ml (± 315-1800 ml). Mean difference between measurements was -12.9 ml (± 178 ml). There was a very good correlation between methods (Spearman's rho?=?0.82, p?<?0.001). Using a cut-ff value of >500 ml, specificity and sensitivity were 85.4 and 85.6%, respectively.

CONCLUSIONS:

The BladderScan® (BVI 9400) measures PVRV precisely and reliably after vaginal delivery and should be preferred over catheterization.

Impactfactor 2.078

Body mass index and sexual function in women with gynaecological cancer

Donkers H, Smits A, Eleuteri A, **Bekkers R**, Massuger L, Galaal K

Psychooncology. 2018 Oct 4. [Epub ahead of print]

OBJECTIVES:

To investigate the association between body mass index (BMI) and sexual functioning in gynaecologic cancer patients. To determine the association between socio-economic deprivation and sexual functioning.

METHODS:

This is a prospective cohort study on women undergoing surgery for suspected or proven gynaecological cancer between September 2014 and February 2016 in the Royal Cornwall Hospital Trust. Patients were invited to participate by completing the Female Sexual Function Index (FSFI) at three time points: preoperative, 3 months postoperative, and 1 year postoperative. A semiparametric model of the FSFI score was used to establish the association between BMI and sexual functioning.

RESULTS:

A total of 257 patients were approached of which 166 patients were included. Fifty-two patients (33.8%) were overweight (BMI, 25-29.9 kg/m2), 44 (28.6%) were obese (BMI, 30-39.9 kg/m2), and a further 20 (13.0%) morbidly obese (BMI = 40 kg/m2). Overweight and obese women reported improved sexual functioning compared with normal-weight women in endometrial, ovarian, and vulvar cancers. Among cervical cancer, worse sexual functioning was seen in women with an increased BMI; however, this was not significant. Younger age was associated with improved sexual function, and sexual functioning was better postoperatively for all patients compared with preoperatively. There was no evidence of relationship between deprivation and sexual functioning in gynaecological cancer patients.

CONCLUSION:

Higher BMI is associated with improved sexual functioning in endometrial, ovarian, and vulvar cancer; however, this was not seen in cervical cancer patients. There is no evidence of correlation between deprivation and sexual functioning.

Impactfactor 3.455

Continuity of care is an important and distinct aspect of childbirth experience: findings of a survey evaluating experienced continuity of care experienced quality of care and women's perception of labor

Perdok H, Verhoeven CJ, van Dillen J, Schuitmaker TJ, Hoogendoorn K, Colli J, Schellevis FG, de Jonge A

BMC Pregnancy Childbirth. 2018 Jan 8 18(1):13

BACKGROUND:

To compare experienced continuity of care among women who received midwife-led versus obstetrician-led care. Secondly, to compare experienced continuity of care with a. experienced quality of care during labor and b. perception of labor.

METHODS:
We conducted a questionnaire survey in a region in the Netherlands in 2014 among 790 women after they gave birth. To measure experienced continuity of care, the Nijmegen Continuity Questionnaire was used. Quality of care during labor was measured with the Pregnancy and Childbirth Questionnaire, and to measure perception of labor we used the Childbirth Perception Scale.
RESULTS:
Three hundred twenty five women consented to participate (41%). Of these, 187 women completed the relevant questions in the online questionnaire. 136 (73%) women were in midwife-led care at the onset of labor, 15 (8%) were in obstetrician-led care throughout pregnancy and 36 (19%) were referred to obstetrician-led care during pregnancy. Experienced personal and team continuity of care during pregnancy were higher for women in midwife-led care compared to those in obstetrician-led care at the onset of labor. Experienced continuity of care was moderately correlated with experienced quality of care although not significantly so in all subgroups. A weak negative correlation was found between experienced personal continuity of care by the midwife and perception of labor.
CONCLUSION:
This study suggests that experienced continuity of care depends on the care context and is significantly higher for women who are in midwife-led compared to obstetrician-led care during labor. It will be a challenge to maintain the high level of experienced continuity of care in an integrated maternity care system. Experienced continuity of care seems to be a distinctive concept that should not be confused with experienced quality of care or perception of labor and should be considered as a complementary aspect of quality of care.

Course of chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among ovarian cancer patients: A longitudinal study

Bonhof CS, Mols F, Vos MC, Pijnenborg JMA, **Boll D**, Vreugdenhil G, Ezendam NPM, van de Poll-Franse LV
Gynecol Oncol. 2018 Jun;149(3):455-463. Epub 2018 Mar 28

OBJECTIVE:
Chemotherapy-induced peripheral neuropathy (CIPN) presents itself as sensory peripheral neuropathy (SPN) or motor peripheral neuropathy (MPN). Our aim was to examine the course of SPN and MPN, and their impact on health-related quality of life (HRQoL) among ovarian cancer patients.
METHODS:
All newly diagnosed ovarian cancer patients from twelve hospitals in the South of the Netherlands were eligible for participation. Patients (N=174) completed questions on CIPN (EORTC QLQ-OV28) and HRQoL (EORTC QLQ-C30) after initial treatment and at 6, 12, and 24months (response rates were 70%, 71%, 58%, and 43% respectively).
RESULTS:
Generalized linear mixed models showed that among chemotherapy-treated patients (N=98), SPN levels were stable over time. For MPN, symptoms significantly improved at 12months. At 2years, 13% still reported high SPN. Also, 11% still reported high MPN. Regarding HRQoL, patients with high SPN reported a worse physical, role, emotional, social, and cognitive functioning compared to those with low SPN. Moreover, those who changed from low to high SPN over time worsened on physical functioning. For MPN, a worse global quality of life and a worse functioning was reported among patients with high MPN. Also, those who changed from low to high MPN over time worsened on global quality of life and on physical, role, social, and cognitive functioning.
CONCLUSIONS:
Among chemotherapy-treated ovarian cancer patients, SPN levels were stable over time. In contrast, MPN symptoms significantly improved at 12months. These symptoms seriously impacted HRQoL. Future studies should examine the impact of different treatment decisions and alterations on CIPN, so recommendations can be made to reduce CIPN (prevalence).

Impactfactor 4.540

Defining hrHPV genotypes in cervical intraepithelial neoplasia by laser capture microdissection supports reflex triage of self-samples using HPV16/18 and FAM19A4/miR124-2 methylation

Leeman A, Ebisch RM, Kasius A, Bosgraaf RP, Jenkins D, van de Sandt MM, de Strooper LM, Heideman DA, Snijders PJ, Massuger LF, **Bekkers RL**, Meijer CJ, van Kemenade FJ, Quint WG, Melchers WJ
Gynecol Oncol. 2018 Nov;151(2):311-318

OBJECTIVE:
HPV16/18 genotyping and detection of hypermethylation of human cell genes involved in cervical oncogenesis have shown promising results in triage of high-risk HPV (hrHPV)-screen positive women on cervical smears. These tests can be performed on self-samples, which contain cervical and vaginal cells. We studied whether a self-sample represents the hrHPV type causing the worst cervical lesion and whether any differences in hypermethylation of FAM19A4/miR124-2 exist between CIN lesions caused by different hrHPV types. These results have important implications for reflex triage of self-samples.
METHODS:
Correlation between genotype found on self-sample using GP5+/6+-PCR-EIA-LMNX and causative hrHPV genotype

in the worst lesion on histology was studied using laser capture microdissection (LCM)-SPF10-PCR (N?=?152). Hypermethylation of FAM19A4/miR124-2 in the self-sample was tested in a quantitative methylation specific PCR and compared between lesions caused by HPV16/18 and other hrHPV genotypes.
RESULTS:
Causative hrHPV genotype of the worst lesion (CIN1, CIN2, CIN3, invasive cervical cancer) was detected on self-sample in 93.4%. HPV16 was the most frequently found genotype on self-sampling (39.2%, 73/186) and causative genotype in CIN3+ (51.4%, 38/74, all detected on self-sample). There were no differences in the percentages of positive FAM19A4/miR124-2 methylation assays between lesions caused by HPV16/18 (73.8% in CIN3+) or other hrHPV genotypes (66.7% in CIN3+) (p?=?0.538).
CONCLUSIONS:
Our results show that hrHPV genotypes found on self-sample were a good representation of hrHPV in the worst CIN lesion and that methylation testing on self-sample for detection of CIN3+ was not significantly different between lesions caused by HPV16/18 and other hrHPV genotypes

Impactfactor 4.540

Does endometrial scratching increase the rate of spontaneous conception in couples with unexplained infertility and a good prognosis (Hunault >?30%)? Study protocol of the SCRaTCH-OFO trial: a randomized controlled trial

Bui BN, Torrance HL, Janssen C, Cohlen B, de Bruin JP, den Hartog JE, van der Linden PJQ, Deurloo KL, Maas JWM, van Oppenraaij R, Cantineau A, Lambalk CB, Visser H, Brinkhuis E, van Disseldorp J, **Schoot BC**, Lardenoije C, van Wely M, Eijkemans MJC, Broekmans FJM

BMC Pregnancy Childbirth. 2018 Dec 29;18(1):511

BACKGROUND:
In the Netherlands, couples with unexplained infertility and a good prognosis to conceive spontaneously (i.e. Hunault >?30%) are advised to perform timed intercourse for at least another 6?months. If couples fail to conceive within this period, they will usually start assisted reproductive technology (ART). However, treatment of unexplained infertility by ART is empirical and can involve significant burdens. Intentional endometrial injury, also called 'endometrial scratching', has been proposed to positively affect the chance of embryo implantation in patients undergoing in vitro fertilization (IVF). It might also be beneficial for couples with unexplained infertility as defective endometrial receptivity may play a role in these women. The primary aim of this study is to determine whether endometrial scratching increases live birth rates in women with unexplained infertility.
METHOD:
A multicentre randomized controlled trial will be conducted in Dutch academic and non-academic hospitals starting from November 2017. A total of 792 women with unexplained infertility and a good prognosis for spontaneous conception <?12?months (Hunault >?30%) will be included, of whom half will undergo endometrial scratching in the luteal phase of the natural cycle. The women in the control group will not undergo endometrial scratching. According to Dutch guidelines, both groups will subsequently perform timed intercourse for at least 6 months. The primary endpoint is cumulative live birth rate. Secondary endpoints are clinical and ongoing pregnancy rate; miscarriage rate; biochemical pregnancy loss; multiple pregnancy rate; time to pregnancy; progression to intrauterine insemination (IUI) or IVF; pregnancy complications; complications of endometrial scratching; costs and endometrial tissue parameters associated with reproductive success or failure. The follow-up duration is 12 months.
DISCUSSION:
Several small studies show a possible beneficial effect of endometrial scratching in women with unexplained infertility trying to conceive naturally or through IUI. However, the quality of this evidence is very low, making it unclear whether these women will truly benefit from this procedure. The SCRaTCH-OFO trial aims to investigate the effect of endometrial scratching on live birth rate in women with unexplained infertility and a good prognosis for spontaneous conception <?12?months.

Impactfactor 2.331

ENdometrial cancer SURvivors' follow-up carE (ENSURE): Less is more? Evaluating patient satisfaction and cost-effectiveness of a reduced follow-up schedule: study protocol of a randomized controlled trial

Ezendam NP, de Rooij BH, Kruitwagen RF, Creutzberg CL, van Loon I, **Boll D**, Vos MC, van de Poll-Franse LV

Trials. 2018 Apr 16;19(1):227

BACKGROUND:
It has often been hypothesized that the frequency of follow-up visits for patients with early-stage endometrial cancer could be decreased. However, studies evaluating effects of a reduced follow-up schedule among this patient group are lacking. The aim of this study is to assess patient satisfaction and cost-effectiveness of a less frequent follow-up schedule compared to the schedule according to the Dutch guideline.
METHODS:
In this multicenter randomized controlled trial, patients diagnosed in the Netherlands with stage 1A and 1B low-risk endometrial cancer, for whom adjuvant radiotherapy is not indicated (n =?282), are randomized. Patients allocated to the intervention group receive four follow-up visits during three years. Patients allocated to the control

group receive 10-13 follow-up visits during five years, according to the Dutch guideline. Patients are asked to fill out a questionnaire at baseline and after 6, 12, 36, and 60 months. Primary outcomes include patient satisfaction with follow-up care and cost-effectiveness. Secondary outcomes include healthcare use, adherence to schedule, health-related quality of life, fear of recurrence, anxiety and depression, information provision, recurrence, and survival. Linear regression analyses will be used to assess differences in patient satisfaction with follow-up care between intervention and control group.
DISCUSSION:
We anticipate that patients in the intervention arm have a similar satisfaction with follow-up care and overall outcomes, but lower healthcare use and costs than patients in the control arm. No differences are expected in quality-adjusted life-years and satisfaction, but the reduced schedule is expected to be cost-saving when implemented in the Netherlands.

Impactfactor 2.067

External validation of a prediction model to select the best day-three embryo for transfer in in vitro fertilization or intracytoplasmatic sperm injection procedures

Blank C, Duijf IT, Slappendel E, Mischi M, Houterman S, Maas JW, de Sutter P, **Schoot BC**

Fertil Steril. 2018 Oct;110(5):917-924

OBJECTIVE:
To evaluate the multivariate embryo selection model by van Loendersloot et al. (2014) (VL) in a different geographical context.
DESIGN:
This is a retrospective external validation study of a 5-year cohort of women undergoing in vitro fertilization or intracytoplasmatic sperm injection.
SETTING:
Two outpatient fertility clinics.
PATIENT(S):
A total of 1,197 women who underwent 1,610 fresh in vitro fertilization or intracytoplasmatic sperm injection cycles with single embryo transfer were included.
INTERVENTION(S):
None.
MAIN OUTCOME MEASURE(S):
The area under the receiver operating characteristics curve for diagnostic efficacy was used to assess the discriminative value of the model. Calibration for testing the validity of the VL model was performed using the Hosmer-Lemeshow goodness-of-fit test and a calibration plot.
RESULT(S):
Three hundred thirty-three patients (21%) achieved a viable pregnancy of at least 11 weeks. The area under the receiver operating characteristics curve using the VL model was 0.68. No significant difference between the predicted implantation rate and the observed implantation rates was showed using the Hosmer-Lemeshow (X2= 6.70). The calibration plot showed an intercept of the regression line of 0.34 and the estimated slope was 0.7
COCLUSION:
The investigated VL model was able to distinguish between higher and lower implantation potential of embryos in our clinical setting.

Impactfactor 4.803

Factors influencing decision-making around opportunistic salpingectomy: a nationwide survey

Steenbeek MP, **van Lieshout LAM**, Aarts JWM, **Piek JMJ**, Coppus SFPJ, Massuger LFAG, Hermens RPM, de Hullu JA

J Gynecol Oncol. 2018 Aug 31[Epub ahead of print]

OBJECTIVE:
To explore current practice and influencing factors on adoption of the opportunistic salpingectomy (OS), particularly regarding the decision making, to eventually enhance the development and implementation of clear guidelines.
METHODS:
This nationwide cross-sectional survey study was conducted in all hospitals in the Netherlands. An anonymous online survey was sent to gynecologists with special interest in gynecological oncology, gynecological endoscopy or urogynecology and all Dutch gynecology trainees. The survey mainly focused on current practice regarding OS and identification of influencing factors on the level of innovation, organization, healthcare professional and individual patient.
RESULTS:
The response rate was 348 out of 597 gynecologists (58.3%) and 142 out of 340 trainees (41.8%). Current practice of discussing and performing the OS varied widely, with ovarian cancer (OC) risk reduction as most important supportive factor on innovation level. Supportive factors on the level of organization and healthcare provider were; working in a non-training hospital, knowledge of current literature and extensive work experience (in years and

annual number of hysterectomies). On individual patient level, a vaginal approach of hysterectomy, negative family history for OC and the presence of firm adhesions were suppressive factors for the OS.
CONCLUSION:
In this study we evaluated the current practice regarding the opportunistic salpingectomy in the Netherlands and identified influencing factors on different levels to raise awareness and attribute to development of a targeted implementation strategy, on both national and international level.

Impactfactor 3.340

Feasibility of Transabdominal Electrohysterography for Analysis of Uterine Activity in Nonpregnant Women

Sammali F, **Kuijsters NP, Schoot BC**, Mischi M, Rabotti C

Reprod Sci. 2018 Jul;25(7):1124-1133

PURPOSE:
Uterine activity plays a key role in reproduction, and altered patterns of uterine contractility have been associated with important physiopathological conditions, such as subfertility, dysmenorrhea, and endometriosis. However, there is currently no method to objectively quantify uterine contractility outside pregnancy without interfering with the spontaneous contraction pattern. Transabdominal electrohysterography has great potential as a clinical tool to characterize noninvasively uterine activity, but results of this technique in nonpregnant women are poorly documented. The purpose of this study is to investigate the feasibility of transabdominal electrohysterography in nonpregnant women.
METHODS:
Longitudinal measurements were performed on 22 healthy women in 4 representative phases of the menstrual cycle. Twelve electrohysterogram-based indicators previously validated in pregnancy have been estimated and compared in the 4 phases of the cycle. Using the Tukey honest significance test, significant differences were defined for P values below .05.
RESULTS:
Half of the selected electrohysterogram-based indicators showed significant differences between menses and at least 1 of the other 3 phases, that is the luteal phase.
CONCLUSION:
Our results suggest transabdominal electrohysterography to be feasible for analysis of uterine activity in nonpregnant women. Due to the lack of a golden standard, this feasibility study is indirectly validated based on physiological observations. However, these promising results motivate further research aiming at evaluating electrohysterography as a method to improve understanding and management of dysfunctions (possibly) related to altered uterine contractility, such as infertility, endometriosis, and dysmenorrhea.

Impactfactor 2.548

Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, **Hermans RHM**, de Hingh IHJT, van der Velden J, Arts HJ, Massuger LFAG, Aalbers AGJ, Verwaal VJ, Kieffer JM, Van de Vijver KK, van Tinteren H, Aaronson NK, Sonke GS

N Engl J Med. 2018 Jan 18 378(3):230-240

BACKGROUND:
Treatment of newly diagnosed advanced-stage ovarian cancer typically involves cytoreductive surgery and systemic chemotherapy. We conducted a trial to investigate whether the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to interval cytoreductive surgery would improve outcomes among patients who were receiving neoadjuvant chemotherapy for stage III epithelial ovarian cancer.
METHODS:
In a multicenter, open-label, phase 3 trial, we randomly assigned 245 patients who had at least stable disease after three cycles of carboplatin (area under the curve of 5 to 6 mg per milliliter per minute) and paclitaxel (175 mg per square meter of body-surface area) to undergo interval cytoreductive surgery either with or without administration of HIPEC with cisplatin (100 mg per square meter). Randomization was performed at the time of surgery in cases in which surgery that would result in no visible disease (complete cytoreduction) or surgery after which one or more residual tumors measuring 10 mm or less in diameter remain (optimal cytoreduction) was deemed to be feasible. Three additional cycles of carboplatin and paclitaxel were administered postoperatively. The primary end point was recurrence-free survival. Overall survival and the side-effect profile were key secondary end points.
RESULTS:
In the intention-to-treat analysis, events of disease recurrence or death occurred in 110 of the 123 patients (89%) who underwent cytoreductive surgery without HIPEC (surgery group) and in 99 of the 122 patients (81%) who underwent cytoreductive surgery with HIPEC (surgery-plus-HIPEC group) (hazard ratio for disease recurrence or death, 0.66; 95% confidence interval [CI], 0.50 to 0.87; P=0.003). The median recurrence-free survival was 10.7 months in the surgery group and 14.2 months in the surgery-plus-HIPEC group. At a median follow-up of 4.7 years, 76 patients (62%) in the surgery group and 61 patients (50%) in the surgery-plus-HIPEC group had died (hazard ratio, 0.67; 95% CI, 0.48 to 0.94; P=0.02). The median overall survival was 33.9 months in the surgery group and 45.7

months in the surgery-plus-HIPEC group. The percentage of patients who had adverse events of grade 3 or 4 was similar in the two groups (25% in the surgery group and 27% in the surgery-plus-HIPEC group, P=0.76).
CONCLUSIONS:
Among patients with stage III epithelial ovarian cancer, the addition of HIPEC to interval cytoreductive surgery resulted in longer recurrence-free survival and overall survival than surgery alone and did not result in higher rates of side effects. (Funded by the Dutch Cancer Society; ClinicalTrials.gov number, NCT00426257 ; EudraCT number, 2006-003466-34 .).

Impactfactor 79.258

Hysteroscopic resection of a uterine caesarean scar defect (niche) in women with postmenstrual spotting: a randomised controlled trial

Vervoort A, van der Voet LF, Hehenkamp W, Thurkow AL, van Kesteren P, Quartero H, Kuchenbecker W, Bongers M, Geomini P, de Vleeschouwer L, van Hooff M, **van Vliet H**, Veersema S, Renes WB, Oude Rengerink K, Zwolsman SE, Brölmann H, Mol B, Huirne J

BJOG. 2018 Feb 125(3):326-334. Epub 2017 Jul 5

OBJECTIVE:
To compare the effectiveness of a hysteroscopic niche resection versus no treatment in women with postmenstrual spotting and a uterine caesarean scar defect.
DESIGN:
Multicentre randomised controlled trial.
SETTING:
Eleven hospitals collaborating in a consortium for women's health research in the Netherlands.
POPULATION:
Women reporting postmenstrual spotting after a caesarean section who had a niche with a residual myometrium of =3 mm, measured during sonohysterography.
METHODS:
Women were randomly allocated to hysteroscopic niche resection or expectant management for 6 months.
MAIN OUTCOME MEASURES:
The primary outcome was the number of days of postmenstrual spotting 6 months after randomisation. Secondary outcomes were spotting at the end of menstruation, intermenstrual spotting, dysuria, sonographic niche measurements, surgical parameters, quality of life, women's satisfaction, sexual function, and additional therapy. Outcomes were measured at 3 months and, except for niche measurements, also at 6 months after randomisation.
RESULTS:
We randomised 52 women to hysteroscopic niche resection and 51 women to expectant management. The median number of days of postmenstrual spotting at baseline was 8 days in both groups. At 6 months after randomisation, the median number of days of postmenstrual spotting was 4 days (interquartile range, IQR 2-7 days) in the intervention group and 7 days (IQR 3-10 days) in the control group (P = 0.04); on a scale of 0-10, discomfort as a result of spotting had a median score of 2 (IQR 0-7) in the intervention group, compared with 7 (IQR 0-8) in the control group (P = 0.02).
CONCLUSIONS:
In women with a niche with a residual myometrium of =3 mm, hysteroscopic niche resection reduced postmenstrual spotting and spotting-related discomfort.

Impactfactor 4.876

Hysteroscopy in the Netherlands and Flanders: A survey amongst practicing gynaecologists

van Wessel S, Hamerlynck T, **Schoot B**, Weyers S

Eur J Obstet Gynecol Reprod Biol. 2018 Apr 223:85-92. Epub 2018 Feb 19

OBJECTIVE:
To gain insight in the current ideas on, and implementation of hysteroscopy amongst practicing gynaecologists in the Netherlands and Flanders.
STUDY DESIGN:
In August 2016 an electronic questionnaire was sent to practising gynaecologist members of the Dutch (N?=?591) and Flemish (N?=?586) Society of Obstetrics and Gynaecology.
RESULTS:
The response rate for the Netherlands was 15.4% (91/591), and for Flanders 27.0% (158/586). Responding gynaecologists have a preference for hysteroscopy for diagnosing and treating most intrauterine pathology. Flemish respondents are more hesitant in opting for hysteroscopy instead of curettage for treatment of polyps and placental remnants. There appears to be a wide diffusion of diagnostic and basic operative hysteroscopy. In contrast to Flanders, responding hysteroscopists from the Netherlands more often perform office hysteroscopic procedures. Hysteroscopic procedures, and office procedures in particular, are now educated during residency. Therefore, recently graduated gynaecologists have a preference for this technique.

CONCLUSION:

Our survey confirms that nowadays the focus of treating intrauterine pathology is on less invasive techniques and preserving the uterus. Dutch responding hysteroscopists have more expertise concerning office hysteroscopy than their Flemish colleagues. Future research on the cost-effectiveness of and optimisation of patient comfort during office hysteroscopy is needed to support its further implementation.

Impactfactor *1.809*

Identification and Validation of a 3-Gene Methylation Classifier for HPV-Based Cervical Screening on Self-Samples

Verlaat W, Snoek BC, Heideman DA, Wilting SM, Snijders PJ, Novianti PW, van Splunter AP, Peeters CF, van Trommel NE, Massuger LF, **Bekkers RL**, Melchers WJ, van Kemenade FJ, Berkhof J, van de Wiel MA, Meijer CJ, Steenbergen RD

Clin Cancer Res. 2018 Jul 15;24(14):3456-3464

Purpose: Offering self-sampling of cervico-vaginal material for high-risk human papillomavirus (hrHPV) testing is an effective method to increase the coverage in cervical screening programs. Molecular triage directly on hrHPV-positive self-samples for colposcopy referral opens the way to full molecular cervical screening. Here, we set out to identify a DNA methylation classifier for detection of cervical precancer (CIN3) and cancer, applicable to lavage and brush self-samples.Experimental Design: We determined genome-wide DNA methylation profiles of 72 hrHPV-positive self-samples, using the Infinium Methylation 450K Array. The selected DNA methylation markers were evaluated by multiplex quantitative methylation-specific PCR (qMSP) in both hrHPV-positive lavage (n = 245) and brush (n = 246) self-samples from screening cohorts. Subsequently, logistic regression analysis was performed to build a DNA methylation classifier for CIN3 detection applicable to self-samples of both devices. For validation, an independent set of hrHPV-positive lavage (n = 199) and brush (n = 287) self-samples was analyzed.Results: Genome-wide DNA methylation profiling revealed 12 DNA methylation markers for CIN3 detection. Multiplex qMSP analysis of these markers in large series of lavage and brush self-samples yielded a 3-gene methylation classifier (ASCL1, LHX8, and ST6GALNAC5). This classifier showed a very good clinical performance for CIN3 detection in both lavage (AUC = 0.88; sensitivity = 74%; specificity = 79%) and brush (AUC = 0.90; sensitivity = 88%; specificity = 81%) self-samples in the validation set. Importantly, all self-samples from women with cervical cancer scored DNA methylation-positive.Conclusions: By genome-wide DNA methylation profiling on self-samples, we identified a highly effective 3-gene methylation classifier for direct triage on hrHPV-positive self-samples, which is superior to currently available methods

Impactfactor *10.199*

Illness perceptions are associated with higher health care use in survivors of endometrial cancer-a study from the population-based PROFILES registry

Thong MSY, Mols F, Kaptein AA, **Boll D**, Vos C, Pijnenborg JMA, van de Poll-Franse LV, Ezendam NPM

Support Care Cancer. 2018 Sep 13. [Epub ahead of print]

OBJECTIVES: According to the Common Sense Model of self-regulation, cancer survivors construct perceptions of their illness as a (mal)adaptive mechanism. These perceptions might impact on health care use. We aimed to explore the association between illness perceptions and health care use in stage I-II endometrial cancer (EC) survivors, and whether these associations differed by time since diagnosis.

METHODS: A survey was conducted in 2008 by the population-based PROFILES registry among EC survivors diagnosed between 1999 and 2007. Survivors (n?=?742, 77% response) completed the Brief Illness Perception Questionnaire (BIPQ) and questions on health care use in the past 12 months. Clinical data were accessed from the Netherlands Cancer Registry. Multiple logistic regression was used to evaluate the relationship between illness perceptions and health care use.

RESULTS: Between 15 and 22% of the survivors had negative illness perceptions. Survivors with more negative perceptions on consequences, timeline, treatment control, identity, cognitive representation, concern, emotion, and emotional representation were more likely to make =?1 visit to their family physician/general practitioner in relation to their cancer when compared with survivors with more positive illness perceptions. More negative perceptions on consequences, timeline, identity, and concern were associated with =?2 general or cancer-related visits to the medical specialists. The association between negative illness perceptions and health care use was more prominent among long-term (>5 years post-diagnosis) EC survivors.

CONCLUSIONS: Negative illness perceptions among EC survivors were associated with higher health care use. For individuals with maladaptive illness perceptions, visits to their health care provider may reduce worry about their illness. Future research might address the effects of intervening in maladaptive illness perceptions on use of health care in this category of survivors.

Impactfactor *2.676*

Implementation of laparoscopic hysterectomy for endometrial cancer over the past decade

Wollinga T, Ezendam NPM, Eggink FA, Smink M, van Hamont D, Pijlman B, Boss E, Robbe EJ, Ngo H, **Boll D**, Mom CH, van der Aa MA, Kruitwagen RFLP, Nijman HW, Pijnenborg JMA

Gynecol Surg. 2018 15(1):7. Epub 2018 Feb 27

Background:
Laparoscopic hysterectomy (LH) for the treatment of early-stage endometrial carcinoma/cancer (EC) has demonstrated to be safe in several randomized controlled trials. Yet, data on implementation of LH in clinical practice are limited. In the present study, implementation of LH for EC was evaluated in a large oncology network in the Netherlands.
Results:
Retrospectively, a total of 556 EC patients with FIGO stage I-II were registered in the selected years. The proportion of LH gradually increased from 11% in 2006 to 85% in 2015. LH was more often performed in patients with low-grade EC and was not related to the studied patient characteristics. The introduction of TLH was frequently preceded by LAVH. Patients treated in teaching hospitals were more likely to undergo a LH compared to patients in non-teaching hospitals. The conversion rate was 7.7%, and the overall complication rates between LH and AH were comparable, but less postoperative complications in LH.
Conclusions:
Implementation of laparoscopic hysterectomy for early-stage EC increased from 11 to 85% in 10 years. Implementation of TLH was often preceded by LAVH and was faster in teaching hospitals.

Impactfactor --

Influence of endometrial thickness on pregnancy rates in modified natural cycle frozen-thawed embryo transfer

Groenewoud ER, Cohlen BJ, Al-Oraiby A, Brinkhuis EA, Broekmans FJM, de Bruin JP, van Dool G, Fleisher K, Friederich J, Goddijn M, Hoek A, Hoozemans DA, Kaaijk EM, Koks CAM, Laven JSE, van der Linden PJQ, Manger AP, **van Rumste M**, Spinder T, Macklon NS

Acta Obstet Gynecol Scand. 2018 Jul 97(7):808-815.Epub 2018 Apr 24

INTRODUCTION:
Pregnancy after frozen-thawed embryo transfer (FET) is a multifactorial process. Although embryo quality is a key factor in determining pregnancy, other factors, including maternal determinants, are also considered to be predictive. Even though an association between endometrial thickness measured by transvaginal ultrasound and pregnancy rates has been reported in patients undergoing various assisted reproductive technology treatments, whether endometrial thickness predicts achieving pregnancy after natural cycle FET (NC-FET) remains unclear.
MATERIAL AND METHODS:
In this cohort study, 463 patients allocated to the modified NC-FET (mNC-FET) arm of a previously published randomized controlled trial were included. Monitoring in mNC-FET cycles consisted of regular ultrasound scans, measuring both dominant follicle and endometrial thickness. When the dominant follicle reached a size of 16-20 mm, an injection of human chorionic gonadotrophin was administered and embryo thawing and transfer planned. No minimal endometrial thickness was defined below which transfer was to be deferred. The primary endpoint was ongoing pregnancy rate.
RESULTS:
Overall, the ongoing pregnancy rate per started FET cycle was 12.5%. Multivariate regression analyses showed that embryo quality was the only significant predictor for ongoing pregnancy. Mean endometrial thickness did not differ between patients achieving ongoing pregnancy and those who did not (9.0 vs. 8.8 mm, p = 0.4). Comparable results were obtained with regard to clinical pregnancy, live birth and miscarriage rates. The area under the receiver operator curve was 0.5, indicating little discriminatory value of endometrial thickness.
CONCLUSIONS:
Given that endometrial thickness was not found to be predictive of pregnancy after mNC-FET, cancellation based on endometrial thickness alone may not be justified.

Impactfactor *2.649*

Interdepartmental Spread of Innovations: A Multicentre Study of the Enhanced Recovery After Surgery Programme

de Groot JJ, Maessen JM, Dejong CH, Winkens B, Kruitwagen RF, Slangen BF, van der Weijden T; all the members of the study group: **Bekkers RL**

World J Surg. 2018 Aug;42(8):2348-2355

BACKGROUND:
Spread of evidence-based innovations beyond pioneering settings is essential to improve quality of care. This study aimed to evaluate the influence of a national project to implement 'Enhanced Recovery After Surgery' (ERAS) among colorectal teams on the spread of this innovation to gynaecological procedures.

METHODS:
A retrospective observational multicentre study was performed of a consecutive sample of patients who underwent major elective gynaecological surgery in 2012-2013. Ten Dutch hospitals (294 patients) had participated in a colorectal breakthrough project implementing ERAS on a nationwide basis and were assigned to the intervention group. Thirteen hospitals (390 patients) that had not participated in this project acted as controls. Outcome measures were time to functional recovery and total length of postoperative hospital stay. Multilevel models adjusted for clustering and baseline demographics were used for analysis. The uptake of ten selected perioperative care elements was evaluated for each hospital.
RESULTS:
The estimated mean difference (95% confidence interval) between the intervention and control hospitals was -0.3 (-0.9 to 0.3) days in the time to recovery and 0.2 (-0.8 to 1.3) days in the total length of hospital stay. The mean (± standard deviation) absolute rate of implemented perioperative care elements per hospital was 28.9 ± 14.9% in the control, versus 29.3 ± 11.1% in the intervention group (p = 0.934).
CONCLUSION:
Initial implementation effects seem to be restricted to the participating teams and do not automatically spread to other surgical teams in the same hospital.

Impactfactor 2.766

Justifying conservative management of CIN2 in women younger than 25?years - A population-based study

Loopik DL, **Bekkers RLM**, Massuger LFAG, Melchers WJG, Siebers AG, Bentley J

Gynecol Oncol. 2018 Nov 7.[Epub ahead of print]

OBJECTIVE:
In 2012, the joint clinical practice guideline from the Society of Obstetricians and Gynaecologists of Canada (SOGC) changed from immediate treatment to a more conservative management of Cervical Intraepithelial Neoplasia (CIN) grade 2 in young women. In this study, the outcomes before and after this management change were reviewed in Nova Scotia, Canada.
METHODS:
A retrospective population-based cohort study was performed among women younger than 25?years with biopsy-proven CIN2, who were diagnosed in one of the colposcopy clinics in Nova Scotia between 2010 and 2014. Regression and progression rates were compared pre- and post-guideline changes.
RESULTS:
Of the 636 women included in the study, 286 women were diagnosed with CIN2 before and 350 women after the management in Nova Scotia was changed. After implementation of the 2012 guidelines patients were more likely to receive conservative management (78.6% versus 44.1%; p?<?0.001); which differs from the patients who underwent treatment during follow-up prior to the change in guidelines (73.4% versus 38.9%; p?<?0.001). Regression occurred in 73.1% of all women, but women seen in the post-guideline change period had a higher regression rate and lower progression rate (p?<?0.05). Histologic results from treatment specimen did not show a significant difference in low-grade or high-grade lesions before or after the guideline had been changed (p?=?0.59).
CONCLUSION:
Conservative management seems a safe and justified approach for women younger than 25?years with CIN2

Impactfactor 4.540

Laparoscopic Sterilization Under Local Anesthesia with Conscious Sedation Versus General Anesthesia

Huppelschoten AG, Bijleveld K, Braams L, **Schoot BC, van Vliet HAAM**

J Minim Invasive Gynecol. 2018 Mar - Apr;25(3):393-401

Authors' Reply. - J Minim Invasive Gynecol. 2018 May - Jun 25(4):740-741. Epub 2018 Jan 31

Female sterilization is the most popular and common contraceptive method worldwide. Because hysteroscopic sterilization techniques are used less often due to side effects, the number of laparoscopic sterilization is increasing. A systematic overview concerning the most optimal anesthetic technique for laparoscopic sterilization is lacking. We performed a systematic review to compare conscious sedation with general anesthesia for laparoscopic sterilization procedures with respect to clinical relevant outcome measures, such as operating times, perioperative parameters and complications, patient comfort, recovery, and patient satisfaction. We searched Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE for randomized controlled trials comparing general anesthesia with conscious sedation for laparoscopic sterilization. Two authors (AGH and HAAMvV) abstracted and entered data into RevMan. Methodologic quality of the included trials was critically appraised. For our main outcome measures mean differences (continuous variables) and risk ratios (dichotomous variables) with 95% confidence intervals using random-effect models were calculated. Four randomized controlled trials were included comparing general anesthesia versus local anesthesia with conscious sedation for laparoscopic sterilization. The methodologic quality of the studies was moderate to good. Both techniques were comparable with regard to operating times, complications, and postoperative pain. However, local anesthesia with conscious sedation showed better results compared with general anesthesia with respect to recovery times, patient complaints of sore throat, and patient recovery and satisfaction. In conclusion, this systematic review about anesthetic techniques for laparoscopic

sterilization showed that both general anesthesia and conscious sedation have no major anesthetic complications and may therefore be safe. Patients might benefit from conscious sedation in terms of recovery times, sore throat, and patient recovery and satisfaction, but only a few studies are included in the review and are relatively old. New research regarding this subject is needed to advise our patients most optimally in the future about the best anesthetic technique to be used when choosing for a laparoscopic sterilization procedure.

Impactfactor 3.061

Long-term outcome of vaginal mesh or native tissue in recurrent prolapse: a randomized controlled trial

Milani AL, **Damoiseaux A**, IntHout J, Kluivers KB, Withagen MIJ

Int Urogynecol J. 2018 Jun;29(6):847-858

INTRODUCTION AND HYPOTHESIS:

Our aim was to evaluate clinically relevant long-term outcomes of transvaginal mesh or native tissue repair in women with recurrent pelvic organ prolapse (POP).

METHODS:

We performed a 7-year follow-up of a randomized controlled trial on trocar-guided mesh placement or native tissue repair in women with recurrent POP. Primary outcome was composite success, defined as absence of POP beyond the hymen, absence of bulge symptoms, and absence of retreatment for POP. Secondary outcomes were adverse events, pain, and dyspareunia. Multiple imputation was used for missing data of composite success and pain; estimates are presented with 95% confidence intervals (CI).

RESULTS:

Between August 2006 and July 2008, 194 women were randomized; 190 underwent surgery. At 7 years, 142 (75%) were available for analysis, of whom, the primary outcome could be calculated in 127. Composite success was 53% (95% CI 41, 66) for mesh and 54% (95% CI 42, 65) for native tissue. Repeat surgery for POP was 25% for mesh and 16% for native tissue (difference 9%; 95% CI -5, 23) and occurred in untreated compartments in the mesh group and treated compartments in the native tissue group. Mesh exposure rate was 42%; pain with mesh 39% and native tissue 50% (difference?- 11%, 95% CI -27, 6); dyspareunia with mesh 20% and native tissue 17% (difference 3%, 95% CI -9, 17).

CONCLUSIONS:

Seven-year composite success rates appeared similar for mesh and native tissue. Mesh did not reduce long-term repeat surgery rates due to de novo POP in nonmesh-treated vaginal compartments. Mesh exposure rates were high, though significant differences in pain and dyspareunia were not detected.

Impactfactor 2.078

Opportunistic salpingectomy in women undergoing hysterectomy: Results from the HYSTUB randomised controlled trial

Van Lieshout LAM, Pijlman B, Vos MC, de Groot MJM, Houterman S, Coppus SFPJ, Harmsen MG, **Vandenput I, Piek JMJ**

Maturitas. 2018 Jan 107:1-6. Epub 2017 Oct 3

OBJECTIVE: To evaluate whether opportunistic salpingectomy in premenopausal women undergoing hysterectomy for benign indications is both hormonally and surgically safe, compared with hysterectomy without salpingectomy.

STUDY DESIGN: In this multicentre randomised controlled trial, women were randomised to undergo either hysterectomy with opportunistic bilateral salpingectomy (intervention group) or standard hysterectomy with preservation of the Fallopian tubes (control group).

MAIN OUTCOME MEASURES: The primary outcome was the difference in serum anti-Müllerian hormone concentration (?AMH), measured pre-surgery and 6 months post-surgery. Secondary outcomes were surgical outcomes and duration of hospital stay. The sample size was powered at 50 participants per group (n=100) to compare ?AMH after hysterectomy with salpingectomy to ?AMH after standard hysterectomy.

RESULTS: Between March 2013 and December 2016, 104 women, aged 30-55 years, were randomly allocated to hysterectomy with opportunistic bilateral salpingectomy (n=52) or standard hysterectomy (n=52). The baseline characteristics did not differ between the two groups. The median ?AMH was -0.14pmol/L (IQR -1.47-0.95) in the intervention group and 0.00pmol/L (IQR -1.05-0.80) in the control group (p=0.49). The addition of salpingectomy did not impair surgical results and it did not affect duration of hospital stay.

CONCLUSION: Addition of opportunistic bilateral salpingectomy during hysterectomy did not result in a larger effect on ovarian reserve when compared with hysterectomy alone, neither did it affect surgical outcomes. Therefore, opportunistic salpingectomy seems to be a safe procedure in premenopausal women undergoing hysterectomy for benign gynaecological conditions

Impactfactor 3.315

Para-aortic lymphadenectomy in advanced stage cervical cancer, a protocol for comparing safety, feasibility and diagnostic accuracy of surgical staging versus PET-CT; PALDISC trial

Tax C, Abbink K, Rovers MM, **Bekkers RL**, Zusterzeel PL

Pilot Feasibility Stud. 2018 Jan 4;4:27

Background:
Currently, a PET-CT is used to assess the need for extended field radiotherapy of para-aortic lymph nodes (PALN) in International Federation of Gynaecology and Obstetrics (FIGO) stage IB2, IIA2-IVA (locally advanced stage) cervical cancer. A small study established a sensitivity and specificity estimate for PALN metastases of 50% (95% CI; 7-93%) and 83% (95% CI; 52-98%), respectively. Surgical staging of PALN may lead to a higher diagnostic accuracy. However, surgical staging of para-aortic lymph nodes in locally advanced stage cervical cancer is not common practice. Therefore, a phase 2 randomised controlled trial is needed to assess its safety and feasibility.
Methods/design:
In addition to standard imaging (MRI or CT scan) with PET-CT, 30 adult women with FIGO stage IB2, IIA2-IVA cervical cancer will be randomised to receive either surgical staging or usual PET-CT staging. Administering extended field radiotherapy will be based on lymphadenectomy results for the intervention group and on the PET-CT results for the control group. Follow-up visits at 0, 3, 6, 9 and 12 months will assess health-related quality of life and progression-free survival.Primary safety and feasibility outcomes of surgical staging will be assessed by calculating means with 95% confidence intervals for duration of surgery, number of complications, blood loss, nodal yield after para-aortic lymphadenectomy and treatment delay due to surgical staging. Secondary patient-centred outcomes on quality of life and first year survival will be documented and compared between the two groups. Estimates of sensitivity, specificity and negative and positive predictive values of MRI, PET-CT and surgical staging will be presented with 95% CI.. All analysis will be performed according to the intention to treat principle.
Discussion:
This study will assess safety and feasibility, expressed as the number and severity of complications, effect on quality of life and the treatment delay due to surgically staging para-aortic lymph nodes in locally advanced cervical cancer. It will provide insight in the diagnostic accuracy of the PET-CT and detection rate of missed (micro)metastases due to surgical staging. This information will be used to assess the necessity for a phase 3 study on the diagnostic accuracy of the PET-CT and surgical staging. If a phase 3 study is deemed necessary, current data can be used for sample size calculation of such a phase 3 study.

Impactfactor --

Patients' information coping styles influence the benefit of a survivorship care plan in the ROGY care trial: New insights for tailored delivery

de Rooij BH, Ezendam NPM, Vos MC, Pijnenborg JMA, **Boll D**, Kruitwagen RFPM, van de Poll-Franse LV

Cancer. 2018 Nov 30. [Epub ahead of print]

Background:
In efforts to improve the implementation of survivorship care plans (SCPs), the authors assessed whether the impact of SCPs on patient-reported outcomes differed between patients with an information-seeking coping style (monitoring) versus those with an information-avoiding coping style (blunting).
METHODS: In the Registration System Oncological Gynecology (ROGY) Care Trial, 12 hospitals in the Netherlands were randomized to deliver SCP care or usual care. All patients with newly diagnosed endometrial and ovarian cancer in the SCP care arm received an SCP that was generated automatically by their oncology provider through the web-based ROGY registration system. Outcomes (satisfaction with information provision and care, illness perceptions, and health care use) were measured directly after initial treatment and after 6, 12, and 24 months. Information coping style was measured at 12 months after initial treatment.
RESULTS: Among patients who had a monitoring coping style (N = 123), those in the SCP care arm reported higher satisfaction with information provision (mean score: 73.9 vs 63.9, respectively; P = .04) and care (mean score: 74.5 vs 69.2, respectively; P = .03) compared with those in the usual care arm. Among patients who had a blunting coping style (N = 102), those in the SCP care arm reported a higher impact of the disease on life (mean score: 5.0 vs 4.5, respectively; P = .02) and a higher emotional impact of the disease (mean score: 5.4 vs 4.2, respectively; P = .01) compared with those in the usual care arm.
CONCLUSIONS: SCPs may be beneficial for patients who desire information about their disease, whereas SCPs may be less beneficial for patients who avoid medical information, suggesting a need for tailored SCP delivery to improve survivorship care.

Impactfactor *6.537*

Peritoneal carcinomatosis after risk-reducing surgery in BRCA1/2 mutation carriers

Harmsen MG, **Piek JMJ**, Bulten J, Casey MJ, Rebbeck TR, Mourits MJ, Greene MH, Slangen BFM, van Beurden M, Massuger LFAG, Hoogerbrugge N, de Hullu JA

Cancer. 2018 Mar 1 124(5):952-959. Epub 2018 Jan 9

BACKGROUND:
Risk-reducing salpingo-oophorectomy (RRSO) is recommended for BRCA1/2 mutation carriers because of their increased risk of ovarian carcinoma. Despite RRSO, metachronous peritoneal carcinomatosis occasionally is diagnosed.
METHODS:
The literature was searched for BRCA1/2 mutation carriers with peritoneal carcinomatosis after risk-reducing

surgery. The authors were asked for additional data. Clinical and histopathological data were descriptively analyzed. Cases were compared with a single-institution control cohort.
RESULTS:
Of 36 cases, 86.1% concerned BRCA1 mutation carriers. The median age of the patients was 52 years (range, 30-71 years) at the time of risk-reducing surgery and 60 years (range, 37-75 years) at the time of diagnosis of peritoneal carcinomatosis. The median interval between the 2 events was 54.5 months (range, 11-292 months). Peritoneal carcinomatosis was mostly high-grade serous carcinoma. Histopathological details of the RRSO specimens were retrieved in 8 cases; 5 (62.5%) were found to have serous tubal intraepithelial carcinoma and 1 had epithelial atypia. Cases were older (P = .025) at the time of risk-reducing surgery and harbored more serous tubal intraepithelial carcinomas (P<.001) compared with women from the control cohort.
CONCLUSIONS:
Metachronous peritoneal carcinomatosis after risk-reducing surgery occurs predominantly in BRCA1 mutation carriers, usually within 5 years. Data have suggested that surgery at a younger age lowers the rates of peritoneal carcinomatosis. These data can be used in the gynecologic counseling of BRCA1/2 mutation carriers. RRSO should include complete salpingectomy. Detailed histopathological examination of specimens removed during RRSO is essential. Cancer 2018;124:952-9. © 2018 American Cancer Society.

Impactfactor *6.537*

Peritoneal NK cells are responsive to IL-15 and percentages are correlated with outcome in advanced ovarian cancer patients

Hoogstad-van Evert JS, Maas RJ, van der Meer J, Cany J, van der Steen S, Jansen JH, Miller JS, **Bekkers R**, Hobo W, Massuger L, Dolstra H

Oncotarget. 2018 Oct 5;9(78):34810-34820

The demonstration that ovarian carcinoma (OC) is an immunogenic disease, opens opportunities to explore immunotherapeutic interventions to improve clinical outcome. In this regard, NK cell based immunotherapy could be promising as it has been demonstrated that OC cells are susceptible to killing by cytokine-stimulated NK cells. Here, we evaluated whether percentage, phenotype, function and IL-15 responsiveness of ascites-derived natural killer (NK) cells is related to progression-free survival (PFS) and overall survival (OS) of advanced stage OC patients. Generally, a lower percentage of NK cells within the lymphocyte fraction was seen in OC ascites (mean 17.4 ± 2.7%) versus benign peritoneal fluids (48.1 ± 6.8%; p < 0.0001). Importantly, a higher CD56+ NK cell percentage in ascites was associated with a better PFS (p = 0.01) and OS (p = 0.002) in OC patients. Furthermore, the functionality of ascites-derived NK cells in terms of CD107a/IFN-? activity was comparable to that of healthy donor peripheral blood NK cells, and stimulation with monomeric IL-15 or IL-15 superagonist ALT-803 potently improved their reactivity towards tumor cells. By showing that a higher NK cell percentage is related to better outcome in OC patients and NK cell functionality can be boosted by IL-15 receptor stimulation, a part of NK cell immunity in OC is further deciphered to exploit NK cell based immunotherapy.

Impactfactor *5.168*

Presence of koilocytosis in low-grade smears of high-risk HPV-positive women is a negative predictor for cervical intraepithelial neoplasia grade 3 or more

Siebers AG, van der Linden H, Vedder JE, **Bekkers RL**, Melchers WL, Bulten J

Cytopathology. 2018 Jun;29(3):275-280

OBJECTIVE:
The Netherlands converted to high-risk (hr)HPV-based screening in 2017. An increase in referral of hrHPV-positive women with low risk for cervical intraepithelial neoplasia grade 3 or more (CIN3+) is anticipated and reduction of unjustified referrals will have priority. The relevance of koilocytosis in relation to the underlying risk of high-grade CIN in a primary HPV screening setting is unclear. The aim was to investigate whether the risk for CIN3+ differs between hrHPV-positive atypical squamous cells of undetermined significance (ASC-US)/low-grade squamous intraepithelial lesion (LSIL) with or without koilocytosis.
METHODS:
Retrospective cohort study, using data from the Dutch national pathology database (PALGA). The population was 1201 hrHPV-positive women with cytological diagnosis of ASC-US/LSIL. Reporting of koilocytosis was assessed as well as detection rates of CIN1 or less, CIN2 and CIN3+ for ASC-US/LSIL cytology stratified by presence or absence of koilocytosis. Crude and adjusted odds ratios were determined.
RESULTS:
Koilocytosis was present in 40.1% of ASC-US and 45.9% of LSIL cases. CIN3+ is significantly less often found when koilocytosis is present (7.8% for hrHPV-positive ASC-US with- vs 15.8% without koilocytosis). For hrHPV-positive LSIL this was 11.7% vs 20.2%. The crude and adjusted odds ratios for CIN3+ was 0.45 for hrHPV-positive ASC-US and 0.52 for hrHPV-positive LSIL.
CONCLUSIONS:
The presence of koilocytosis is a negative predictor of CIN3+. The risk of hrHPV-positive ASC-US with koilocytosis is in the same range as hrHPV-positive/cytology negative cases and in a setting of primary hrHPV screening these

cases could be followed conservatively by repeat cytology. The results should be confirmed by the first data from the Dutch HPV-based screening programme.

Impactfactor 1.376

Primum non nocere: earlier cessation of glucose monitoring is possible

Blank C, van Dillen J, Hogeveen M

Eur J Pediatr. 2018 Aug;177(8):1239-1245

Newborns are at relatively high risk for developing hypoglycaemia in the first 24 h after birth. Well-known risk factors are prematurity, small for gestational age (SGA) or large for gestational age (LGA), and maternal pre-existent or gestational diabetes mellitus. Prolonged hypoglycaemia is associated with poor neurodevelopmental outcomes; hence, prevention through proper monitoring and treatment is important. Given the ongoing debate concerning frequency and duration of screening for neonatal hypoglycaemia, therefore, we investigated the frequency and duration of glucose monitoring safe to discover neonatal hypoglycaemia in different risk groups. Data of newborns at risk for hypoglycaemia were retrospectively collected and analysed. Blood glucose concentrations were measured 1, 3, 6, 12, and 24 h after birth. Moderate hypoglycaemia was defined as a blood glucose concentration of <?2.2 mM and severe hypoglycaemia as a concentration of <?1.5 mM. Of 1570 newborns, 762 (48.5%) had at least one episode of hypoglycaemia in the first 24 h after birth; 30.6% of them had severe hypoglycaemia (all in the first 9 h after birth). Only three SGA and two LGA newborns had a first moderate asymptomatic hypoglycaemic episode beyond 12 h after birth. The incidence of hypoglycaemia increased with accumulation of multiple risk factors.

CONCLUSION:

Safety of limiting the monitoring to 12 h still has to be carefully evaluated in the presence of SGA or LGA newborns; however, our results suggest that 12 h is enough for late preterm newborns (>?34 weeks) and maternal diabetes. What is Known: • Newborns are at relatively high risk for developing hypoglycaemia and such hypoglycaemia is associated with adverse neurodevelopmental outcomes. • Proper glucose monitoring and prompt treatment in case of neonatal hypoglycaemia are necessary. What is New: • Glucose monitoring 12 h after birth is proficient for most newborns at risk. • Maternal diabetes leads to the highest risk of early neonatal hypoglycaemia and newborns with more than one risk factor are at increased risk of hypoglycaemia

Impactfactor 2.242

Screening for persistent high-risk HPV infections may be a valuable screening method for young women; A retrospective cohort study

Ebisch RM, Ketelaars PJ, van der Sanden WM, Schmeink CE, Lenselink CH, Siebers AG, Massuger LF, Melchers WJ, **Bekkers RL**

PLoS One. 2018 Oct 24;13(10):e0206219

INTRODUCTION: Screening of young women is often discouraged because of the high risk of unnecessary diagnostics or overtreatment. Multiple countries therefore use cytology instead of high risk human papillomavirus (hrHPV)-testing as screening method for young women because of the limited specificity of hrHPV-testing. The objective of this study was to investigate how hrHPV screening before the age of 30, can be used to reduce the future prevalence of high-grade cervical lesions in young women.

METHODS: We retrospectively analyzed follow-up data from a cohort study on HPV prevalence in unscreened Dutch women aged 18-29 years. Women performed multiple self-collected cervico-vaginal samples for HPV detection and genotyping. At least one valid cervical pathology result was obtained from 1,018 women. Women were categorized as hrHPV negative, cleared- or persistent hrHPV infection. Anonymized follow-up data for each group was obtained. Composite outcome measures were defined as; normal, low-grade squamous intraepithelial lesion (LSIL) or high-grade squamous intraepithelial lesion (HSIL). The association between prior hrHPV status and cytology and histology outcome was analyzed.

RESULTS: After exclusion, a pathology result was registered for 962 women. The prevalence of HSIL was 19.3% in women with a persistent HPV infection at a younger age. This is significantly higher (p<0,001) compared with the HSIL prevalence of 1.5% in HPV-negative women, and 3.1% (n = 8) in women who cleared the hrHPV infection in the past.

CONCLUSION: Women with a persistent hrHPV infection in their 20s, show an increased prevalence of HSIL lesions in their early 30s. Screening for persistent hrHPV infections, instead of cytology screening before the age of 30, can be used to reduce the future prevalence of cervical cancer in young women.

Impactfactor 2.766

Surgical management of pelvic organ prolapse.

Maher CF, Baessler KK, Barber MD, Cheong C, Consten ECJ, Cooper KG, Deffieux X, **Dietz V**, Gutman RE, van Iersel JJ, Nager CW, Sung VW, de Tayrac R.

Climacteric. 2018 Dec 21:1-7. [Epub ahead of print]

Despite pelvic organ prolapse being a universal problem experienced in nearly 50% of parous women, the surgical management of vaginal prolapse remains an enigma to many, with wide variation in the rates and types of

intervention performed. As part of the 6th International Consultation on Incontinence (ICI) our committee, charged with producing an evidence-based report on the surgical management of prolapse, produced a pathway for the surgical management of prolapse. The 2017 ICI surgical management of prolapse evidence-based pathway will be presented and summarized. Weaknesses of the data and pathway will be discussed and avenues for future research proposed.

Impactfactor 2.807

Surgical margins in squamous cell carcinoma, different for the vulva?

Pleunis N, Leermakers ME, van der Wurff AA, Klinkhamer PJ, Ezendam NP, **Boll D**, de Hullu JA, Pijnenborg JM

Eur J Surg Oncol. 2018 Oct;44(10):1555-1561

INTRODUCTION:

The recommended pathological resection margin (8 mm) for vulvar squamous cell carcinoma (SCC) is broader than for SCC located elsewhere, and does not depend on tumor grade or lesion size. Our aim is to evaluate the resection margin in vulvar SCC in relation to local recurrence, and to determine the impact of other prognostic factors.

MATERIALS AND METHODS:

Data of all surgically treated patients at the Gynecological Oncology Center South with vulvar SCC, FIGO IB-IIIC, between 2005 and 2015 were analysed retrospectively. The relation between the pathological resection margin and other clinicopathological factors with the risk of local recurrence was analysed.

RESULTS:

In this cohort of 167 patients, the tumor was radically removed in 87% of the patients. Yet, in 57% the pathological resection margin was <8 mm. Including re-excisions, the median closest margin was 7.0 mm. There was no significant difference in the risk of local recurrence for a resection margin <8 mm or =8 mm (25.0% (n = 20) and 22.2% (n = 16)), nor in the median resection margin of patients with or without local recurrence (6.5 mm and 7.0 mm). Lichen sclerosus was the only significant risk factor for local recurrence.

CONCLUSION:

A pathological resection margin <8 mm was not related to an increased risk of local recurrence. The most important predictor of local recurrence was the presence of lichen sclerosus. A resection margin <8 mm in vulvar SCC can therefore be accepted, especially in tumors located close to clitoris, urethra or anus.

Impactfactor 3.688

Survivorship care plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients: the ROGY care trial

de Rooij BH, Ezendam NPM, Nicolaije KAH, Lodder P, Vos MC, Pijnenborg JMA, **Boll D**, Kruitwagen RFPM, van de Poll-Franse LV

Qual Life Res. 2018 Jun 27(6):1533-1544. Epub 2018 Mar 6

PURPOSE: Prior results from the registration system oncological gynecology (ROGY) care trial showed that survivorship care plans (SCPs) increased threatening illness perceptions in gynecological cancer survivors, but it remained unclear whether this would result in poorer physical and psychosocial outcomes. The aim of the current study is to assess the direct and indirect effects of SCPs on health-related quality of life (HRQoL) and anxiety and depression, through illness perceptions.

METHODS: Twelve hospitals in the South of the Netherlands were randomized to providing 'SCP care' or 'usual care.' Newly diagnosed endometrial and ovarian cancer patients completed questionnaires after initial treatment (endometrial, 221 [75%]; ovarian, 174 [71%]) and after 6, 12, and 24 months. SCPs were automatically generated after initial treatment by the oncology providers through the web-based ROGY. Illness perceptions were measured after initial treatment and HRQoL and anxiety and depression after 6, 12, and 24 months.

RESULTS: Structural equation models showed that endometrial cancer patients who experienced more symptoms or concern due to the SCP reported worse social functioning (ß?=?-?0.82; p?=?0.01) and more fatigue, insomnia, pain, and anxiety (ß?=?0.58-0.86, p?<?0.05) within 12 months after treatment. Ovarian cancer patients who had lower trust that the treatment would cure their disease due to the SCP reported worse emotional functioning 6 months after treatment (ß?=?0.27, p?=?0.02).

CONCLUSIONS: Current results show that SCPs may have negative effects on HRQoL and anxiety in patients who experience more threatening illness perceptions due to the SCP. We should be aware of the potential negative consequences of SCPs.

Impactfactor 2.392

The impact of the survivorship care plan on health care use: 2-year follow-up results of the ROGY care trial

Jeppesen MM, Ezendam NPM, Pijnenborg JMA, Caroline Vos M, **Boll D**, Kruitwagen RFPM, Jensen PT, van de Poll-Franse LV

J Cancer Surviv. 2018 Feb 12(1):18-27. Epub 2017 Sep 5

PURPOSE:

The purpose of this paper was to assess the impact of survivorship care plan (SCP) provision and moderating factors on health care use following endometrial cancer treatment.

METHODS:
Women newly diagnosed with endometrial cancer were included in a pragmatic cluster randomized trial at 12 hospitals in the Netherlands and were randomly assigned to SCP or usual care (n = 221; 75% response). The SCP was generated using the web-based Registrationsystem Oncological GYnecology (ROGY) and provided tailored information regarding disease, treatment, and possible late-effects. Cancer-related use of general practitioner, specialist, and additional health care was collected through questionnaires after diagnosis and at 6-, 12-, and 24-month follow-up and compared using linear multilevel regression analyses.
RESULTS:
Women who received an SCP had more cancer-related primary care visits compared to the usual care arm during the first year after diagnosis (ß = 0.7, p < 0.01). At 6-month follow-up, women in the SCP group used more additional health care compared to women receiving usual care (24 vs. 11%, p = 0.04). Women with anxious symptoms (p = 0.03) and women who received radiotherapy (p = 0.01) had a higher primary care use within the first year after treatment, when receiving an SCP.
CONCLUSIONS:
The SCP increases primary health care consumption the first year after treatment, particularly in women treated with radiotherapy and women with anxious symptoms.
IMPLICATIONS FOR CANCER SURVIVORS:
These findings imply that the SCP enables women in need of supportive care to seek relevant care at an early stage after treatment. Whether this results in improved patient-reported outcomes in the long-term needs to be further studied.

Impactfactor 3.713

The randomised uterine septum transsection trial (TRUST): design and protocol

Rikken JF, Kowalik CR, Emanuel MH, Bongers MY, Spinder T, de Kruif JH, Bloemenkamp KW, Jansen FW, Veersema S, Mulders AG, Thurkow AL, Hald K, Mohazzab A, Khalaf Y, Clark TJ, Farrugia M, **van Vliet H**, Stephenson MS, van der Veen F, van Wely M, Mol BW, Goddijn M

BMC Womens Health. 2018 Oct 5;18(1):163

BACKGROUND:
A septate uterus is a uterine anomaly that may affect reproductive outcome, and is associated with an increased risk for miscarriage, subfertility and preterm birth. Resection of the septum is subject of debate. There is no convincing evidence concerning its effectiveness and safety. This study aims to assess whether hysteroscopic septum resection improves reproductive outcome in women with a septate uterus.
METHODS/DESIGN:
A multi-centre randomised controlled trial comparing hysteroscopic septum resection and expectant management in women with recurrent miscarriage or subfertility and diagnosed with a septate uterus. The primary outcome is live birth, defined as the birth of a living foetus beyond 24 weeks of gestational age. Secondary outcomes are ongoing pregnancy, clinical pregnancy, miscarriage and complications following hysteroscopic septum resection. The analysis will be performed according to the intention to treat principle. Kaplan-Meier curves will be constructed, estimating the cumulative probability of conception leading to live birth rate over time. Based on retrospective studies, we anticipate an improvement of the live birth rate from 35% without surgery to 70% with surgery. To demonstrate this difference, 68 women need to be randomised.
DISCUSSION:
Hysteroscopic septum resection is worldwide considered as a standard procedure in women with a septate uterus. Solid evidence for this recommendation.

Impactfactor 1.806

The role of positive psychological changes in anxiety and depression of patients with ovarian tumors and their partners: an observational study from the population-based PROFILES registry

Camara C, Caroline Vos M, de Rooij BH, Pijnenborg JMA, **Boll D**, van de Poll-Franse LV1, Ezendam NPM

Support Care Cancer. 2018 Jun 29. epub ahead of print

PURPOSE:
It is unknown whether positive psychological changes (e.g., in life perspective, self-perception, and social relationships) after being diagnosed with ovarian cancer can reduce anxiety and depression in patients and their partners. The first aim of the present study was to assess differences in anxiety and depression between patients diagnosed with an ovarian tumor and their partners. The second aim was to explore the mutual associations of patients' and partners' posttraumatic growth and their anxiety and depressive symptoms.
METHODS:
Participants included 130 Dutch couples of which one partner was diagnosed with a borderline ovarian tumor or ovarian cancer between 2000 and 2010, as registered by the Netherlands Cancer Registry. In September 2011, a questionnaire was sent including the Hospital Anxiety and Depression Scale (anxiety and depression) and Cancer Survivors (Partners) Unmet Needs measure (positive psychological changes).

RESULTS:
A one-way multivariate analysis of variance showed that patients reported higher anxiety than partners, without differences in depression. Contrasting to our expectations, an actor-partner interdependence model revealed no mutual dyadic associations between positive psychological changes and anxiety or depressive symptoms.
CONCLUSIONS:
Based on these findings, positive psychological change seems to be an independent construct unrelated to anxiety or depression in couples diagnosed with ovarian tumors. Still, as ovarian tumor patients and partners suffer from high anxiety and depression, further research investigating how these feelings can be reduced in couples dealing with an ovarian tumor is necessary.
Impactfactor 2.676

Intensive Care

ABCDE of prehospital ultrasonography: a narrative review

Ketelaars R, **Reijnders G**, van Geffen GJ, Scheffer GJ, Hoogerwerf N

Crit Ultrasound J. 2018 Aug 8;10(1):17

Prehospital point-of-care ultrasound used by nonradiologists in emergency medicine is gaining ground. It is feasible on-scene and during aeromedical transport and allows health-care professionals to detect or rule out potential harmful conditions. Consequently, it impacts decision-making in prioritizing care, selecting the best treatment, and the most suitable transport mode and destination. This increasing relevance of prehospital ultrasonography is due to advancements in ultrasound devices and related technology, and to a growing number of applications. This narrative review aims to present an overview of prehospital ultrasonography literature. The focus is on civilian emergency (trauma and non-trauma) setting. Current and potential future applications are discussed, structured according to the airway, breathing, circulation, disability, and environment/exposure (ABCDE) approach. Aside from diagnostic implementation and specific protocols, procedural guidance, therapeutic ultrasound, and challenges are reviewed.

Impactfactor --

An alternative ICU staffing model: implementation of the non-physician provider

Kreeftenberg HG, **Aarts JT**, de Bie A, **Bindels AJGH, Roos AN**, van der Voort PHJ

Neth J Med. 2018 May;76(4):176-183

INTRODUCTION: Literature in Europe regarding implementation of nurse practitioners or physician assistants in the intensive care unit (ICU) is lacking, while some available studies indicate that this concept can improve the quality of care and overcome physician shortages on ICUs. The aim of this study is to provide insight on how a Dutch ICU implemented non-physician providers (NPP), besides residents, and what this staffing model adds to the care on the ICU.

METHODS: This paper defines the training course and job description of NPPs on a Dutch ICU. It describes the number and quality of invasive interventions performed by NPPs, residents, and intensivists during the years 2015 and 2016. Salary scales of NPPs and residents are provided to describe potential cost-effectiveness.

RESULTS: The tasks of NPPs on the ICU are equal to those of the residents. Analysis of the invasive interventions performed by NPPs showed an incidence of central venous catheter insertion for NPPs of 20 per fulltime equivalent (FTE) and for residents 4.3 per FTE in one year. For arterial catheters the NPP inserted 61.7 per FTE and the residents inserted 11.8 per FTE. The complication rate of both groups was in line with recent literature. Regarding their salary: after five years in service an NPP earns more than a starting resident.

CONCLUSION:

This is the first European study which describes the role of NPPs on the ICU and shows that practical interventions normally performed by physicians can be performed with equal safety and quality by NPPs.

Impactfactor *1.156*

Early prognostication after cardiac arrest: Are we getting closer?

Kamps M, Hoedemaekers C

Resuscitation. 2018 Aug;129:A3-A4

Comment in

Authors' comments on two published resuscitation editorials. [Resuscitation. 2018]

Comment on

Neurophysiological and neuroradiological multimodal approach for early poor outcome prediction after cardiac arrest. [Resuscitation. 2018]

Impactfactor *5.863*

RegressionExplorer: Interactive Exploration of Logistic Regression Models with Subgroup Analysis

Dingen D, Veer MV, Houthuizen P, **Mestrom EHJ**, Korsten EHHM, Bouwman ARA, Wijk JV

IEEE Trans Vis Comput Graph. 2018 Sep 13. [Epub ahead of print]

We present RegressionExplorer, a Visual Analytics tool for the interactive exploration of logistic regression models. Our application domain is Clinical Biostatistics, where models are derived from patient data with the aim to obtain clinically meaningful insights and consequences. Development and interpretation of a proper model requires domain expertise and insight into model characteristics. Because of time constraints, often a limited number of candidate models is evaluated. RegressionExplorer enables experts to quickly generate, evaluate, and compare many different models, taking the workflow for model development as starting point. Global patterns in parameter values of candidate models can be explored effectively. In addition, experts are enabled to compare candidate models across multiple subpopulations. The insights obtained can be used to formulate new hypotheses or to steer model development. The effectiveness of the tool is demonstrated for two uses cases: prediction of a cardiac conduction disorder in patients after receiving a heart valve implant and prediction of hypernatremia in critically ill patients.

Impactfactor *3.078*

Inwendige Geneeskunde

A cost analysis of upfront DPYD genotype-guided dose individualisation in fluoropyrimidine-based anticancer therapy

Henricks LM, Lunenburg CATC, de Man FM, Meulendijks D, Frederix GWJ, Kienhuis E, **Creemers GJ**, Baars A, Dezentjé VO, Imholz ALT, Jeurissen FJF, Portielje JEA, Jansen RLH, Hamberg P, Ten Tije AJ, Droogendijk HJ, Koopman M, Nieboer P, van de Poel MHW, Mandigers CMPW, Rosing H, Beijnen JH, et al

Eur J Cancer. 2018 Dec 10 107:60-67. [Epub ahead of print]

BACKGROUND:
Fluoropyrimidine therapy including capecitabine or 5-fluorouracil can result in severe treatment-related toxicity in up to 30% of patients. Toxicity is often related to reduced activity of dihydropyrimidine dehydrogenase, the main metabolic fluoropyrimidine enzyme, primarily caused by genetic DPYD polymorphisms. In a large prospective study, it was concluded that upfront DPYD-guided dose individualisation is able to improve safety of fluoropyrimidine-based therapy. In our current analysis, we evaluated whether this strategy is cost saving.
METHODS:
A cost-minimisation analysis from a health-care payer perspective was performed as part of the prospective clinical trial (NCT02324452) in which patients prior to start of fluoropyrimidine-based therapy were screened for the DPYD variants DPYD*2A, c.2846A>T, c.1679T>G and c.1236G>A and received an initial dose reduction of 25% (c.2846A>T, c.1236G>A) or 50% (DPYD*2A, c.1679T>G). Data on treatment, toxicity, hospitalisation and other toxicity-related interventions were collected. The model compared prospective screening for these DPYD variants with no DPYD screening. One-way and probabilistic sensitivity analyses were also performed.
RESULTS:
Expected total costs of the screening strategy were €2599 per patient compared with €2650 for non-screening, resulting in a net cost saving of €51 per patient. Results of the probabilistic sensitivity and one-way sensitivity analysis demonstrated that the screening strategy was very likely to be cost saving or worst case cost-neutral.
CONCLUSIONS:
Upfront DPYD-guided dose individualisation, improving patient safety, is cost saving or cost-neutral but is not expected to yield additional costs. These results endorse implementing DPYD screening before start of fluoropyrimidine treatment as standard of care

Impactfactor 7.191

Acute hepatitis C in HIV-negative men who have sex with men in the Netherlands and Belgium: a call for action

Boerekamps A, Wouters K, **Ammerlaan HS**, Götz HM, Laga M, Rijnders BJ

Sex Transm Infect. 2018 Jun;94(4):297

Geen abstract beschikbaar

Impactfactor 1.981

An alternative ICU staffing model: implementation of the non-physician provider

Kreeftenberg HG, Aarts JT, **de Bie A**, Bindels AJGH, Roos AN, van der Voort PHJ

Neth J Med. 2018 May;76(4):176-183

INTRODUCTION:
Literature in Europe regarding implementation of nurse practitioners or physician assistants in the intensive care unit (ICU) is lacking, while some available studies indicate that this concept can improve the quality of care and overcome physician shortages on ICUs. The aim of this study is to provide insight on how a Dutch ICU implemented non-physician providers (NPP), besides residents, and what this staffing model adds to the care on the ICU.
METHODS:
This paper defines the training course and job description of NPPs on a Dutch ICU. It describes the number and quality of invasive interventions performed by NPPs, residents, and intensivists during the years 2015 and 2016. Salary scales of NPPs and residents are provided to describe potential cost-effectiveness.
RESULTS:
The tasks of NPPs on the ICU are equal to those of the residents. Analysis of the invasive interventions performed by NPPs showed an incidence of central venous catheter insertion for NPPs of 20 per fulltime equivalent (FTE) and for residents 4.3 per FTE in one year. For arterial catheters the NPP inserted 61.7 per FTE and the residents inserted 11.8 per FTE. The complication rate of both groups was in line with recent literature. Regarding their salary: after five years in service an NPP earns more than a starting resident.
CONCLUSION:
This is the first European study which describes the role of NPPs on the ICU and shows that practical interventions normally performed by physicians can be performed with equal safety and quality by NPPs.

Impactfactor 1.156

Betere overleving na een Staphylococcus aureus-bacteriëmie bij betrokkenheid van het antibioticateam en bundelaanpak?

M. van den Hurk, J. Fonville, **H.S.M. Ammerlaan**, C. Miedema, S. Sanders, I Overdevest

TVI : tijdschrift voor infectieziekten, 2018;13(1):3-10

Staphylococcus aureus is een van de meest voorkomende verwekkers van een bacteriëmie. Een Staphylococcus aureus-bacteriëmie (SAB) heeft een hoge mortaliteit, mede door een vaak gecompliceerd beloop met strooihaarden. Uit literatuuronderzoek blijkt dat een bundelaanpak en de betrokkenheid van een multidisciplinair antibioticateam de uitkomst van SAB significant verbeteren. We hebben retrospectief beoordeeld wat de invloed is van ons antibioticateam op de aanpak van SAB en op de mortaliteit en het recidiefrisico voor de patiënt. Tevens werd onderzocht welke onderdelen in het behandeltraject de meeste invloed hadden op de prognose van de patiënt.

Impactfactor --

Capecitabine-Associated Terminal Ileitis

van Hellemond IE, Thijs AM, Creemers GJ

Case Rep Oncol. 2018 Oct 22;11(3):654-659

Capecitabine is an oral fluoropyrimidine used as adjuvant and palliative chemotherapy in patients with colorectal cancer. Diarrhea is a well-known side effect of capecitabine and 5-fluorouracil agents. We present a case with terminal ileitis as a rare adverse event of capecitabine treatment. Capecitabine-induced terminal ileitis is likely to be underreported. It should be considered more often as a cause of severe and atypical complaints of diarrhea during treatment with capecitabine or other 5-fluorouracil agents.

Impactfactor --

Case series on acute HCV in HIV-negative men in regular clinical practice: a call for action

Boerekamps A, Wouters K, **Ammerlaan HSM**, Götz HM, Laga M, Rijnders BJ

Neth J Med. 2018 Oct;76(8):374-378

BACKGROUND:

The evidence that HIV treatment as prevention (TasP) and HIV pre-exposure prophylaxis (PrEP) reduces the risk of HIV transmission is overwhelming. But as PrEP and TasP can lead to increased sexual mixing between HIV positive and negative men who have sex with men (MSM), sexually transmitted infections such as acute hepatitis C (HCV), which were thought to be limited to HIV-infected MSM, could become more frequent in HIV uninfected MSM as well. The objective of this study was to describe a series of cases of sexually transmitted HCV infections in HIV-uninfected MSM in the Netherlands and Belgium.

METHODS:

Through the Dutch Acute HCV in HIV Study (a Dutch-Belgian prospective multicentre study on the treatment of acute HCV infection, NCT02600325) and the Be-PrEP-ared study (a PrEP project in Antwerp, EudraCT2015-000054-37) several acute HCV infections were detected in HIV-negative men.

RESLTS:

A newly acquired HCV infection was diagnosed in ten HIV-negative MSM. HCV was diagnosed at a sexually transmitted infection (STI) clinic (n = 2), by their general practitioner (n = 2), by their HIV physician (n = 1) or at a PrEP clinic (n = 5). Ten patients reported unprotected anal intercourse and four had a concomitant STI at the time of HCV diagnosis. Six patients reported using drugs during sex.

CONCLUSIONS:

Our observation calls for a larger nationwide epidemiological study on the prevalence, incidence and risk factors of HCV infection in HIV-uninfected MSM. In the changing landscape of TasP and PrEP, reliable and up-to-date epidemiological data on HCV among HIV-uninfected MSM are needed and will help in developing evidence-based testing policies.

Impactfactor *1.156*

Comorbidities associated with higher von Willebrand factor (VWF) levels may explain the age-related increase of VWF in von Willebrand disease

Atiq F, Meijer K, Eikenboom J, Fijnvandraat K, Mauser-Bunschoten EP, van Galen KP, **Nijziel MR**, Ypma PF, de Meris J, Laros-van Gorkom BA, van der Bom JG, de Maat MP, Cnossen MH, Leebeek FW; WiN study group

Br J Haematol. 2018 Jul;182(1):93-105

Some comorbidities, such as hypertension, are associated with higher von Willebrand factor (VWF) levels in the general population. No studies have been conducted to assess this association in patients with von Willebrand disease (VWD). Therefore, we studied this association in patients with type 1 (n = 333) and type 2 (n = 203) VWD from the 'WiN" study. VWF antigen (VWF:Ag) was higher in type 1 VWD patients with hypertension [difference: 0·23 iu/ml, 95% confidence interval (CI): 0·11-0·35], diabetes mellitus (0·11 iu/ml, 95% CI: -0·02 to 0·23), cancer (0·14 iu/ml, 95% CI: 0·03-0·25) and thyroid dysfunction (0·14 iu/ml, 95% CI: 0·03-0·26) than in patients without these comorbidities (all corrected for age, sex and blood group). Similar results were observed for VWF collagen binding

capacity (VWF:CB), VWF activity as measured by the VWF monoclonal antibody assay (VWF:Ab) and factor VIII (FVIII) coagulant activity (FVIII:C). In type 1 VWD, age was associated with higher VWF:Ag (0·03 iu/ml; 95% CI: 0·01-0·04), VWF:CB (0·02 iu/ml; 95% CI: 0·00-0·04), VWF:Ab (0·04 iu/ml; 95% CI: 0·02-0·06) and FVIII:C (0·03 iu/ml; 95% CI: 0·01-0·06) per decade increase. After adjustment for relevant comorbidities, these associations were no longer significant. Despite the higher VWF and FVIII levels, type 1 VWD patients with comorbidities had more bleeding episodes, particularly during surgery. There was no association between comorbidities and VWF/FVIII levels or bleeding phenotype in type 2 VWD patients. In conclusion, comorbidities are associated with higher VWF and FVIII levels in type 1 VWD and may explain the age-related increase of VWF and FVIII levels.

Impactfactor 5.128

Conservative care as a treatment option for patients aged 75 years and older with CKD stage V: a National survey in the Netherlands

Susanto C, Kooman J, Courtens AM, **Konings CJAM**

Eur Geriatr Med. 2018;9(2):235-242. Epub 2018 Feb 12

Background and objectives:

Conservative care for patients aged 75 years and older with CKD stage 5 as a treatment option besides dialysis was proposed officially in the Netherlands in October 2016. This national survey showed the current implementation of this option in Netherlands nephrology departments.

Design setting participants and measurement:

A web-based survey was sent to medical managers of 60 nephrology departments in the Netherlands in August 2016.

Results:

Twenty-one medical managers (35%) completed the survey. The term "conservative care" is frequently used and well known. The estimated number of patients in whom the decision for maximal conservative care was made in 2015 was 310 of 2249 patients with CKD stage 5 age 75 years and older (range 5-50 patients per department). 164 patients became symptomatic and received no dialysis. There is no official registration for this treatment option and patient category. The practice patterns vary widely. Only one of 21 respondents reported a conservative care outpatient clinic. Formal training or education regarding conservative care is not available in most of departments. 95% of respondents discussed this treatment option with their patients. General practitioners are always being informed about their patient's decision. Their main role is providing or organizing palliative care support at the end of life and discussing advance care planning. Most respondents (86%) considered to include their patients in a prospective multicentre observational study, conservative care versus dialysis.

Conclusions:

Conservative care as a treatment option for patients with CKD stage 5 aged 75 years and older is well established. The practice patterns are varied in the Netherlands. Follow-up studies are needed to see whether the new multidisciplinary guideline facilitates harmonization of practice pattern. Funding is needed to optimize the implementation of conservative care.

Impactfactor 1.169

Development of diagnostic prediction tools for bacteraemia caused by third-generation cephalosporin-resistant enterobacteria in suspected bacterial infections: a nested case-control study

Rottier WC, van Werkhoven CH, Bamberg YR, Dorigo-Zetsma JW, van de Garde EM, van Hees BC, Kluytmans JA, Kuck EM, van der Linden PD, Prins JM, Thijsen SF, Verbon A, Vlaminckx BJ, **Ammerlaan HS**, Bonten MJ

Clin Microbiol Infect. 2018 Dec;24(12):1315-1321

OBJECTIVES:

Current guidelines for the empirical antibiotic treatment predict the presence of third-generation cephalosporin-resistant enterobacterial bacteraemia (3GCR-E-Bac) in case of infection only poorly, thereby increasing unnecessary carbapenem use. We aimed to develop diagnostic scoring systems which can better predict the presence of 3GCR-E-Bac.

METHODS:

A retrospective nested case-control study was performed that included patients =18 years of age from eight Dutch hospitals in whom blood cultures were obtained and intravenous antibiotics were initiated. Each patient with 3GCR-E-Bac was matched to four control infection episodes within the same hospital, based on blood-culture date and onset location (community or hospital). Starting from 32 commonly described clinical risk factors at infection onset, selection strategies were used to derive scoring systems for the probability of community- and hospital-onset 3GCR-E-Bac.

RESULTS:

3GCR-E-Bac occurred in 90 of 22 506 (0.4%) community-onset infections and in 82 of 8110 (1.0%) hospital-onset infections, and these cases were matched to 360 community-onset and 328 hospital-onset control episodes. The derived community-onset and hospital-onset scoring systems consisted of six and nine predictors, respectively. With selected score cut-offs, the models identified 3GCR-E-Bac with sensitivity equal to existing guidelines (community-onset: 54.3%; hospital-onset: 81.5%). However, they reduced the proportion of patients classified as

at risk for 3GCR-E-Bac (i.e. eligible for empirical carbapenem therapy) with 40% (95%CI 21-56%) and 49% (95%CI 39-58%) in, respectively, community-onset and hospital-onset infections.

CONCLUSIONS:

These prediction scores for 3GCR-E-Bac, specifically geared towards the initiation of empirical antibiotic treatment, may improve the balance between inappropriate antibiotics and carbapenem overuse.

Impactfactor 5.394

Double-Balloon Endoscopy after Incomplete Colonoscopy and Its Comparison with Computed Tomography Colonography

Hermans C, Zee DV, Gilissen L

Clin Endosc. 2018 Jan 51(1):66-71. Epub 2018 Jan 10

BACKGROUND/AIMS:

Because of the national screening program for colorectal carcinoma in The Netherlands, the number of colonoscopies has increased. In case of incomplete colonoscopy, computed tomography colonography (CTC) and double-balloon colonoscopy (DBc) are alternative options. This study evaluated cecal intubation rate and pathology detection rate in the previously unexplored part of the colon, complication rate of DBc, and CTC results after incomplete colonoscopy.

METHODS:

Retrospective observational study in a tertiary referral hospital regarding DBc and CTC reports from cases with incomplete colonoscopy.

RESULTS:

Sixty-three DBcs were performed after incomplete colonoscopy. Cecal intubation rate was 95%. Detection rate was 58% (5% carcinoma and 3% high-grade dysplastic adenoma). CTC preceded 54% of DBcs and 62% of CTC findings were confirmed. In 16%, a biopsy was taken, and in 60%, an intervention (mostly polypectomy) was performed. One major complication (1.5%) occurred, i.e., arterial bleeding due to polypectomy necessitating right hemicolectomy. CTC (n=213) showed a possible lesion in 35%, and could be confirmed by follow-up endoscopy or surgery in 65%.

CONCLUSIONS:

DBc is effective and safe for completion of colon inspection in incomplete colonoscopy. In patients with a high likelihood of pathology, DBc is preferred over CTC.

Impactfactor --

DPYD genotype-guided dose individualisation of fluoropyrimidine therapy in patients with cancer: a prospective safety analysis

Henricks LM, Lunenburg CA, de Man FM, Meulendijks D, Frederix GW, Kienhuis E, **Creemers GJ**, Baars A, Dezentjé VO, Imholz AL, Jeurissen FJ, Portielje JE, Jansen RL, Hamberg P, Ten Tije AJ, Droogendijk HJ, Koopman M, Nieboer P, van de Poel MHW, Mandigers CM, Rosing H, Beijnen JH, Werkhoven EV, van Kuilenburg AB, van Schaik RH, Mathijssen RH, Swen JJ, Gelderblom H, Cats A, Guchelaar HJ, Schellens JHM

Lancet Oncol. 2018 Nov;19(11):1459-1467

BACKGROUND:

Fluoropyrimidine treatment can result in severe toxicity in up to 30% of patients and is often the result of reduced activity of the key metabolic enzyme dihydropyrimidine dehydrogenase (DPD), mostly caused by genetic variants in the gene encoding DPD (DPYD). We assessed the effect of prospective screening for the four most relevant DPYD variants (DPYD*2A [rs3918290, c.1905+1G>A, IVS14+1G>A], c.2846A>T [rs67376798, D949V], c.1679T>G [rs55886062, DPYD*13, I560S], and c.1236G>A [rs56038477, E412E, in haplotype B3]) on patient safety and subsequent DPYD genotype-guided dose individualisation in daily clinical careMETHODS:
In this prospective, multicentre, safety analysis in 17 hospitals in the Netherlands, the study population consisted of adult patients (=18 years) with cancer who were intended to start on a fluoropyrimidine-based anticancer therapy (capecitabine or fluorouracil as single agent or in combination with other chemotherapeutic agents or radiotherapy). Patients with all tumour types for which fluoropyrimidine-based therapy was considered in their best interest were eligible. We did prospective genotyping for DPYD*2A, c.2846A>T, c.1679T>G, and c.1236G>A. Heterozygous DPYD variant allele carriers received an initial dose reduction of 25% (c.2846A>T and c.1236G>A) or 50% (DPYD*2A and c.1679T>G), and DPYD wild-type patients were treated according to the current standard of care. The primary endpoint of the study was the frequency of severe (National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 grade =3) overall fluoropyrimidine-related toxicity across the entire treatment duration. We compared toxicity incidence between DPYD variant allele carriers and DPYD wild-type patients on an intention-to-treat basis, and relative risks (RRs) for severe toxicity were compared between the current study and a historical cohort of DPYD variant allele carriers treated with full dose fluoropyrimidine-based therapy (derived from a previously published meta-analysis). This trial is registered with ClinicalTrials.gov, number NCT02324452, and is complete.

FINDINGS:

Between April 30, 2015, and Dec 21, 2017, we enrolled 1181 patients. 78 patients were considered non-evaluable,

because they were retrospectively identified as not meeting inclusion criteria, did not start fluoropyrimidine-based treatment, or were homozygous or compound heterozygous DPYD variant allele carriers. Of 1103 evaluable patients, 85 (8%) were heterozygous DPYD variant allele carriers, and 1018 (92%) were DPYD wild-type patients. Overall, fluoropyrimidine-related severe toxicity was higher in DPYD variant carriers (33 [39%] of 85 patients) than in wild-type patients (231 [23%] of 1018 patients; p=0·0013). The RR for severe fluoropyrimidine-related toxicity was 1·31 (95% CI 0·63-2·73) for genotype-guided dosing compared with 2·87 (2·14-3·86) in the historical cohort for DPYD*2A carriers, no toxicity compared with 4·30 (2·10-8·80) in c.1679T>G carriers, 2·00 (1·19-3·34) compared with 3·11 (2·25-4·28) for c.2846A>T carriers, and 1·69 (1·18-2·42) compared with 1·72 (1·22-2·42) for c.1236G>A carriers.
INTERPRETATION:
Prospective DPYD genotyping was feasible in routine clinical practice, and DPYD genotype-based dose reductions improved patient safety of fluoropyrimidine treatment. For DPYD*2A and c.1679T>G carriers, a 50% initial dose reduction was adequate. For c.1236G>A and c.2846A>T carriers, a larger dose reduction of 50% (instead of 25%) requires investigation. Since fluoropyrimidines are among the most commonly used anticancer agents, these findings suggest that implementation of DPYD genotype-guided individualised dosing should be a new standard of care.

Impactfactor 36.418

Effect of Neoadjuvant Chemoradiotherapy on Health-Related Quality of Life in Esophageal or Junctional Cancer: Results From the Randomized CROSS Trial

Noordman BJ, Verdam MGE, Lagarde SM, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, van Laarhoven HWM, Nieuwenhuijzen GAP, Hospers GAP, Bonenkamp JJ, Cuesta MA, Blaisse RJB, Busch OR, Ten Kate FJW, **Creemers GM**, Punt CJA, Plukker JTM, Verheul HMW, Spillenaar Bilgen EJ, van Dekken H, van der Sangen MJC, et al

J Clin Oncol. 2018 Jan 20 36(3):268-275. Epub 2017 Nov 21

Purpose To compare pre-agreed health-related quality of life (HRQOL) domains in patients with esophageal or junctional cancer who received neoadjuvant chemoradiotherapy (nCRT) followed by surgery or surgery alone. Secondary aims were to examine the effect of nCRT on HRQOL before surgery and the effect of surgery on HRQOL. Patients and Methods Patients were randomly assigned to nCRT (carboplatin plus paclitaxel with concurrent 41.4-Gy radiotherapy) followed by surgery or surgery alone. HRQOL was measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) and -Oesophageal Cancer Module (QLQ-OES24) questionnaires pretreatment and at 3, 6, 9, and 12 months postoperatively. The nCRT group also received preoperative questionnaires. Physical functioning (PF; QLQ-C30) and eating problems (EA; QLQ-OES24) were chosen as predefined primary end points. Predefined secondary end points were global QOL (GQOL; QLQ-C30), fatigue (FA; QLQ-C30), and emotional problems (EM; QLQ-OES24). Results A total of 363 patients were analyzed. No statistically significant differences in postoperative HRQOL were found between treatment groups. In the nCRT group, PF, EA, GQOL, FA, and EM scores deteriorated 1 week after nCRT (Cohen's d: -0.93, P < .001; 0.47, P < .001; -0.84, P < .001; 1.45, P < .001; and 0.32, P = .001, respectively). In both treatment groups, all end points declined 3 months postoperatively compared with baseline (Cohen's d: -1.00, 0.33, -0.47, -0.34, and 0.33, respectively; all P < .001), followed by a continuous gradual improvement. EA, GQOL, and EM were restored to baseline levels during follow-up, whereas PF and FA remained impaired 1 year postoperatively (Cohen's d: 0.52 and -0.53, respectively; both P < .001). Conclusion Although HRQOL declined during nCRT, no effect of nCRT was apparent on postoperative HRQOL compared with surgery alone. In addition to the improvement in survival, these findings support the view that nCRT according to the Chemoradiotherapy for Esophageal Cancer Followed by Surgery Study-regimen can be regarded as a standard of care.

Impactfactor 26.303

Feasibility and effectiveness of trifluridine/tipiracil in metastatic colorectal cancer: real-life data from The Netherlands

Kwakman JJM, Vink G, Vestjens JH, Beerepoot LV, de Groot JW, Jansen RL, Opdam FL, Boot H, **Creemers GJ**, van Rooijen JM, Los M, Vulink AJE, Schut H, van Meerten E, Baars A, Hamberg P, Kapiteijn E, Sommeijer DW, Punt CJA, Koopman M

Int J Clin Oncol. 2018 Jun;23(3):482-489. Epub 2017 Dec 4

BACKGROUND:
The RECOURSE trial showed clinical efficacy for trifluridine/tipiracil for refractory metastatic colorectal cancer patients. We assessed the feasibility and effectiveness of trifluridine/tipiracil in daily clinical practice in The Netherlands.
METHODS:
Medical records of patients from 17 centers treated in the trifluridine/tipiracil compassionate use program were reviewed and checked for RECOURSE eligibility criteria. Baseline characteristics, safety, and survival times were compared, and prespecified baseline characteristics were tested in multivariate analyses for prognostic significance on overall survival (OS).

RESULTS:
A total of 136 patients with a median age of 62 years were analyzed. Forty-three patients (32%) did not meet the RECOURSE eligibility criteria for not having received all prior standard treatments (n = 35, 26%) and/or ECOG performance status (PS) 2 (n = 12, 9%). The most common grade =3 toxicities were neutropenia (n = 44, 32%), leukopenia (n = 8, 6%), anemia (n = 7, 5%), and fatigue (n = 7, 5%). Median progression-free survival (PFS) and median OS were 2.1 (95% CI, 1.8-2.3) and 5.4 months (95% CI, 4.0-6.9), respectively. Patients with ECOG PS 2 had a worse median OS (3.2 months) compared to patients with ECOG PS 0-1 (5.9 months). ECOG PS, KRAS-mutation status, white blood cell count, serum lactate dehydrogenase, and alkaline phosphatase were prognostic factors for OS.
CONCLUSIONS:
Our data show that treatment with trifluridine/tipiracil in daily clinical practice is feasible and safe. Differences in patient characteristics between our population and the RECOURSE study population should be taken into account in the interpretation of survival data. Our results argue against the use of trifluridine/tipiracil in patients with ECOG PS 2.

Impactfactor 2.610

Health-related quality of life in end-stage renal disease patients: the effects of starting dialysis in the first year after the transition period

Broers NJH, Martens RJH, Canaud B, Cornelis T, Dejagere T, Diederen NMP, Hermans MMH, **Konings CJAM**, Stifft F, Wirtz JJJM, Leunissen KML, van der Sande FM, Kooman JP

Int Urol Nephrol. 2018 Jun 50(6):1131-1142. . Epub 2018 Mar 26

BACKGROUND/AIMS:
Prevalent dialysis patients have low scores of health-related quality of life (HRQOL) which are associated with increased risk of hospitalization and mortality. Also in CKD-5 non-dialysis patients, HRQOL scores seem to be lower as compared with the general population. This study firstly aimed to compare HRQOL between CKD-5 non-dialysis and prevalent dialysis patients in a cross-sectional analysis and to assess longitudinal changes over 1 year after the dialysis initiation. Secondly, the correlation between HRQOL and physical activity (PA) was explored.
METHODS:
Cross-sectional 44 CKD-5 non-dialysis, 29 prevalent dialysis, and 20 healthy controls were included. HRQOL was measured by Short Form-36 questionnaires to measure physical and mental domains of health expressed by the physical component summary (PCS) and mental component summary (MCS) scores. PA was measured by a SenseWear™ pro3. Longitudinally, HRQOL was assessed in 38 CKD-5 non-dialysis patients (who were also part of the cross-sectional analysis), before dialysis initiation until 1 year after dialysis initiation.
RESULTS:
PCS scores were significantly lower both in CKD-5 non-dialysis patients and in prevalent dialysis patients as compared with healthy controls (p?<?0.001). MCS scores were significantly lower in both CKD-5 non-dialysis patients (p?=?0.003), and in dialysis patients (p?=?0.022), as compared with healthy controls. HRQOL scores did not change significantly from the CKD-5 non-dialysis phase into the first year after dialysis initiation. PA was significantly related to PCS in both CKD-5 non-dialysis patients (r?=?0.580; p?<?0.001), and dialysis patients (r?=?0.476; p?=?0.009).
CONCLUSIONS:
HRQOL is already low in the CKD-5 non-dialysis phase. In the first year after dialysis initiation, HRQOL did not change significantly. Given the correlation between PCS score and PA, physical activity programs may be potential tools to improve HRQOL in both CKD-5 non-dialysis as well as in prevalent dialysis patients.

Impactfactor 1.692

Impact of Surgical Approach on Long-term Survival in Esophageal Adenocarcinoma Patients With or Without Neoadjuvant Chemoradiotherapy

Noordman BJ, van Klaveren D, van Berge Henegouwen MI, Wijnhoven BPL, Gisbertz SS, Lagarde SM, van der Gaast A, Hulshof MCCM, Biermann K, Steyerberg EW, van Lanschot JJB; also on behalf of the CROSS-study group: Nieuwenhuijzen GA, **Creemers GJ**, Sangen M van der

Ann Surg. 2018 May;267(5):892-897

OBJECTIVE:
To compare overall survival in patients with esophageal adenocarcinoma who underwent transhiatal esophagectomy (THE) with limited lymphadenectomy or transthoracic esophagectomy (TTE) with extended lymphadenectomy with or without neoadjuvant chemoradiotherapy (nCRT).
BACKGROUND:
The application of neoadjuvant therapy might change the association between the extent of lymphadenectomy and survival in patients with esophageal adenocarcinoma. This may influence the choice of surgical approach in patients treated with nCRT.
METHODS:
Patients with potentially curable subcarinal esophageal adenocarcinoma treated with surgery alone or nCRT

followed by surgery in 7 centers were included. The effect of surgical approach on overall survival, differentiated by the addition or omission of nCRT, was analyzed using a multivariable Cox regression model that included well-known prognostic factors and factors that might have influenced the choice of surgical approach.
RESULTS:
In total, 701 patients were included, of whom 318 had TTE with extended lymphadenectomy and 383 had THE with limited lymphadenectomy. TTE had differential effects on survival (P for interaction = 0.02), with a more favorable prognostic effect in patients who were treated with surgery alone [hazard ratio (HR) = 0.77, 95% confidence interval (CI) 0.58-1.03]. This association was statistically significant in a subgroup of patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 0.62, 95% CI 0.43-0.90). The favorable prognostic effect of TTE over THE was absent in the nCRT and surgery group (HR = 1.16, 95% CI 0.80-1.66) and in the subgroup of nCRT patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 1.00, 95% CI 0.61-1.68).
CONCLUSIONS:
Compared to surgery alone, the addition of nCRT may reduce the need for TTE with extended lymphadenectomy to improve long-term survival in patients with esophageal adenocarcinoma.

Impactfactor 1.536

Interactions Between Malnutrition, Inflammation, and Fluid Overload and Their Associations With Survival in Prevalent Hemodialysis Patients

Dekker MJ, Konings C, Canaud B, van der Sande FM, Stuard S, Raimann JG, Öztürk E, Usvyat L, Kotanko P, Kooman JP

J Ren Nutr. 2018 Nov;28(6):435-444

OBJECTIVE:
Predialysis fluid overload (FO) in hemodialysis (HD) patients is associated with an increased risk of death, further increased by the presence of inflammation. Malnutrition is also associated with outcome. Study objectives were, firstly, to investigate if the presence of FO is associated with malnutrition and whether this association is influenced by the presence of inflammation. Second, we assessed the associations of FO, malnutrition, and inflammation with outcome individually and in combination.
DESIGN:
International cohort study.
SETTING:
European patients of the Monitoring Dialysis Outcome Initiative cohort where bioimpedance and C-reactive protein measurements are performed as standard of care.
SUBJECTS:
8883 prevalent HD patients.
MAIN OUTCOME MEASURE:
Body composition, nutritional and inflammation status were assessed during a 3-month baseline period, and all-cause mortality was noted during 1 year follow-up. Malnutrition was defined as a lean tissue index <10th percentile (of age and gender matched healthy controls), FO as a predialysis overhydration >+1.1 L and inflammation as a C-reactive protein > 6.0 mg/L. We used Cox models to investigate the association with outcome.
RESULTS:
The presence of malnutrition was associated with higher levels of FO, this amount further increased when inflammation was present. Only 11.6% of the patients did not have any of the 3 risk factors and only 6.5% of the patients were only malnourished, which was not associated with an increased risk of death (Hazard Ratio [HR] 1.22 [95% Confidence Interval [CI]: 0.75-1.97]), whereas the combination of severe malnutrition, FO, and inflammation comprised the highest risk of death (HR 5.89 [95% CI: 2.28-8.01]).
CONCLUSION:
In HD patients, predialysis FO associates with both malnutrition and the presence of inflammation, with the highest levels of FO observed when both are present. Malnutrition as singular risk factor was not associated with increased mortality risk. The highest mortality risk was observed in patients where all 3 risk factors were present.

Impactfactor 2.651

Intermittent versus continuous first-line treatment for HER2-negative metastatic breast cancer: the Stop & Go study of the Dutch Breast Cancer Research Group (BOOG)

Claessens AK, Bos ME, Lopez-Yurda M, Bouma JM, Rademaker-Lakhai JM, Honkoop AH, de Graaf H, van Druten E, **van Warmerdam LJ**, van der Sangen MJ, Tjan-Heijnen VC, Erdkamp FL, Dutch Breast Cancer Research Group (BOOG)Breast Cancer Res Treat. 2018 Nov;172(2):413-423

PURPOSE:
We determined if intermittent first-line treatment with paclitaxel plus bevacizumab was not inferior to continuous treatment in patients with HER2-negative, advanced breast cancer.
METHODS:
Patients were randomized to 2?×?4 cycles or continuous 8 cycles of paclitaxel plus bevacizumab, followed by bevacizumab maintenance treatment until disease progression or unacceptable toxicity. The primary endpoint was

overall progression-free survival (PFS). A proportional-hazards regression model was used to estimate the HR. The upper limit of the two-sided 95% CI for the HR was compared with the non-inferiority margin of 1.34.
RESULTS:
A total of 420 patients were included with well-balanced characteristics. In the intention-to-treat analysis, median overall PFS was 7.4 months (95% CI 6.4-10.0) for intermittent and 9.7 months (95% CI 8.9-10.3) for continuous treatment, with a stratified HR of 1.17 (95% CI 0.88-1.57). Median OS was 17.5 months (95% CI 15.4-21.7) versus 20.9 months (95% CI 17.8-24.0) for intermittent versus continuous treatment, with a HR of 1.38 (95% CI 1.00-1.91). Safety results and actually delivered treatments revealed longer durations of treatment in the continuous arm, without significant unexpected findings.
CONCLUSION:
Intermittent first-line treatment cannot be recommended in patients with HER2-negative advanced breast cancer.

Impactfactor 3.605

Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial

Noordman BJ, Wijnhoven BPL, Lagarde SM, Boonstra JJ, Coene PPLO, Dekker JWT, Doukas M, van der Gaast A, Heisterkamp J, Kouwenhoven EA, Nieuwenhuijzen GAP, Pierie JEN, Rosman C, van Sandick JW, van der Sangen MJC, Sosef MN, Spaander MCW, Valkema R, van der Zaag ES, Steyerberg EW, van Lanschot JJB SANO-study group.: **Creemers GJ**, Schoon EJ, Wyndaele D

BMC Cancer. 2018 Feb 6 18(1):142

BACKGROUND:
Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard treatment for locally advanced oesophageal cancer. With this treatment, 29% of patients have a pathologically complete response in the resection specimen. This provides the rationale for investigating an active surveillance approach. The aim of this study is to assess the (cost-)effectiveness of active surveillance vs. standard oesophagectomy after nCRT for oesophageal cancer.
METHODS:
This is a phase-III multi-centre, stepped-wedge cluster randomised controlled trial. A total of 300 patients with clinically complete response (cCR, i.e. no local or disseminated disease proven by histology) after nCRT will be randomised to show non-inferiority of active surveillance to standard oesophagectomy (non-inferiority margin 15%, intra-correlation coefficient 0.02, power 80%, 2-sided a 0.05, 12% drop-out). Patients will undergo a first clinical response evaluation (CRE-I) 4-6 weeks after nCRT, consisting of endoscopy with bite-on-bite biopsies of the primary tumour site and other suspected lesions. Clinically complete responders will undergo a second CRE (CRE-II), 6-8 weeks after CRE-I. CRE-II will include 18F-FDG-PET-CT, followed by endoscopy with bite-on-bite biopsies and ultra-endosonography plus fine needle aspiration of suspected lymph nodes and/or PET- positive lesions. Patients with cCR at CRE-II will be assigned to oesophagectomy (first phase) or active surveillance (second phase of the study). The duration of the first phase is determined randomly over the 12 centres, i.e., stepped-wedge cluster design. Patients in the active surveillance arm will undergo diagnostic evaluations similar to CRE-II at 6/9/12/16/20/24/30/36/48 and 60 months after nCRT. In this arm, oesophagectomy will be offered only to patients in whom locoregional regrowth is highly suspected or proven, without distant dissemination. The main study parameter is overall survival; secondary endpoints include percentage of patients who do not undergo surgery, quality of life, clinical irresectability (cT4b) rate, radical resection rate, postoperative complications, progression-free survival, distant dissemination rate, and cost-effectiveness. We hypothesise that active surveillance leads to non-inferior survival, improved quality of life and a reduction in costs, compared to standard oesophagectomy.
DISCUSSION:
If active surveillance and surgery as needed after nCRT leads to non-inferior survival compared to standard oesophagectomy, this organ-sparing approach can be implemented as a standard of care.

Impactfactor 3.288

Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2): a multicentre, open-label, randomised, phase 3 trial

van Ramshorst MS, van der Voort A, van Werkhoven ED, Mandjes IA, Kemper I, Dezentjé VO, Oving IM, Honkoop AH, Tick LW, van de Wouw AJ, Mandigers CM, **van Warmerdam LJ**, Wesseling J, Vrancken Peeters MT, Linn SC, Sonke GS; Dutch Breast Cancer Research Group (BOOG)

Lancet Oncol. 2018 Dec;19(12):1630-1640

BACKGROUND:
The optimal chemotherapy backbone for dual HER2 blockade in the neoadjuvant setting for early breast cancer is unknown. We investigated whether the addition of anthracyclines would improve pathological complete response compared with a carboplatin-taxane regimen, when given in combination with the HER2-targeted agents trastuzumab and pertuzumab.
METHODS:
The TRAIN-2 study is an open-label, randomised, controlled, phase 3 trial being done in 37 hospitals in the Netherlands. We recruited patients aged 18 years or older with previously untreated, histologically confirmed stage

II-III HER2-positive breast cancer. Patients were randomly allocated using central randomisation software (1:1 ratio) with minimisation without a random component, stratified by tumour stage, nodal stage, oestrogen receptor status, and age, to receive 5-fluorouracil (500 mg/m2), epirubicin (90 mg/m2), and cyclophosphamide (500 mg/m2) every 3 weeks fo days 1 and 8) every 3 weeks for six cycles, or to receive nine cycles of paclitaxel and carboplatin at the same dose and schedule as in the anthracycline group. Patients in both study groups received trastuzumab (6 mg/kg,r three cycles followed by paclitaxel (80 mg/m2 on days 1 and 8) and carboplatin (area under the concentration-time curve [AUC] 6 mg/mL per min on day 1 or optionally, as per hospital preference, AUC 3 mg/mL per min on loading dose 8 mg/kg) and pertuzumab (420 mg, loading dose 840 mg) concurrently with all chemotherapy cycles. The primary endpoint was the proportion of patients who achieved a pathological complete response in breast and axilla (ypT0/is ypN0) in the intention-to-treat population. Safety was analysed in patients who received at least one treatment cycle according to actual treatment received. This trial is registered with ClinicalTrials.gov, number NCT01996267, and follow-up for long-term outcome is ongoing.

FINDINGS:

Between Dec 9, 2013, and Jan 14, 2016, 438 patients were enrolled and randomly assigned to the two treatment groups (219 patients to each group), of whom 418 were evaluable for the primary endpoint (212 in the anthracycline group and 206 in the non-anthracycline group). The median follow-up for all patients was 19 months (IQR 16-23 months). A pathological complete response was recorded in 141 (67%, 95% CI 60-73) of 212 patients in the anthracycline group and in 140 (68%, 61-74) of 206 in the non-anthracycline group (p=0·95). One patient randomly allocated to the non-anthracycline group did receive anthracyclines and was thus included in the anthracycline group for safety analyses; therefore, for the safety analyses there were 220 patients in the anthracycline group and 218 in the non-anthracycline group. Serious adverse events were reported in 61 (28%) of 220 patients in the anthracycline group and in 49 (22%) of 218 in the non-anthracycline group. The most common adverse events of any cause were grade 3 or worse neutropenia (in 131 [60%] of 220 patients in the anthracycline group vs 118 [54%] of 218 in the non-anthracycline group), grade 3 or worse diarrhoea (26 [12%] vs 37 [18%]), and grade 2 or worse peripheral neuropathy (66 [30%] vs 68 [31%]), with no substantial differences between the groups. Grade 3 or worse febrile neutropenia was more common in the anthracycline group than in the non-anthracycline group (23 [10%] vs three [1%], p<0·0001). Symptomatic left ventricular systolic dysfunction was rare in both groups (two [1%] of 220 vs 0 of 218). One patient in the anthracycline group died because of a pulmonary embolism, which was possibly treatment related.

INTERPRETATION:

In view of the high proportion of pathological complete responses recorded in both groups and the fact that febrile neutropenia was more frequent in the anthracycline group, omitting anthracyclines from neoadjuvant treatment regimens might be a preferred approach in the presence of dual HER2 blockade in patients with early HER2-positive breast cancer. Long-term follow-up is required to confirm these results

Impactfactor *36.418*

Pre-dialysis fluid status pre-dialysis systolic blood pressure and outcome in prevalent haemodialysis patients: results of an international cohort study on behalf of the MONDO initiative

Dekker M, **Konings C**, Canaud B, Carioni P, Guinsburg A, Madero M, van der Net J, Raimann J, van der Sande F, Stuard S, Usvyat L, Wang Y, Xu X, Kotanko P, Kooman J

Nephrol Dial Transplant. 2018 Nov 1 33(11):2027-2034

Background: Pre-dialysis fluid overload (FO) associates with mortality and causes elevated pre-dialysis systolic blood pressure (pre-SBP). However, low pre-SBP is associated with increased mortality in haemodialysis patients. The objective of this study was to investigate the interaction between pre-dialysis fluid status (FS) and pre-SBP in association with mortality.

Methods: We included all patients from the international Monitoring Dialysis Outcome Initiative (MONDO) database with a pre-dialysis multifrequency bioimpedance spectroscopy measurement in the year 2011. We used all parameters available during a 90-day baseline period. All-cause mortality was recorded during 1-year follow-up. Associations with outcome were assessed with Cox models and a smoothing spline Cox analysis.

Results: We included 8883 patients. In patients with pre-dialysis FO (>+1.1 to?+2.5 L), pre-SBP <110 mmHg was associated with an increased risk of death {hazard ratio (HR) 1.52 [95% confidence interval (CI) 1.06-2.17]}. An increased risk of death was also associated with pre-dialysis fluid depletion (FD;?<-1.1 L) combined with a pre-SBP?<140 mmHg. In normovolemic (NV) patients, low pre-SBP?<110 mmHg was associated with better survival [HR 0.46 (95% CI 0.23-0.91)]. Also, post-dialysis FD associated with a survival benefit. Results were similar when inflammation was present. Only high ultrafiltration rate could not explain the higher mortality rates observed.

Conclusion: The relation between pre-SBP and outcome is dependent on pre-dialysis FS. Low pre-SBP appears to be disadvantageous in patients with FO or FD, but not in NV patients. Post-dialysis FD was found to associate with improved survival. Therefore, we suggest interpreting pre-SBP levels in the context of FS and not as an isolated marker.

Impactfactor *4.600*

Predicting breast and axillary response after neoadjuvant treatment for breast cancer: The role of histology vs receptor status

Vugts G, Van den Heuvel F, Maaskant-Braat AJ, Voogd AC, **Van Warmerdam LJ**, Nieuwenhuijzen GA, Van der Sangen MJ

Breast J. 2018 Nov;24(6):894-901

PURPOSE:
Neoadjuvant systemic treatment (NST) is increasingly administered in breast cancer patients. This study was conducted to identify predictors for tumor response in the breast and axilla.
METHODS:
All female patients with nonmetastatic, noninflammatory breast cancer receiving NST between 2003-2013 at the Catharina Cancer Institute in Eindhoven, The Netherlands, were included.
RESULTS:
The majority of 216 of the 337 patients receiving NST (65%) presented with a cT2 tumor. In 159 patients (47%), the axilla was clinically node positive. A pathologic complete response (pCR) in the breast was achieved in 83 patients (24.6%), and a pCR in the axilla in 65 node-positive patients (40.9%). The triple-negative (OR 4.29, 95% CI 2.15-8.55) and hormone receptor (HR)-negative/HER2-positive tumors (OR 3.73, 95% CI 1.59-8.75) were associated with in-breast pCR. Patients with invasive lobular carcinoma (ILC) were less likely to experience in-breast pCR (OR 0.10, 95% CI 0.01-0.73) than those with invasive ductal cancer. Axillary pCR was found in 65 clinically node-positive patients (41%). Axillary pCR was more likely to occur in HR-positive/HER2-positive (OR 6.24, 95% CI 1.86-20.90) and HR-negative/HER2-positive tumors (OR 6.41, 95% CI 1.95-21.06), compared to HER2-negative disease. In-breast pCR was strongly associated with axillary pCR (OR 10.89, 95% CI 4.20-28.22).
CONCLUSION:
Response to NST in the breast and axilla is largely determined by receptor status, with high pCR rates occurring in HER2-positive and triple-negative tumors. For axillary pCR, in-breast pCR and HER2-positive disease are the most important predictive factors.

Impactfactor 2.424

Preliminary results of a cohort study of induction chemotherapy-based treatment for locally recurrent rectal cancer

van Zoggel DMGI, Bosman SJ, Kusters M, Nieuwenhuijzen GAP, Cnossen JS, **Creemers GJ**, van Lijnschoten G, Rutten HJT

Br J Surg. 2018 Mar;105(4):447-452.Epub 2017 Nov 23

BACKGROUND:
A significant number of patients treated for locally recurrent rectal cancer have local or systemic failure, especially after incomplete surgical resection. Neoadjuvant treatment regimens in patients who have already undergone preoperative (chemo)radiotherapy for the primary tumour are limited. The objective of the present study was to evaluate the influence of a neoadjuvant regimen incorporating induction chemotherapy (ICT) in patients with locally recurrent rectal cancer who had preoperative (chemo)radiotherapy for the primary cancer or an earlier local recurrence.
METHODS:
Patients were treated with a sequential neoadjuvant regimen including three or four cycles of 5-fluorouracil and oxaliplatin-containing chemotherapy. When no progressive disease was found at evaluation, neoadjuvant treatment was continued with chemoradiation therapy (CRRT) using 30?Gy with concomitant capecitabine. If there was a response to ICT, the patient was advised to continue with systemic chemotherapy after CRRT as consolidation chemotherapy while waiting for resection. These patients were compared with patients who received CRRT alone in the same time interval.
RESULTS:
Of 58 patients who had ICT, 32 (55 per cent) had surgery with clear resection margins, of whom ten (17 per cent) exhibited a pathological complete response (pCR). The remaining 26 patients had 23 R1 and three R2 resections. In 71 patients who received CRRT, a similar rate of R0 (35 patients) and R1 (36) resection was found (P?=?0·506), but only three patients (4 per cent) had a pCR (P?=?0·015).
CONCLUSION:
The incorporation of ICT in neoadjuvant regimens for locally recurrent rectal cancer is a promising strategy.

Impactfactor 5.433

Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer

Schaap DP, Ogura A, Nederend J, Maas M, Cnossen JS, **Creemers GJ**, van Lijnschoten I, Nieuwenhuijzen GA, Rutten HJ, Kusters M

Br J Surg. 2018 Dec;105(13):1844-1852

BACKGROUND:
Lateral nodal disease in rectal cancer remains a subject of debate and is treated differently in the East and the West.

The predictive value of lateral lymph node and MRI-detected extramural vascular invasion (mrEMVI) features on oncological outcomes was assessed in this study.
METHODS:
In this retrospective cohort study, data on patients with cT3-4 rectal cancer within 8?cm from the anal verge were considered over a 5-year period (2009-2013). Lateral lymph node size, malignant features and mrEMVI features were evaluated and related to oncological outcomes.
RESULTS:
In total, 192 patients were studied, of whom 30 (15·6 per cent) underwent short-course radiotherapy and 145 (75·5 per cent) received chemoradiotherapy. A lateral lymph node short-axis size of 10?mm or more was associated with a significantly higher 5-year lateral/presacral local recurrence rate of 37 per cent, compared with 7·7 per cent in nodes smaller than 10?mm (P?=?0·041). Enlarged nodes did not result in a higher 5-year rate of distant metastasis (23 per cent versus 27·7 per cent in nodes smaller than 10?mm; P?=?0·563). However, mrEMVI positivity was related to more metastatic disease (5-year rate 43 versus 26·3 per cent in the mrEMVI-negative group; P?=?0·014), but not with increased lateral/presacral recurrence. mrEMVI occurred in 46·6 per cent of patients with nodes smaller than 10?mm, compared with 29 per cent in patients with nodes of 10?mm or larger (P?=?0·267).
CONCLUSION:
Although lateral nodal disease is more a local problem, mrEMVI mainly predicts distant recurrence. The results of this study showed an unacceptably high local recurrence rate in patients with a short axis of 10?mm or more, despite neoadjuvant (chemo)radiotherapy

Impactfactor *5.433*

Review: Pathology and Its Clinical Relevance of Mucinous Appendiceal Neoplasms and Pseudomyxoma Peritonei

Legué LM, Creemers GJ, de Hingh IHJT, Lemmens VEPP, Huysentruyt CJ

Clin Colorectal Cancer. 2018 Dec 6. pii: S1533-0028(18)30467-5. [Epub ahead of print]

Until recently, many classifications existed for the terminology and histopathologic classification of appendiceal mucinous neoplasms, mucinous appendiceal adenocarcinomas, and pseudomyxoma peritonei (PMP). A major accomplishment was achieved by consensus-based histopathologic classifications on behalf of the Peritoneal Surface Oncology Group International regarding mucinous appendiceal tumours and PMP. As different classifications were used over the years and also owing to the rare nature of these tumors, many clinicians are not familiar with the terminology and the impact on patient management. Hence, an overview concerning mucinous appendiceal neoplasms, mucinous appendiceal adenocarcinomas, and PMP is provided to serve as an introduction into the basic morphology of these tumors with tentative recommendations for management.

Impactfactor *3.861*

Salivary cortisol in the diagnosis of adrenal insufficiency: cost efficient and patient friendly

Langelaan MLP, **Kisters JMH, Oosterwerff MM**, Boer AK

Endocr Connect. 2018 Apr 7(4):560-566. Epub 2018 Mar 12

Saliva as a diagnostic tool is patient friendly and offers analytical advantages. Hormonal analysis of saliva is not influenced by changes in concentrations of binding globulins as the free concentration of the hormones is measured. Analysis of salivary cortisol is common practice in the diagnostic work-up of hypercortisolism. We investigated the potential role of measuring salivary cortisol when adrenal insufficiency (AI) is suspected, to reduce the numbers of ACTH stimulation tests. Over a period of 6 years, patients undergoing an ACTH stimulation test (tetracosactide, 250?µg) in our hospital were included. Plasma cortisol (Elecsys, Cobas, Roche Diagnostics) and salivary cortisol and cortisone (LC-MS/MS) were determined at t?=?0, 30 and 60?min after stimulation. Based on peak plasma cortisol levels, AI was ruled out in 113 patients and was established in 16 patients. Patients without AI displayed maximal salivary cortisol concentrations of 12.6-123.4?nmol/L (95th percentile) after stimulation, as opposed to 0.5-15.2?nmol/L in AI patients. At t?=?0?min, a minimal salivary cortisol concentration of 1.0?nmol/L was observed in patients without AI, whereas AI patients had a maximum concentration of 5.9?nmol/L. Using these cut-off values, 34% of the initial patient group could be diagnosed without an ACTH stimulation test (28% >5.9?nmol/L, 6% <1.0?nmol/L). A novel diagnostic algorithm, including early morning salivary cortisol analysis can reduce the numbers of ACTH stimulation tests in patients suspected of AI. This patient-friendly method can thereby reduce total health care costs.

Impactfactor *3.041*

Salvage endoscopic resection in patients with esophageal adenocarcinoma after chemoradiotherapy

Noordzij IC, Curvers WL, Huysentruyt CJ, Nieuwenhuijzen GA, **Creemers GJ**, van der Sangen MJ, Schoon EJ

Endosc Int Open. 2018 Sep;6(9):E1126-E1129

Background and study aims For early esophageal adenocarcinoma, endoscopic resection is an accepted curative treatment with an excellent long-term prognosis. Case series from Japan have reported endoscopic resection of residual esophageal squamous cell carcinoma after chemoradiotherapy. This is the first report describing endoscopic resection of residual esophageal adenocarcinoma after chemoradiotherapy. Two patients with

advanced esophageal adenocarcinoma had been treated with chemoradiotherapy because comorbidity precluded esophageal resection. When residual tumor was observed endoscopically, complete remission was achieved by salvage endoscopic therapy alone or in combination with argon plasma coagulation (APC). Both patients achieved long-term sustained remission and died of non-tumor-related causes.

Impactfactor --

The administration of adjuvant chemo(-immuno) therapy in the post ACOSOG-Z0011 era; a population based study

Poodt IGM, Rots ML, Vugts G, van Dalen T, Kuijer A, **Vriens BEPJ**, Nieuwenhuijzen GAP, Schipper RJ

Eur J Surg Oncol. 2018 Aug 44(8):1151-1156. Epub 2018 Mar 14

PURPOSE:

The ACOSOG-Z0011-study has resulted in a trend to a more conservative treatment of the axilla for selected sentinel-node-positive patients. However, axillary nodal involvement has always been an important factor for tumor staging and tailoring adjuvant chemotherapy plans. This study evaluates the impact of omitting completion axillary lymph node dissection (cALND) on the administration of adjuvant chemo (-immuno)therapy in Dutch clinical T1-2N0M0 (cT1-2N0M0) sentinel-node-positive breast cancer patients.

METHODS:

Data were obtained from the nationwide NABON breast cancer audit. Descriptive analyses were used to demonstrate trends in axillary surgery and adjuvant chemo (-immuno)therapy. Multivariable logistic regression analyses were used to identify factors associated with the prescription of chemo (-immuno)therapy.

RESULTS:

In this cohort of 4331 patients, the omission of a cALND increased from 34% to 92%, and the administration of chemo (-immuno)therapy decreased from 68% to 55%, between 2011 and 2015 ($P < 0.001$). Patients treated with cALND had an OR of 2.2 for receiving adjuvant chemo (-immuno)therapy compared with SLNB only patients. Lower age, a hormone receptor (HR) status other than HR-positive, HER2-negative, increasing tumor grade and stage, and a lymph node status = pN2 were independently associated with a higher probability of chemo (-immuno)therapy ($P < 0.05$).

CONCLUSIONS:

This study showed that Dutch cT1-2N0M0 sentinel node-positive breast cancer patients treated with cALND had a higher independent probability for receiving adjuvant chemo (-immuno)therapy compared with SLNB only patients, even when corrected for lymph node status and HR-status. Probably, the decisions to administer adjuvant chemo (-immuno)therapy were not only based on guidelines and tumor characteristics, but also on the preferences from physicians and patients.

Impactfactor *3.688*

The interrelation between FGF23 and glucose metabolism in humans

Ursem SR, Vervloet MG, Büttler RM, Ackermans MT, **Oosterwerff MM**, Eekhoff EM, Lips P, Serlie MJ, la Fleur SE, Heijboer AC

J Diabetes Complications. 2018 Sep;32(9):845-850

AIMS:

Different studies point to a link between glucose metabolism and Fibroblast Growth Factor 23 (FGF23), an osteocyte-derived phosphaturic hormone. We aimed to investigate in humans the effect of (I) a glucose load and (II) a hyperinsulinemic-euglycemic clamp on FGF23 concentrations and conversely (III) the effect of a diet-induced increase in FGF23 concentration on glucose and insulin concentrations.

METHODS:

Plasma cFGF23 concentrations were measured during: I. an oral glucose tolerance test in eight adults with impaired glucose tolerance and vitamin D deficiency and II. a hyperinsulinemic-euglycemic clamp in nine healthy adults. III. Serum glucose and insulin concentrations were measured in nine healthy adults receiving a single-day phosphate-enriched or -restricted diet.

RESULTS:

I. A glucose load decreased FGF23 and phosphate concentrations. II. The hyperinsulinemic-euglycemic clamp decreased phosphate concentrations, but did not affect FGF23 concentrations. III. Fasting insulin and glucose concentrations remained unchanged after a diet-induced increase in FGF23 concentration.

CONCLUSIONS:

An oral glucose load in vitamin D deficient patients with impaired glucose metabolism decreased FGF23 concentrations, which cannot be attributed to changes in insulin concentration. Thus, bone may react rapidly after glucose loading by alternating FGF23 secretion. A diet-induced increase in FGF23 concentrations did not affect fasting glucose or insulin levels.

Impactfactor *2.792*

The Value of (18)F-FDG PET/CT in Diagnosis and During Follow-up in 273 Patients with Chronic Q Fever

Kouijzer IJE, Kampschreur LM, Wever PC, Hoekstra C, van Kasteren MEE, de Jager-Leclercq MGL, Nabuurs-Franssen MH, Wegdam-Blans MCA, **Ammerlaan HSM**, Buijs J, Geus-Oei LF, Oyen WJG, Bleeker-Rovers CP

J Nucl Med. 2018 Jan 59(1):127-133. Epub 2017 May 25

In 1%-5% of all acute Q fever infections, chronic Q fever develops, mostly manifesting as endocarditis, infected aneurysms, or infected vascular prostheses. In this study, we investigated the diagnostic value of 18F-FDG PET/CT in chronic Q fever at diagnosis and during follow-up. Methods: All adult Dutch patients suspected of chronic Q fever who were diagnosed since 2007 were retrospectively included until March 2015, when at least one 18F-FDG PET/CT scan was obtained. Clinical data and results from 18F-FDG PET/CT at diagnosis and during follow-up were collected. 18F-FDG PET/CT scans were prospectively reevaluated by 3 nuclear medicine physicians using a structured scoring system. Results: In total, 273 patients with possible, probable, or proven chronic Q fever were included. Of all 18F-FDG PET/CT scans performed at diagnosis, 13.5% led to a change in diagnosis. Q fever-related mortality rate in patients with and without vascular infection based on 18F-FDG PET/CT was 23.8% and 2.1%, respectively (P = 0.001). When 18F-FDG PET/CT was added as a major criterion to the modified Duke criteria, 17 patients (1.9-fold increase) had definite endocarditis. At diagnosis, 19.6% of 18F-FDG PET/CT scans led to treatment modification. During follow-up, 57.3% of 18F-FDG PET/CT scans resulted in treatment modification. Conclusion:18F-FDG PET/CT is a valuable technique in diagnosis of chronic Q fever and during follow-up, often leading to a change in diagnosis or treatment modification and providing important prognostic information on patient survival.

Impactfactor *7.439*

Tongue necrosis

Hems MA, **Aarnoudse AL, Douwes-Draaijer P**

Neth J Med. 2018 May;76(4):202-203

Geen abstract beschikbaar

Impactfactor *1.156*

Training for Medical Oncologists on Shared Decision-Making About Palliative Chemotherapy: A Randomized Controlled Trial

Henselmans I, van Laarhoven HWM, de Haes HCJM, Tokat M, Engelhardt EG, van Maarschalkerweerd PEA, Kunneman M, Ottevanger PB, Dohmen SE, **Creemers GJ**, Sommeijer DW, de Vos FYFL, Smets EMA

Oncologist. 2018 Jun 29. pii: theoncologist.2018-0090. [Epub ahead of print]

MATERIALS AND METHODS:

A randomized controlled trial comparing training with standard practice was conducted. Medical oncologists and oncologists-in-training (n?=?31) participated in a video-recorded, standardized patient assessment at baseline (T0) and after 4 months (T1, after training). The training was based on a four-stage SDM model and consisted of a reader, two group sessions (3.5 hours each), a booster session (1.5 hours), and a consultation card. The primary outcome was observed SDM as assessed with the Observing Patient Involvement scale (OPTION12) coded by observers blinded for arm. Secondary outcomes were observed SDM per stage, communication skills, and oncologists' satisfaction with communication.

RESULTS:

The training had a significant and large effect on observed SDM in the simulated consultations (Cohen's f?=?0.62) and improved observed SDM behavior in all four SDM stages (f?=?0.39-0.72). The training improved oncologists' information provision skills (f?=?0.77), skills related to anticipating/responding to emotions (f?=?0.42), and their satisfaction with the consultation (f?=?0.53).

CONCLUSION:

Training medical oncologists in SDM about palliative systemic treatment improves their performance in simulated consultations. The next step is to examine the effect of such training on SDM in clinical practice and on patient outcomes.

IMPLICATIONS FOR PRACTICE:

Systemic treatment for advanced cancer offers uncertain and sometimes limited benefit, while the burden can be high. Hence, applying the premises of shared decision-making (SDM) is recommended. SDM is increasingly advocated based on the ethical imperative to provide patient-centered care and the increasing evidence for beneficial patient outcomes. Few studies examined the effectiveness of SDM training in robust designs. This randomized controlled trial demonstrated that SDM training (10 hours) improves oncologists' performance in consultations with standardized patients. The next step is to examine the effect of training on oncologists' performance and patient outcomes in clinical practice.

Impactfactor *5.306*

Kindergeneeskunde

Betere overleving na een Staphylococcus aureus-bacteriëmie bij betrokkenheid van het antibioticateam en bundelaanpak?

M. van den Hurk, J. Fonville, H.S.M. Ammerlaan, **C. Miedema**, S. Sanders, I Overdevest

TVI : tijdschrift voor infectieziekten, 2018;13(1):3-10

Staphylococcus aureus is een van de meest voorkomende verwekkers van een bacteriëmie. Een Staphylococcus aureus-bacteriëmie (SAB) heeft een hoge mortaliteit, mede door een vaak gecompliceerd beloop met strooihaarden. Uit literatuuronderzoek blijkt dat een bundelaanpak en de betrokkenheid van een multidisciplinair antibioticateam de uitkomst van SAB significant verbeteren. We hebben retrospectief beoordeeld wat de invloed is van ons antibioticateam op de aanpak van SAB en op de mortaliteit en het recidiefrisico voor de patiënt. Tevens werd onderzocht welke onderdelen in het behandeltraject de meeste invloed hadden op de prognose van de patiënt.

Impactfactor --

Long-term follow-up after bilateral percutaneous epiphysiodesis around the knee to reduce excessive predicted final height

Goedegebuure WJ, Jonkers F, Boot AM, Bakker-van Waarde WM, **van Tellingen V**, Heeg M, **Odink R**J, van Douveren F, Besselaar AT, van der Steen MC

Arch Dis Child. 2018 Mar;103(3):219-223. Epub 2017 Oct 13

CONTEXT:
Percutaneous epiphysiodesis (PE) around the knee to reduce predicted excessive final height. Studies until now included small numbers of patients and short follow-up periods.
OBJECTIVE AND DESIGN:
This Dutch multicentre, long-term, retrospective, follow-up study aimed to assess adult height (AH), complications, knee function and patient satisfaction after PE. The primary hypothesis was that PE around the knee in constitutionally tall boys and girls is an effective treatment for reducing final height with low complication rates and a high level of patient satisfaction.
PARTICIPANTS:
77 treated adolescents and 60 comparisons.
INTERVENTION:
Percutaneous epiphysiodesis.
OUTCOME:
AH, complications, knee function, satisfaction.
RESULTS:
In the PE-treated group, final height was 7.0?cm (±6.3?cm) lower than predicted in boys and 5.9?cm (±3.7?cm) lower than predicted in girls. Short-term complications in file search were seen in 5.1% (three infections, one temporary nerve injury), one requiring reoperation. Long-term complications in file search were seen in 2.6% (axis deformity 1.3%, prominent head of fibula 1.3%). No significant difference in knee function was found between treated cases and comparisons. Satisfaction was high in both the comparison and PE groups; most patients in the PE group recommended PE as the treatment for close relatives with tall stature.
CONCLUSION:
PE is safe and effective in children with predicted excessive AH. There was no difference in patient satisfaction between the PE and comparison group. Careful and detailed counselling is needed before embarking on treatment.

Impactfactor *3.258*

Klinische Fysica

American Association of Physicists in Medicine Task Group 263: Standardizing Nomenclatures in Radiation Oncology

Mayo CS, Moran JM, Bosch W, Xiao Y, McNutt T, Popple R, Michalski J, Feng M, Marks LB, Fuller CD, Yorke E, Palta J, Gabriel PE, Molineu A, Matuszak MM, Covington E, Masi K, Richardson SL, Ritter T, Morgas T, Flampouri S, Santanam L, Moore JA, Purdie TG, Miller RC, **Hurkmans C**, Adams J, Jackie Wu QR, Fox CJ, Siochi RA, Brown NL, Verbakel W, Archambault Y, Chmura SJ, Dekker AL, Eagle DG, Fitzgerald TJ, Hong T, Kapoor R, Lansing B, Jolly S, Napolitano ME, Percy J, Rose MS, Siddiqui S, Schadt C, Simon WE, Straube WL, St James ST, Ulin K, Yom SS, Yock TI

Int J Radiat Oncol Biol Phys. 2018 Mar 15 100(4):1057-1066. Epub 2017 Dec 15

A substantial barrier to the single- and multi-institutional aggregation of data to supporting clinical trials, practice quality improvement efforts, and development of big data analytics resource systems is the lack of standardized nomenclatures for expressing dosimetric data. To address this issue, the American Association of Physicists in Medicine (AAPM) Task Group 263 was charged with providing nomenclature guidelines and values in radiation oncology for use in clinical trials, data-pooling initiatives, population-based studies, and routine clinical care by standardizing: (1) structure names across image processing and treatment planning system platforms; (2) nomenclature for dosimetric data (eg, dose-volume histogram [DVH]-based metrics); (3) templates for clinical trial groups and users of an initial subset of software platforms to facilitate adoption of the standards; (4) formalism for nomenclature schema, which can accommodate the addition of other structures defined in the future. A multisociety, multidisciplinary, multinational group of 57 members representing stake holders ranging from large academic centers to community clinics and vendors was assembled, including physicists, physicians, dosimetrists, and vendors. The stakeholder groups represented in the membership included the AAPM, American Society for Radiation Oncology (ASTRO), NRG Oncology, European Society for Radiation Oncology (ESTRO), Radiation Therapy Oncology Group (RTOG), Children's Oncology Group (COG), Integrating Healthcare Enterprise in Radiation Oncology (IHE-RO), and Digital Imaging and Communications in Medicine working group (DICOM WG); A nomenclature system for target and organ at risk volumes and DVH nomenclature was developed and piloted to demonstrate viability across a range of clinics and within the framework of clinical trials. The final report was approved by AAPM in October 2017. The approval process included review by 8 AAPM committees, with additional review by ASTRO, European Society for Radiation Oncology (ESTRO), and American Association of Medical Dosimetrists (AAMD). This Executive Summary of the report highlights the key recommendations for clinical practice, research, and trials.

Impactfactor 5.554

Applicability of a prognostic CT-based radiomic signature model trained on stage I-III non-small cell lung cancer in stage IV non-small cell lung cancer

De Jong E*, van Elmpt W Rizzo S Colarieti A Spitaleri G Leijenaar R Jochems A Hendriks L Troost E Reymen B Dingemans A Lambin P

Lung Cancer. 2018 Oct;124:6-11. Epub 2018 Jul 20

OBJECTIVES:

Recently it has been shown that radiomic features of computed tomography (CT) have prognostic information in stage I-III non-small cell lung cancer (NSCLC) patients. We aim to validate this prognostic radiomic signature in stage IV adenocarcinoma patients undergoing chemotherapy.

MATERIALS AND METHODS:

Two datasets of chemo-naive stage IV adenocarcinoma patients were investigated, dataset 1: 285 patients with CTs performed in a single center; dataset 2: 223 patients included in a multicenter clinical trial. The main exclusion criteria were EGFR mutation or unknown mutation status and non-delineated primary tumor. Radiomic features were calculated for the primary tumor. The c-index of cox regression was calculated and compared to the signature performance for overall survival (OS).

RESULTS:

In total CT scans from 195 patients were eligible for analysis. Patients having a prognostic index (PI) lower than the signature median (n?=?92) had a significantly better OS than patients with a PI higher than the median (n?=?103, HR 1.445, 95% CI 1.07-1.95, p?=?0.02, c-index 0.576, 95% CI 0.527-0.624).

CONCLUSION:

The radiomic signature, derived from daily practice CT scans, has prognostic value for stage IV NSCLC, however the signature performs less than previously described for stage I-III NSCLC stages. In the future, machine learning techniques can potentially lead to a better prognostic imaging based model for stage IV NSCLC.

Impactfactor 4.486

**Ten tijde van publicatie verbonden aan: The D-Lab: Decision Support for Precision Medicine, GROW-School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht*

Beam characterisation of the 1.5 T MRI-linac

Woodings SJ, **Bluemink JJ**, de Vries JHW, Niatsetski Y, van Veelen B, Schillings J, Kok JGM, Wolthaus JWH, Hackett SL, van Asselen B, van Zijp HM, Pencea S, Roberts DA, Lagendijk JJW, Raaymakers BW

Phys Med Biol. 2018 Apr 19;63(8):085015

As a prerequisite for clinical treatments it was necessary to characterize the Elekta 1.5 T MRI-linac 7 MV FFF radiation beam. Following acceptance testing, beam characterization data were acquired with Semiflex 3D (PTW 31021), microDiamond (PTW 60019), and Farmer-type (PTW 30013 and IBA FC65-G) detectors in an Elekta 3D scanning water phantom and a PTW 1D water phantom. EBT3 Gafchromic film and ion chamber measurements in a buildup cap were also used. Special consideration was given to scan offsets, detector effective points of measurement and avoiding air gaps. Machine performance has been verified and the system satisfied the relevant beam requirements of IEC60976. Beam data were acquired for field sizes between 1??×??1 and 57??×??22?cm2. New techniques were developed to measure percentage depth dose (PDD) curves including the electron return effect at beam exit, which exhibits an electron-type practical range of [Formula: see text] cm. The Lorentz force acting on the secondary charged particles creates an asymmetry in the crossline profiles with an average shift of??+0.24?cm. For a 10??×??10?cm2 beam, scatter from the cryostat contributes 1% of the dose at isocentre. This affects the relative output factors, scatter factors and beam profiles, both in-field and out-of-field. The average 20%-80% penumbral width measured for small fields with a microDiamond detector at 10?cm depth is 0.50?cm. MRI-linac penumbral widths are very similar to that of the Elekta Agility linac MLC, as is the near-surface dose PDD(0.2?cm)??=??57%. The entrance surface dose is??~36% of [Formula: see text]. Cryostat transmission is quantified for inclusion within the treatment planning system. As a result, the 1.5 T MRI-linac 7 MV FFF beam has been characterised for the first time and is suitable for clinical use. This was a key step towards the first clinical treatments with the MRI-linac, which were delivered at University Medical Center Utrecht in May 2017

Impactfactor 2.665

**Ten tijde van publicatie verbonden aan: Department of Radiotherapy, UMC Utrecht*

ESTRO ACROP guidelines for target volume definition in the treatment of locally advanced non-small cell lung cancer

Nestle U, De Ruysscher D, Ricardi U, Geets X, Belderbos J, Pottgen C, Dziadiuszko R, Peeters S, Lievens Y, **Hurkmans C**, Slotman B, Ramella S, Faivre-Finn C, McDonald F, Manapov F, Putora PM, LePechoux C, Van Houtte P

Radiother Oncol. 2018 Apr 127(1):1-5. Epub 2018 Mar 28

Radiotherapy (RT) plays a major role in the curative treatment of locally advanced non-small cell lung cancer (NSCLC). Therefore, the ACROP committee was asked by the ESTRO to provide recommendations on target volume delineation for standard clinical scenarios in definitive (chemo)radiotherapy (RT) and adjuvant RT for locally advanced NSCLC. The guidelines given here are a result of the evaluation of a structured questionnaire followed by a consensus discussion, voting and writing procedure within the committee. Hence, we provide advice for methods and time-points of diagnostics and imaging before the start of treatment planning and for the mandatory and optional imaging to be used for planning itself. Concerning target volumes, recommendations are given for GTV delineation of primary tumour and lymph nodes followed by issues related to the delineation of CTVs for definitive and adjuvant radiotherapy. In the context of PTV delineation, recommendations about the management of geometric uncertainties and target motion are given. We further provide our opinions on normal tissue delineation and organisational and responsibility questions in the process of target volume delineation. This guideline intends to contribute to the standardisation and optimisation of the process of RT treatment planning for clinical practice and prospective studies.

Impactfactor 4.942

Feasibility of state of the art PET/CT systems performance harmonisation

Kaalep A, Sera T, **Rijnsdorp S**, Yaqub M, Talsma A, Lodge MA, Boellaard R

Eur J Nucl Med Mol Imaging. 2018 Jul 45(8):1344-1361. Epub 2018 Mar 2

PURPOSE:

The objective of this study was to explore the feasibility of harmonising performance for PET/CT systems equipped with time-of-flight (ToF) and resolution modelling/point spread function (PSF) technologies. A second aim was producing a working prototype of new harmonising criteria with higher contrast recoveries than current EARL standards using various SUV metrics.

METHODS:

Four PET/CT systems with both ToF and PSF capabilities from three major vendors were used to acquire and reconstruct images of the NEMA NU2-2007 body phantom filled conforming EANM EARL guidelines. A total of 15 reconstruction parameter sets of varying pixel size, post filtering and reconstruction type, with three different acquisition durations were used to compare the quantitative performance of the systems. A target range for recovery curves was established such that it would accommodate the highest matching recoveries from all investigated systems. These updated criteria were validated on 18 additional scanners from 16 sites in order to demonstrate the scanners' ability to meet the new target range.

RESULTS:
Each of the four systems was found to be capable of producing harmonising reconstructions with similar recovery curves. The five reconstruction parameter sets producing harmonising results significantly increased SUVmean (25%) and SUVmax (26%) contrast recoveries compared with current EARL specifications. Additional prospective validation performed on 18 scanners from 16 EARL accredited sites demonstrated the feasibility of updated harmonising specifications. SUVpeak was found to significantly reduce the variability in quantitative results while producing lower recoveries in smaller (=17 mm diameter) sphere sizes.
CONCLUSIONS:
Harmonising PET/CT systems with ToF and PSF technologies from different vendors was found to be feasible. The harmonisation of such systems would require an update to the current multicentre accreditation program EARL in order to accommodate higher recoveries. SUVpeak should be further investigated as a noise resistant alternative quantitative metric to SUVmax.

Impactfactor *7.704*

Impact of brachytherapy technique (2D versus 3D) on outcome following radiotherapy of cervical cancer

Derks K, **Steenhuijsen JLG**, van den Berg HA, Houterman S, Cnossen J, **van Haaren P**, De Jaeger K

J Contemp Brachytherapy. 2018 Feb 10(1):17-25. Epub 2018 Feb 22

Purpose:
The purpose of this study was to analyze the effect of 2D conventional brachytherapy (CBT) compared to 3D MRI-guided brachytherapy (IGBT) with and without the use of interstitial needles on local control, overall survival, and toxicity in patients treated for cervical cancer with radiation or chemoradiation.
Material and methods:
A retrospective analysis was performed of biopsy-proven FIGO IB-IVA cervical cancer patients, treated with primary radiation or chemoradiation, followed by brachytherapy (BT) between January 1997 and July 2016. Endpoints were local control, overall survival, and toxicity.
Results:
Of 126 patients included, 35 have been treated with CBT, 31 with IGBT without needles (IC), and 60 with IGBT with needles (ICIS). External beam radiotherapy (EBRT) had mostly been delivered concurrently with chemotherapy (weekly cisplatin). Overall local control was 93% after 1 year, and 88% after 3 years. Overall 3-year survival was 75%, and 5-year survival was 66%. The 3D technique (IGBT cohorts) showed a trend for an improved local control and overall survival ($p = 0.05$) compared to the 2D technique (CBT cohort). A decrease in toxicity was observed from 17% (2D cohort) to 12% (3D cohort). The use of interstitial needles was associated with a higher high-risk clinical target volume (HR-CTV) dose (11.3 Gy vs. 9.9 Gy) and a lower D2cc bladder dose (10.9 Gy vs. 14.7 Gy, both $p < 0.01$).
Conclusions:
In cervical cancer treatment, the use of a 3D brachytherapy technique (MRI-guided with or without interstitial needles) showed a trend towards an increased local control and improved overall survival with reduced toxicity, compared to the conventional 2D brachytherapy technique. The use of interstitial needles allowed dose sculpting, resulting in delivery of higher doses to the HR-CTV, while reducing radiation doses to organs at risk, such as the bladder.

Impactfactor --

Inter-reader variability of SPECT MPI readings in low- and middle-income countries: Results from the IAEA-MPI Audit Project (I-MAP)

Dondi M, Rodella C, Giubbini R, Camoni L, Karthikeyan G, Vitola JV, Einstein AJ, **Arends BJ**, Morozova O, Pascual TN, Paez D I-MAP investigators..

J Nucl Cardiol. 2018 Aug 30. [Epub ahead of print]

BACKGROUND:
Consistency of results between different readers is an important issue in medical imaging, as it affects portability of results between institutions and may affect patient care. The International Atomic Energy Agency (IAEA) in pursuing its mission of fostering peaceful applications of nuclear technologies has supported several training activities in the field of nuclear cardiology (NC) and SPECT myocardial perfusion imaging (MPI) in particular. The aim of this study was to verify the outcome of those activities through an international clinical audit on MPI where participants were requested to report on studies distributed from a core lab.
METHODS:
The study was run in two phases: in phase 1, SPECT MPI studies were distributed as raw data and full processing was requested as per local practice. In phase 2, images from studies pre-processed at the core lab were distributed. Data to be reported included summed stress score (SSS); summed rest score (SRS); summed difference score (SDS); left ventricular (LV) ejection fraction (EF) and end- diastolic volume (EDV). Qualitative appraisals included the assessment of perfusion and presence of ischemia, scar or mixed patterns, presence of transient ischemic dilation (TID), and risk for cardiac events (CE). Twenty-four previous trainees from low- and middle-income countries participated (core participants group) and their results were assessed for inter-observer variability in each of the

two phases, and for changes between phases. The same evaluations were performed for a group of eleven international experts (experts group). Results were also compared between the groups.
RESULTS:
Expert readers showed an excellent level of agreement for all parameters in both phase 1 and 2. For core participants, the concordance of all parameters in phase 1 was rated as good to excellent. Two parameters which were re-evaluated in phase 2, namely SSS and SRS, showed an increased level of concordance, up to excellent in both cases. Reporting of categorical variables by expert readers remained almost unchanged between the two phases, while core participants showed an increase in phase 2. Finally, pooled LVEF values did not show a significant difference between core participants and experts. However, significant differences were found between LVEF values obtained using different software packages for cardiac analysis.
CONCLUSIONS:
In this study, inter-observer agreement was moderate-to-good for core group readers and good-to-excellent for expert readers. The quality of reporting is affected by the quality of processing. These results confirm the important role of the IAEA training activities in improving imaging in low- and middle-income countries.

Impactfactor *3.847*

Monte Carlo Based Dose Assessment for 90Y Radioembolization, A Comparison between 99mtc-MAA SPECT/CT and 90Y-Microspheres PET

Rijnsdorp S, Oprea-Lager D, de Vries J, van Lingen A

To Physics Journal 2018;1(2):83-94

The aim of this research was to assess the agreement between the distribution of technetium-99m macroaggregated albumin (MAA) and yttrium-90 microspheres in radioembolization of the liver, as well as the correspondence between the desired radiation dose and the true radiation dose in the target area.
Materials and Methods: The relative distribution of yttrium-90 microspheres was estimated in 5 patients, using the activity distributions from technetium-99m MAA SPECT/CT and yttrium-90 PET/CT imaging. A Monte Carlo simulation using these relative activity distributions was used to calculate the radiation dose to the liver.
Results and Discussion:
A large difference in radiation dose was found when comparing technetium-99m MAA and yttrium-90 microspheres distributions. In addition, the distribution of yttrium-90 microspheres in the liver, obtained from the PET images, was highly inhomogeneous.
Relative technetium-99m MAA distribution does not necessarily comply with the distribution of yttrium-90 microspheres. Therefore, technetium-99m MAA scans cannot directly be used for prospective radiation dose assessment. Due to the inhomogeneity of the distribution of yttrium-90 microspheres, the estimated radiation dose in large parts of the targeted lobe(s) is smaller than the desired radiation dose.

Impactfactor *--*

Optimal image guided radiation therapy strategy for organs at risk sparing in radiotherapy of the prostate including pelvic lymph nodes

van Nunen A, van der Toorn PPG, Budiharto TCG, **Schuring D**

Radiother Oncol. 2018 Apr 127(1):68-73. Epub 2018 Mar 2

BACKGROUND AND PURPOSE:
Purpose of this study was to quantify the OAR dose for different position correction strategies, and to determine which strategy is most optimal for treating patients on the prostate and pelvic lymph nodes.
MATERIALS AND METHODS:
For 30 patients, four different treatment plans were made reflecting different correction strategies: online correction on bony anatomy; offline correction on bony anatomy; online correction on the prostate fiducials; using 1?cm margins around both CTVs. The dose to the PTVs and OARs was quantified and a pairwise statistical analysis was performed.
RESULTS:
No statistically significant differences were observed in the dose to the PTVs, ensuring that any OAR sparing is not caused by differences in PTV coverage. Dose to the rectum and anal canal was lowest when applying an online correction on prostate fiducials, although the total PTV volume was higher. Dose to the small bowel bag and femoral heads was slightly higher compared to online correction on bony structures, but well within clinically acceptable limits.
CONCLUSION:
Although the total PTV volume is higher when applying an online correction on the prostate, this strategy leads to the most optimal sparing of relevant OARs, at the cost of a slightly higher dose to the femoral heads and small bowel bag.

Impactfactor *4.942*

Photons protons or carbon ions for stage I non-small cell lung cancer - Results of the multicentric ROCOCO in silico study

Wink KCJ, Roelofs E, Simone CB 2nd, Dechambre D, Santiago A, van der Stoep J, **Dries W**, Smits J, Avery S, Ammazzalorso F, Jansen N, Jelen U, Solberg T, de Ruysscher D, Troost EGC

Radiother Oncol. 2018 Jul 128(1):139-146. Epub 2018 Mar 12

PURPOSE:
To compare dose to organs at risk (OARs) and dose-escalation possibility for 24 stage I non-small cell lung cancer (NSCLC) patients in a ROCOCO (Radiation Oncology Collaborative Comparison) trial.
METHODS:
For each patient, 3 photon plans [Intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT) and CyberKnife], a double scattered proton (DSP) and an intensity-modulated carbon-ion (IMIT) therapy plan were created. Dose prescription was 60?Gy (equivalent) in 8 fractions.
RESULTS:
The mean dose and dose to 2% of the clinical target volume (CTV) were lower for protons and ions compared with IMRT (p?<?0.01). Doses to the lungs, heart, and mediastinal structures were lowest with IMIT (p?<?0.01), doses to the spinal cord were lowest with DSP (p?<?0.01). VMAT and CyberKnife allowed for reduced doses to most OARs compared with IMRT. Dose escalation was possible for 8 patients. Generally, the mediastinum was the primary dose-limiting organ.
CONCLUSION:
On average, the doses to the OARs were lowest using particles, with more homogenous CTV doses. Given the ability of VMAT and CyberKnife to limit doses to OARs compared with IMRT, the additional benefit of particles may only be clinically relevant in selected patients and thus should be carefully weighed for every individual patient.

Impactfactor 4.942

Quality assurance of four-dimensional computed tomography in a multicentre trial of stereotactic body radiotherapy of centrally located lung tumours

Marie Lambrecht, Jan-Jakob Sonke, Ursula Nestle,, Heike Peulen, Damien C. Weber, Marcel Verheij, **Coen W. Hurkmans**

Physics and Imaging in Radiation Oncology 2018;8:57-62

Background and Purpose:
Extensive radiation therapy quality assurance (RTQA) programs are needed when advanced radiotherapy treatments are used. As part of the RTQA four dimensional computed tomography (4DCT)imaging performance needs to be assessed. Here we present the RTQA data related to 4DCT procedures used within the context of stereotactic body radiotherapy(SBRT) of centrally located lung tumours. It provides an overview of the 4DCT acquisition methods and achievable accuracy of imaging lung tumour volumes.
Materials and Methods:
3DCT and 4DCT images were acquired from a CIRS phantom with spheres of 7.5 and 12.5 mm radius using the institutional scan protocols. Regular asymmetric tumour motion was simulated withvarying amplitude sand periods. Target volumes were reconstructed using auto-contouring with scanner specific thresholds. Volume and amplitudes deviations were assessed.
Results:
Although acquisition parameters were rather homogeneous over the eleven institutions analysed, volume deviations were observed. Average volume deviations for the 12.5mm spherewere 15%(-4%to69%) at end of inspiration, 2% (-2% to 9.0%) at end of expiration and 12% (0% to 36%) at mid-ventilation. For the 7.5mm sphere deviations were 13% (-99% to 65%), 16% (-34% to 66%) and 1% (-13% to 20%), respectively.
The amplitude deviation was generally within 2mm although underestimations up to 6mm were observed.
Conclusions:
The expiration phase was the most accurate phase to define the tumour volume and should be preferred for GTV delineation of tumours exhibiting large motion causing motion artefacts when using mid-ventilation or tracking techniques. The large variation found among the institutions indicated that further improvements in 4DCT imaging were possible. Recommendations for 4DCT QA have been formulated.

Impactfactor --

Radiotherapy quality assurance for the RTOG 0834/EORTC 26053-22054/NCIC CTG CEC.1/CATNON intergroup trial "concurrent and adjuvant temozolomide chemotherapy in newly diagnosed non-1p/19q deleted anaplastic glioma": Individual case review analysis

Abrunhosa-Branquinho AN, Bar-Deroma R, Collette S, Clementel E, Liu Y, **Hurkmans CW**, Feuvret L, Van Beek K, van den Bent M, Baumert BG, Weber DC

Radiother Oncol. 2018 May;127(2):292-298. Epub 2018 Mar 29

BACKGROUND:
The EORTC phase III 26053-22054/ RTOG 0834/NCIC CTG CEC.1/CATNON intergroup trial was designed to evaluate the impact on concurrent and adjuvant temozolomide chemotherapy in newly diagnosed non-1p/19q deleted anaplastic gliomas. The primary endpoint was overall survival. We report the results of retrospective individual case reviews (ICRs) for the first patient randomized per institution to detect the compliance with the study protocol.
MATERIAL AND METHODS:
Sixty-nine institutions were required to submit the radiotherapy plan of their first randomized patient. Full digital datasets uploaded to the EORTC server were assessed by three independent and blinded reviewers through the EORTC radiotherapy quality assurance platform.
RESULTS:
Sixty-two (90%) of sixty-nine ICRs were received and assessable. Of the 62 cases, 22 were evaluated as per protocol (35.5%), 11 as acceptable variation (17.7%) and 29 were classified as unacceptable variations (46.8%). Most common unacceptable variations were related to the PTV dose (n?=?19, 31%) and delineation (n?=?17, 27%) processes.
CONCLUSIONS:
The ICR analysis showed a significant number of unacceptable variations with potential impact on tumor control and/or toxicity profile. Prospective ICRs are encouraged for future studies to prevent and correct protocol violations before start of treatment.

Impactfactor 4.942

Radiotherapy quality assurance of SBRT for patients with centrally located lung tumours within the multicentre phase II EORTC Lungtech trial: Benchmark case results

Marie Lambrecht , Enrico Clementel, Jan-Jacob Sonke, Ursula Nestle, Sonja Adeba, Mathias Guckenberger, Nicolaus Andratschke, Damien C. Weber, Marcel Verheij, **Coen W. Hurkmans**

Radiotherapy and Oncology 2018; 23 oct, online 21 dec 2018

Purpose
To report on the benchmark case (BC) study performed in the context of the European Organisation for Research and Treatment of Cancer prospective multicentre Lungtech trial of SBRT for patients with inoperable centrally located lung tumours.
Methods and materials
Target volume and organs at risk (OARs) delineations first needed to be acceptable before the treatment plan was reviewed. Retrospectively, Dice similarity coefficients of the OARs and the target volumes were calculated and a set of gold standard contours adapted for each institution margins was applied on the accepted dose submissions to evaluate the influence of acceptable delineation variations on dosimetry.
Results
Twenty-five institutions participated. Five BCs were accepted at the first attempt. Twenty institutions had to revise their delineation at least once and seven had to revise their planning once. The V60 Gy dose coverage improved significantly (p?=?0.05) between the first and final submissions from median (range) 94.8% (22.5–97.8) to 95.3% (70.5–99.3). The median Dice coefficient varied significantly between OARs: The lowest values were found for the brachial plexus 0.25 (0.01–0.54) and the highest for the spinal cord 0.89 (0.71–0.95). The mean PTV Dice coefficient was 0.82 (0.48–0.92). Applying the gold standard contours, only one institution remained compliant with the dose coverage criteria with V60 Gy median (range) of 83.4% (54.2–93.9).
Conclusions
Clinical guidelines and radiotherapy protocols are not a substitute for timely radiotherapy quality assurance procedures, which improve dose coverage significantly. Delineation remains the main source of BC rejection and plan review without first reviewing delineation may not be efficient. Our results show that delineation variations seem to have a larger influence on PTV coverage than variations in planning and irradiation techniques and thus suggest that dose tolerance criteria should preferably take into account the accuracy of delineation.

Impactfactor 4.942

Remote beam output audits: A global assessment of results out of tolerance

Stephen F. Kry, Christine B. Peterson, Rebecca M. Howell, Joanna Izewska e, Jessica Lye, Catharine H. Clark, Mitsuhiro Nakamura, **Coen Hurkmans**, Paola Alvarez, Andrew Alves, Tomislav Bokulic, David Followill, Pavel Kazantsev, Jessica Lowenstein, Andrea Molineu, Jacob Palmer, Susan A. Smith, Paige Taylor, Paulina Wesolowska, Ivan Williams

Physics and Imaging in Radiation Oncology 2018;7:39-44

Background and purpose:
Remote beam output audits, which independently measure an institution ’s machine calibration, are a common component of independent radiotherapy peer review. This work reviews the results and trends of these audit results across several organisations and geographical regions.
Materials and methods:

10Beam output audit results from the Australian Clinical Dosimetry Services, International Atomic Energy Agency, Imaging and Radiation Oncology Core, and Radiation Dosimetry Services were evaluated from 2010 to the present. The rate of audit results outside a ± 5% tolerance was evaluated for photon and electron beams as a function of the year of irradiation and nominal beam energy. Additionally, examples of confirmed calibration errors were examined to provide guidance to clinical physicists and auditing bodies.
Results:
Of the 210,167 audit results, 1323 (0.63%) were outside of tolerance. There was a clear trend of improved audit performance for more recent dates, and while all photon energies generally showed uniform rates of results out of tolerance, low (6 MeV) and high (=18 MeV) energy electron beams showed significantly elevated rates. Twentynine confirmed calibration errors were explored and attributed to a range of issues, such as equipment failures, errors in setup, and errors in performing the clinical reference calibration. Forty-two percent of these confirmed errors were detected during ongoing periodic monitoring, and not at the time of the first audit of the machine.
Conclusions:
Remote beam output audits have identified, and continue to identify, numerous and often sub-stantial beam calibration errors.

Impactfactor --

Spiraling contaminant electrons increase doses to surfaces outside the photon beam of an MRI-linac with a perpendicular magnetic field

Hackett SL, van Asselen B, Wolthaus JWH, **Bluemink JJ***, Ishakoglu K, Kok J, Lagendijk JJW, Raaymakers BW
Phys Med Biol. 2018 May 1;63(9):095001

The transverse magnetic field of an MRI-linac sweeps contaminant electrons away from the radiation beam. Films oriented perpendicular to the magnetic field and 5?cm from the radiation beam edge show a projection of the divergent beam, indicating that contaminant electrons spiral along magnetic field lines and deposit dose on surfaces outside the primary beam perpendicular to the magnetic field. These spiraling contaminant electrons (SCE) could increase skin doses to protruding regions of the patient along the cranio-caudal axis. This study investigated doses from SCE for an MRI-linac comprising a 7 MV linac and a 1.5 T MRI scanner. Surface doses to films perpendicular to the magnetic field and 5?cm from the radiation beam edge showed increased dose within the projection of the primary beam, whereas films parallel to the magnetic field and 5?cm from the beam edge showed no region of increased dose. However, the dose from contaminant electrons is absorbed within a few millimeters. For large fields, the SCE dose is within the same order of magnitude as doses from scattered and leakage photons. Doses for both SCE and scattered photons decrease rapidly with decreasing beam size and increasing distance from the beam edge.

Impactfactor *2.665*
**Ten tijde van publicatie verbonden aan: Department of Radiotherapy, UMC Utrecht,*

Systematic review of the diagnostic value of magnetic resonance imaging for early glottic carcinoma

van Egmond SL, Stegeman I, Pameijer FA, **Bluemink JJ***, Terhaard CH, Janssen LM
Laryngoscope Investig Otolaryngol. 2018 Feb 5;3(1):49-55. eCollection 2018 Feb

Objective:
In early glottic cancer, accurate assessment of tumor extension, including depth infiltration, is of great importance for both staging, therapeutic approach and systematic comparison of data. Our goal was to assess the diagnostic value of MRI in pre-therapeutic staging of primary early stage (T1 and T2) glottic carcinoma.
Study design:
Systematic review of literature.
Methods:
We conducted a systematic search in Pubmed, Embase, and Scopus up to September 23, 2016. Included studies were selected and critically appraised for relevance and validity.
Results:
Seven out of 938 unique articles were selected, including 64 cases. MRI over-staged 6% and under-staged 13% of cT1 and cT2 tumors. However, available data is heterogeneous, very limited and mainly based on subanalysis of a small amount of patients. Reported MRI protocols appear to be suboptimal for small laryngeal lesions. Diagnostic value of MRI for subtle depth infiltration or laryngeal anatomical subsites (eg, laryngeal ventricle, vocal cord, etc.) could not be assessed.
Conclusions:
More studies are needed to assess the diagnostic value of MRI for small glottic tumors.

Impactfactor: --
**Ten tijde van publicatie verbonden aan: Department of Radiotherapy UMC Cancer Center University Medical Center Utrecht Utrecht*

What you see is (not) what you get: tools for a non-radiologist to evaluate image quality in lung cancer

de Jong EEC*, Hendriks LEL, van Elmpt W, Gietema HA, Hofman PAM, De Ruysscher DKM, Dingemans AC

Lung Cancer. 2018 Sep;123:112-115. Epub 2018 Jul 18

Medical images are an integral part of oncological patient records and they are reviewed by many different specialists. Therefore, it is important that besides imaging experts, other clinicians are also aware that the diagnostic value of a scan is influenced by the applied imaging protocol. Based on two clinical lung cancer trials, we experienced that, even within a study protocol, there is a large variability in imaging parameters, which has direct impact on the interpretation of the image. These two trials were: 1) the NTR3628 in which the added value of gadolinium magnetic resonance imaging (Gd-MRI) to dedicated contrast enhanced computed tomography (CE-CT) for detecting asymptomatic brain metastases in stage III non-small cell lung cancer (NSCLC) was investigated and 2) a sub-study of the NVALT 12 trial (NCT01171170) in which repeated 18?F-fludeoxyglucose positron emission tomography (18F-FDG-PET) imaging for early response assessment was investigated. Based on the problems encountered in the two trials, we provide recommendations for non-radiology clinicians, which can be used in daily interpretation of imaging. Variations in image parameters cannot only influence trial results, but sub-optimal imaging can also influence treatment decisions in daily lung cancer care, when a physician is not aware of the scanning details.

Impactfactor: 4.486

**Ten tijde van publicatie verbonden aan: The D-Lab: Decision Support for Precision Medicine, GROW-School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht*

Kwaliteit

Health insurance outcome-based purchasing: The case of hospital contracting for cardiac interventions in the Netherlands

D. van Veghel, **D. N. Schulz**, A. H. M. van Straten, T. A. Simmers, A. Lenssen, L. Kuijten-Slegers, F. van Eenennaam, M. A. Soliman Hamad, B. A. de Mol & L. R. C. Dekker

INTERNATIONAL JOURNAL OF HEALTHCARE MANAGEMENT, 2018;11(4):371-8

Innovative forms of value-based purchasing contracts, based on outcome instead of volume, are imperative to face the imminent cost crisis in health care. The objective of this study was to design and implement a model for an outcome-based purchasing contract between a hospital and a health insurance company. The model was implemented in 2015. A study cohort (n = 14,944) from patients with coronary artery disease or atrial fibrillation treated in 2014 was compared to a historical reference cohort from patients treated between 2010 and 2013. The outcome measures and the model are based on Porter's value-based healthcare principles. Improvements in outcomes were observed, leading to a financial incentive to be spent on further quality improvement. Implementation of this model is a first step towards enabling inclusion of patient-relevant outcomes in purchasing for healthcare. It aligns the focus of health insurance companies and hospitals on patient value.

Impactfactor --

Longgeneeskunde

Box-ticking and Olympic high jumping - Physicians' perceptions and acceptance of national physician validation systems

Sehlbach C, Govaerts MJB, Mitchell S, Rohde GGU, **Smeenk FWJM**, Driessen EW

Med Teach. 2018 Sep;40(9):886-891. Epub 2018 May 24

PURPOSE:
National physician validation systems aim to ensure lifelong learning through periodic appraisals of physicians' competence. Their effectiveness is determined by physicians' acceptance of and commitment to the system. This study, therefore, sought to explore physicians' perceptions and self-reported acceptance of validation across three different physician validation systems in Europe.
MATERIALS AND METHODS:
Using a constructivist grounded-theory approach, we conducted semi-structured interviews with 32 respiratory specialists from three countries with markedly different validation systems: Germany, which has a mandatory, credit-based system oriented to continuing professional development; Denmark, with mandatory annual dialogs and ensuing, non-compulsory activities; and the UK, with a mandatory, portfolio-based revalidation system. We analyzed interview data with a view to identifying factors influencing physicians' perceptions and acceptance.
RESULTS:
Factors that influenced acceptance were the assessment's authenticity and alignment of its requirements with clinical practice, physicians' beliefs about learning, perceived autonomy, and organizational support.
CONCLUSIONS:
Users' acceptance levels determine any system's effectiveness. To support lifelong learning effectively, national physician validation systems must be carefully designed and integrated into daily practice. Involving physicians in their design may render systems more authentic and improve alignment between individual ambitions and the systems' goals, thereby promoting acceptance.

Impactfactor *2.450*

Certified ...now what?" On the Challenges of Lifelong Learning: Report from an AMEE 2017 Symposium

Sehlbach C, Balzan M, Bennett J, Prior Filipe H, Thinggaard E, **Smeenk F**

J Eur CME. 2018 Jan 25 7(1):1428025. eCollection 2018

The increasing mobility of patients and healthcare professionals across the countries of Europe has highlighted the wide variations in both medical training, and provision of medical competency and skills. The maintenance of the standards defining competency and skills have national and international implications and have proved challenging for national regulatory bodies. Thus each nation has introduced different types of Continuing Professional Development (CPD), recertification and relicensing systems. At the Symposium entitled: " 'Certified … now what?' On the Challenges of Lifelong Learning" in August 2017 at the Association for Medical Education in Europe (AMEE) annual conference, we reviewed differing European national relicensing systems were reviewed. The review highlighted various lifelong learning and competence assessment approaches using examples from different medical specialties across several European countries.

Impactfactor --

De waarde van een astma-adviespolikliniek* : Een effectieve service voor patiënt én huisarts

Gillis RME, van Litsenburg W, van Balkom RH, Muris JW, **Smeenk FW**

Ned Tijdschr Geneeskd. 2018 Jun 21;162. pii: D2424

Doel
Het evalueren van het effect van een astma-adviespolikliniek (ADP) als service voor huisartsen.
Opzet
Retrospectieve studie.
Methode
Alle 659 patiënten die in de periode mei 2011-augustus 2015 door de huisarts waren verwezen naar de ADP in het Catharina Ziekenhuis te Eindhoven en bij wie de huisarts de diagnose ‘astma’ vermoedde, werden geïncludeerd in deze studie. Op de ADP werd een anamnese afgenomen en lichamelijk onderzoek en histamineprovocatietest verricht. Indien noodzakelijk werd er aanvullend onderzoek verricht. Op grond van de bevindingen werd het medicamenteuze beleid bijgesteld. Wij evalueerden de overeenstemming tussen de werkdiagnose van de huisarts en de diagnose die was gesteld door de ADP en welke consequenties dit had voor de medicamenteuze behandeling.
Resultaten
Bij 52% (n = 340) van alle patiënten werd de diagnose ‘astma’ uitgesloten en bij 42% (n = 275) werd de diagnose ‘astma’ bevestigd. De aangepaste diagnose resulteerde bij meer dan de helft van alle patiënten in een verandering van de medicatie. Het ‘one-stop-shop’-principe van de ADP werd bereikt bij 53% van alle patiënten.
Conclusie
Een ADP is een effectieve ondersteuning voor huisartsen bij de astmadiagnostiek. Dit kan het probleem van over- en onderdiagnose verminderen en daarmee leiden tot betere behandelstrategieën voor de patiënt.

Impactfactor --

* Dubbelpublicatie: Dit onderzoek werd eerder gepubliceerd in Primary Care Respiratory Medicine (2017;27:35) met als titel The contribution of an asthma diagnostic consultation service in obtaining an accurate asthma diagnosis for primary care patients: results of a real-life study.

Diagnosis of vertebral deformities on chest CT and DXA compared to routine lateral thoracic spine X-ray

van Dort MJ, **Romme EAPM, Smeenk FWJM**, Geusens PPPM, Wouters EFM, van den Bergh JP

Osteoporos Int. 2018 Jun 29(6):1285-1293. Epub 2018 Feb 12

X-ray, CT and DXA enable diagnosis of vertebral deformities. For this study, level of agreement of vertebral deformity diagnosis was analysed. We showed that especially on subject level, these imaging techniques could be used for opportunistic screening of vertebral deformities in COPD patients.

INTRODUCTION:

X-ray and CT are frequently used for pulmonary evaluation in patients with chronic obstructive pulmonary disease (COPD) and also enable to diagnose vertebral deformities together with dual-energy X-ray absorptiometry (DXA) imaging. The aim of this research was to study the level of agreement of these imaging modalities for diagnosis of vertebral deformities from T4 to L1.

METHODS:

Eighty-seven subjects (mean age of 65; 50 males; 57 COPD patients) who had X-ray, chest CT (CCT) and DXA were included. Evaluable vertebrae were scored twice using SpineAnalyzer™ software. ICCs and kappas were calculated to examine intra-observer variability. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the receiver operating characteristic curve (AUROC) were calculated to compare vertebral deformities diagnosed on the different imaging modalities.

RESULTS:

ICCs for height measurements were excellent (>?0.94). Kappas were good to excellent (0.64-0.77). At vertebral level, the AUROC was 0.85 for CCT vs. X-ray, 0.74 for DXA vs. X-ray and 0.77 for DXA vs. CCT. Sensitivity (51%-73%) and PPV (57%-70%) were fair to good; specificity and NPV were excellent (=?96%). At subject level, the AUROC values were comparable.

CONCLUSIONS:

Reproducibility of height measurements of vertebrae is excellent with all three imaging modalities. On subject level, diagnostic performance of CT (PPV 79-82%; NPV 90-93%), and to a slightly lesser extend of DXA (PPV 73-77%; NPV 80-89%), indicates that these imaging techniques could be used for opportunistic screening of vertebral deformities in COPD patients.

Impactfactor 3.856

Doctors on the move: a European case study on the key characteristics of national recertification systems

Sehlbach C, Govaerts MJ, Mitchell S, Rohde GG, **Smeenk FW**, Driessen EW

BMJ Open. 2018 Apr 17;8(4):e019963

OBJECTIVES: With increased cross-border movement, ensuring safe and high-quality healthcare has gained primacy. The purpose of recertification is to ensure quality of care through periodically attesting doctors' professional proficiency in their field. Professional migration and facilitated cross-border recognition of qualifications, however, make us question the fitness of national policies for safeguarding patient care and the international accountability of doctors.

DESIGN AND SETTING: We performed document analyses and conducted 19 semistructured interviews to identify and describe key characteristics and effective components of 10 different European recertification systems, each representing one case (collective case study). We subsequently compared these systems to explore similarities and differences in terms of assessment criteria used to determine process quality.

RESULTS: Great variety existed between countries in terms and assessment formats used, targeting cognition, competence and performance (Miller's assessment pyramid). Recertification procedures and requirements also varied significantly, ranging from voluntary participation in professional development modules to the mandatory collection of multiple performance data in a competency-based portfolio. Knowledge assessment was fundamental to recertification in most countries. Another difference concerned the stakeholders involved in the recertification process: while some systems exclusively relied on doctors' self-assessment, others involved multiple stakeholders but rarely included patients in assessment of doctors' professional competence. Differences between systems partly reflected different goals and primary purposes of recertification.

CONCLUSION: Recertification systems differ substantially internationally with regard to the criteria they apply to assess doctors' competence, their aims, requirements, assessment formats and patient involvement. In the light of professional mobility and associated demands for accountability, we recommend that competence assessment includes patients' perspectives, and recertification practices be shared internationally to enhance transparency. This can help facilitate cross-border movement, while guaranteeing high-quality patient care.

Impactfactor 2.413

Een niet-rokende vrouw met een kleincellig longcarcinoom met een mutatie in het epidermale groeifactorreceptor (EGFR)-gen | A female never-smoker with small cell lung cancer and an epidermal growth factor receptor (EGFR) mutation

drs. B.H.G. de Bruijn, **dr. E.A.P.M. Romme**, drs. J. Stavast, dr. N.A. 't Hart, dr. J.P.F.H.A. Simons

Ned Tijdschr Oncol 2018;15:297-301

Geen abstract beschikbaar

Impactfactor --

Effectiveness of Pulmonary Rehabilitation in Patients With Chronic Obstructive Pulmonary Disease With Different Degrees of Static Lung Hyperinflation

Vanfleteren MJ, Koopman M, Spruit MA, Pennings HJ, **Smeenk F**, Pieters W, van den Bergh JJ, Michels AJ, Wouters EF, Groenen MT, Franssen FM, Vanfleteren LE

Arch Phys Med Rehabil. 2018 Nov 99(11):2279-2286.e3. Epub 2018 Jun 12

OBJECTIVE:
To evaluate the effect of pulmonary rehabilitation (PR) on exercise performance and quality of life in patients with chronic obstructive pulmonary disease (COPD) with different degrees of static lung hyperinflation (LH).
DESIGN:
Retrospective cohort study.
SETTING:
PR network.
PARTICIPANTS:
A cohort of 1981 patients with COPD (55% men; age: 66.8±9.3y; forced expiratory volume in the first second%: 50.7±19.5; residual volume [RV]%: 163.0±49.7).
INTERVENTION:
An interdisciplinary PR program for patients with COPD consisting of 40 sessions.
MAIN OUTCOME MEASURES:
Participants were stratified into 5 quintiles according to baseline RV and were evaluated on the basis of pre- and post-PR 6-minute walk distance (6MWD), constant work rate test (CWRT), and Saint George's Respiratory Questionnaire (SGRQ), among other clinical parameters.
RESULTS:
With increasing RV quintile, patients were younger, more frequently women, had lower forced expiratory volume in the first second%, lower body mass index and fat-free mass index, shorter 6MWD, shorter CWRT, and worse SGRQ scores (P<.01). All RV strata improved after PR in all 3 outcomes (P<.001). Nevertheless, higher, compared to lower RV categories, had lower ?CWRT (P<.01) but similar ?6MWD (P=.948) and ?SGRQ (P=.086) after PR.
CONCLUSIONS:
LH in COPD is related to younger age, female sex, lower body weight, worse exercise capacity and health status, but did not prevent patients from benefitting from PR. LH, however, influences walking and cycling response after PR differently.

Impactfactor *3.077*

ERS Congress highlight: educational forum on continuing professional development

Sehlbach C, Farr A, Allen M, Guiral JG, **Wielders PL**, Stolz D, Rohde G

Breathe (Sheff). 2018 Jun;14(2):e12-e16

The ERS International Congress educational forum brings together experts to advance respiratory medicine

Impactfactor --

High Imminent Vertebral Fracture Risk in Subjects With COPD With a Prevalent or Incident Vertebral Fracture

van Dort MJ, Geusens P, Driessen JH, **Romme EA, Smeenk FW**, Wouters EF, van den Bergh JP

J Bone Miner Res. 2018 Jul 33(7):1233-1241. Epub 2018 Apr 17

Subjects with chronic obstructive pulmonary disease (COPD) have an increased risk of vertebral fractures (VFs); however, VF incidence is largely unknown. Therefore, the aim of our study was to determine the incidence of new and/or worsening VF in subjects with COPD. Smokers and subjects with COPD (GOLD II-IV) from the ECLIPSE study with complete set of chest CT scans (baseline and 1- and 3-year follow-up) to evaluate vertebrae T1 down to L1 were included. If a VF was diagnosed on the last scan, detailed VF assessment of the previous scans was performed. VFs were scored according to the method of Genant as mild, moderate, or severe. Main outcome measure was the cumulative incidence of new and/or worsening VF at subject level, within 1 and 3 years. Of 1239 subjects (mean age 61 years, 757 males [61%], 999 subjects with COPD), 253 (20.5%) had =1 prevalent VF. The cumulative incidence of VFs was 10.1% within 1 year and 24.0% within 3 years. After adjustment for age, sex, body mass index (BMI), pack-years, and smoking status, prevalence and incidence were similar between smokers and COPD GOLD stages. Within 1 year, 29.2% of the subjects with a prevalent VF had an incident VF, compared with 5.1% in absence of prevalent VF (hazard ratio [HR]?=?5.1; 95% confidence interval [CI] 3.6-7.4) and 58.5% versus 15.0% within 3 years

(HR?=?3.6; 95% CI 2.9-4.6). The incidence of VF was higher with increasing number and severity of prevalent VFs. Among subjects having an incident VF within the first year, 57.3% had a subsequent VF within the next 2 years. In this study, more than half of the smokers and subjects with COPD with a prevalent VF or an incident VF within the first year sustained a subsequent VF within 3 years. The 3-year risk was even higher in the presence of multiple or severe prevalent VFs.

Impactfactor 6.314

Interprofessional Pulmocheck care pathway: An innovative approach to managing pediatric asthma care in the Netherlands

Meuwissen JMJE, Heynens J, Dauven T, Crasborn L, **Smeenk FWJM**, van der Weijden T, Muris JWM

J Asthma. 2018 Jul;55(7):779-784.Epub 2017 Oct 13

OBJECTIVES:

Under-diagnosis and suboptimal asthma control in children persists. An innovative care pathway was developed by a hospital department of pediatrics with the aim to detect pulmonary problems in children and provide appropriate treatment possibilities through systematic feedback towards the referring primary care physician. Primary care physicians can use this pathway to refer children with asthma-like symptoms for a one-day assessment. Goals are to measure the usage of the pathway by primary care general practitioners (GPs), the outcomes in terms of new diagnoses of asthma, the reduction in regular referrals, generated recommendations/therapy and the adequacy of asthma follow-up.

METHODS:

We collected all feedback letters sent to the GP concerning children who underwent the Pulmocheck in 2010, 2011 and 2012. Furthermore, all GPs, who had referred a child to the Pulmocheck in this period and that subsequently was diagnosed with asthma and was further managed in primary care, were sent a follow-up questionnaire in 2014.

RESULTS:

There were 121 referrals from 51 GPs in 3 years to this pathway. In 59.5% of these referrals a new diagnosis of asthma was established. In 90.9% one or more changes in clinical management were advised. The response rate to the follow-up questionnaires was 65.7% of which 4.8% of the children with new established asthma were reviewed four times or more in the follow-up period, 17.4% two times, 65.2% once, and in 8.7% were not followed.

CONCLUSIONS:

The specialty pediatric asthma care pathway revealed a high number of children with newly diagnosed asthma, but was also helpful to exclude this diagnosis. However, the referral rate of GPs to this pathway was low, but in the children, that were referred several changes in the clinical management were advised and the frequency of monitoring of the children with diagnosed asthma was not in accordance with the asthma guidelines.

Impactfactor 2.014

Utilization of Molecular Testing and Survival Outcomes of Treatment with First- or Second-line Tyrosine Kinase Inhibitors in Advanced Non-small Cell Lung Cancer in a Dutch Population

Sluga R, **VAN DEN Borne BEEM**, Roepman P, Peters BJM, Kastelijn EA, Schramel FMNH

Anticancer Res. 2018 Jan 38(1):393-400

BACKGROUND/AIM:

Epidermal growth factor receptor (EGFR) mutation testing is standard-of-care for advanced non-small cell lung cancer (NSCLC). Outcomes of second-/third-line compared to first-line tyrosine kinase inhibitors (TKIs) have shown conflicting results. We investigated utilization of molecular diagnostics and the outcomes of treatment with first-/second-line TKIs in patients with advanced NSCLC.

MATERIALS AND METHODS:

Retrospective analysis was carried out of 2,206 patients with stage IIIb/IV NSCLC treated between 2008 and 2014 in four hospitals in the Netherlands.

RESULTS:

The rate of performing molecular diagnostics increased from 20.8% to 74.4% in the study period. The median overall survival of EGFR mutation-positive patients treated with TKIs was superior compared to EGFR mutation-negative patients treated with chemotherapy (720 vs. 274 days, $p<0.0001$). No difference in overall survival was found between EGFR mutation-positive patients treated only with TKIs compared to those treated with chemotherapy prior to TKIs, or upon progression under TKIs.

CONCLUSION:

The rate of EGFR testing has improved, increasing the number of patients eligible for targeted therapy. Chemotherapy, prior or subsequent to TKIs, for the treatment of EGFR mutation-positive patients, did not result in significantly better overall survival compared to that achieved with TKIs alone.

Impactfactor 1.865

Maag-Darm-Leverziekten

A prospective multicenter study using a new multiband mucosectomy device for endoscopic resection of early neoplasia in Barrett's esophagus

Pouw RE, Beyna T, Belghazi K, Koch AD, **Schoon EJ**, Haidry R, Weusten BL, Bisschops R, Shaheen NJ, Wallace MB Marcon N, Heise-Ginsburg , Gotink AW, Wang KK, Leggett CL, Ortiz-Fernández-Sordo J, Ragunath K, DiPietro M, Pech O, Neuhaus H, Bergman JJ

Gastrointest Endosc. 2018 Oct;88(4):647-654

BACKGROUND AND AIMS:

Early neoplasia in Barrett's esophagus (BE) can be effectively and safely removed by endoscopic resection (ER) using multiband mucosectomy (MBM). This study aimed to document performance of a novel MBM device designed for improved visualization, easier passage of accessories, and better suction power compared with other marketed MBM devices.

METHODS:

This international, single-arm, prospective registry in 14 referral centers (Europe, 10; United States, 3; Canada, 1) included patients with early BE neoplasia scheduled for ER. The primary endpoint was successful ER defined as complete resection of the delineated area in 1 procedure. Secondary outcomes were adverse events and procedure time.

RESULTS:

A total of 332 lesions was included in 291 patients (248 men; mean age, 67 years [standard deviation, 9.6]). ER indication was high-grade dysplasia in 64%, early adenocarcinoma in 19%, lesion with low-grade dysplasia in 11%, and a lesion without definite histology in 6%. Successful ER was reached in 322 of 332 lesions (97%; 95% confidence interval [CI], 94.6%-98.4%). A perforation occurred in 3 of 332 procedures (.9%; 95% CI, .31%-2.62%), all were managed endoscopically, and patients were admitted with intravenous antibiotics during days 2, 3, and 9. Postprocedural bleeding requiring an intervention occurred in 5 of 332 resections (1.5%; 95% CI, .65%-3.48%). Dysphagia requiring dilatation occurred in 11 patients (3.8%; 95% CI, 2.1%-6.6%). Median procedure time was 16 minutes (interquartile range, 12.0-26.0).

CONCLUSIONS:

In expert hands, the novel MBM device proved to be effective for resection of early neoplastic lesions in BE, with successful ER in 97% of procedures. Severe adverse events were rare and were effectively managed endoscopically or conservatively.

Impactfactor 7.204

A single-step sizing and radiofrequency ablation catheter for circumferential ablation of Barrett's esophagus: Results of a pilot study

Belghazi K, Pouw RE, Sondermeijer C, Meijer SL, **Schoon EJ**, Koch AD, Weusten B, Bergman J

United European Gastroenterol J. 2018 Aug;6(7):990-999

Background:

The 360 Express balloon catheter (360 Express) has the ability to self-adjust to the esophageal lumen, ensuring optimal tissue contact.

Objective:

The objective of this article is to evaluate the efficacy and safety of the 360 Express for radiofrequency ablation (RFA) treatment of Barrett's esophagus (BE).

Methods:

BE patients with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or early cancer (EC) were included. Visible lesions were removed by endoscopic resection (ER) prior to RFA. RFA was performed with the 360 Express using the standard ablation regimen (12J/cm2-clean-12J/cm2). Primary outcome: BE regression percentage at three months. Secondary outcomes: procedure time, adverse events, complete eradication of dysplasia (CE-D) and intestinal metaplasia (CE-IM).

Results:

Thirty patients (median BE C4M6) were included. Eight patients underwent ER prior to RFA. Median BE regression: 90%. Median procedure time: 31 minutes. Adverse events (13%): laceration (n?=?1); atrial fibrillation (n?=?1); vomiting and dysphagia (n?=?1); dysregulated diabetes (n?=?1). After subsequent treatment CE-D and CE-IM was achieved in 97% and 87%, respectively. In 10% a stenosis developed during additional treatment requiring a median of one dilation.

Conclusion:

This study shows that circumferential RFA using the 360 Express may shorten procedure time, while maintaining efficacy compared to standard circumferential RFA

Impactfactor 3.477

A Systematic Review and Meta-Analysis on Outcomes and Complications of Percutaneous Endoscopic Versus Radiologic Gastrostomy for Enteral Feeding

Strijbos D, Keszthelyi D, Bogie RMM, **Gilissen LPL**, Lacko M, Hoeijmakers JGJ, van der Leij C, de Ridder R, de Haan MW, Masclee AAM

J Clin Gastroenterol. 2018 Oct;52(9):753-764

BACKGROUND:

The optimal technique for long-term enteral feeding has not yet been established. Both percutaneous endoscopic gastrostomy (PEG) and percutaneous radiologic gastrostomy (PRG) are widely used. Aim was to extensively review outcomes of PEG and PRG.

MATERIALS AND METHODS:

A systematic review using Medline, Embase, and Cochrane was performed, using standardized tools for assessing bias. Main outcomes were infectious and tube-related complications, procedure related and 30-day mortality. Pooled risk differences (RDs) with corresponding 95% confidence intervals (95% CIs) were calculated using random effects. Arcsine transformations were applied.

RESULTS:

In total, 344 studies were identified, of which 16 were included, reporting on 934 PEGs and 1093 PRGs. No differences were found for infectious complications [RD, 0.03 (-0.05 to 0.11)], procedure-related mortality [RD, 0.01 (-0.04 to 0.06)], or 30-day mortality [RD, 0.06 (-0.01 to 0.13)]. Tube-related complications were higher in PRG [RD, 0.16 (0.06-0.26)]. Subgroup analysis was performed for head and neck cancer (HNC) and motor neuron disease. In HNC, this revealed significantly lower tube-related complications and procedure-related mortality after PEG. In motor neuron disease, no differences were seen. The level of evidence appears sufficient considering the low degree of heterogeneity.

CONCLUSIONS:

No differences were found with regard to mortality or infectious complications. PEG showed lower risk of tube-related complications. Subgroup analysis revealed PEG to be favorable in HNC based on lower rates of procedure-related mortality and tube-related complications. Local experience and availability should be taken into account in the decision process.

Impactfactor 2.968

Blue-light imaging has an additional value to white-light endoscopy in visualization of early Barrett's neoplasia: an international multicenter cohort study

de Groof AJ, Swager AF, Pouw RE, Weusten BLAM, **Schoon EJ**, Bisschops R, Pech O, Meining A, Neuhaus H, **Curvers WL**, Bergman JJGHM.

Gastrointest Endosc. 2018 Nov 9. pii: S0016-5107(18)33259-0. [Epub ahead of print]

BACKGROUND AND AIMS:

Endoscopic features of early neoplasia in Barrett's esophagus (BE) are subtle. Blue-light imaging (BLI) may improve visualization of neoplastic lesions. The aim of this study was to evaluate BLI in visualization of Barrett's neoplasia.

METHODS:

Corresponding white-light endoscopy (WLE) and BLI images of 40 BE lesions were obtained prospectively and assessed by 6 international experts in 3 assessments. Each assessment consisted of overview and magnification images. Assessments were as follows: assessment 1, WLE only; assessment 2, BLI only; and assessment 3, corresponding WLE and BLI images. Outcome parameters were as follows: (1) appreciation of macroscopic appearance and surface relief (visual analog scale scores); (2) ability to delineate lesions (visual analog scale scores); (3) preferred technique for delineation (ordinal scores); and (4) quantitative agreement on delineations (AND/OR scores).

RESULTS:

Experts appreciated BLI significantly better than WLE for visualization of macroscopic appearance (median 8.0 vs 7.0, $P < .001$) and surface relief (8.0 vs 6.0, $P < .001$). For both overview and magnification images, experts appreciated BLI significantly better than WLE for ability to delineate lesions (8.0 vs 6.0, $P < .001$ and 8.0 vs 5.0, $P < .001$). There was no overall significant difference in AND/OR scores of WLE + BLI when compared with WLE, yet agreement increased significantly with WLE + BLI for cases with a low baseline AND/OR score on WLE, both in overview (mean difference, 0.15; $P = .015$) and magnification (mean difference, 0.10; $P = .01$).

CONCLUSIONS:

BLI has additional value for visualization of BE neoplasia. Experts appreciated BLI better than WLE for visualization and delineation of BE neoplasia. Quantitative agreement increased significantly when BLI was offered next to WLE for lesions that were hard to delineate with WLE alone.

Impactfactor 7.204

Cancer risk perception in relation to associated symptoms in Barrett's patients: A cross sectional study on quality of life

van der Ende-van Loon MC, Rosmolen WD, Houterman S, **Schoon EJ, Curvers WL**

United European Gastroenterol J. 2018 Nov;6(9):1316-1322

Background:

Barrett's oesophagus affects patients' quality of life and may be a psychological burden due to the threat of developing an oesophageal adenocarcinoma.

Objective:

Assessing the oesophageal adenocarcinoma risk perceived by non-dysplastic Barrett's oesophagus patients and its association with quality of life, illness perception and reflux symptoms.

Methods:

This cross-sectional questionnaire study included 158 Barrett's oesophagus non-dysplastic patients aged 18-75 years. Based on their annual and lifetime oesophageal adenocarcinoma risk estimations measured with the Magnifier Scale, patients were classified as overestimating or underestimating. Associations between the groups where assed on demographics, reflux symptoms and results of the Outcomes Study Short-Form-36 (SF-36) and the Brief Illness Perception Questionnaire (B-IPQ).

Results:

The annual oesophageal adenocarcinoma risk was overestimated by 41%. Overestimating patients had lower means on the SF-36 domains: bodily pain (annual p?=?0.007 and lifetime p?=?0.014), general health (annual p?=?0.011 and lifetime p?=?0.014), vitality (annual p?=?0.030), physical functioning (lifetime p?=?0.028), worse illness perception (total score p?=?0.001) and significantly more reflux symptoms.

Conclusions:

Overestimation of the oesophageal adenocarcinoma risk by Barrett's oesophagus patients was associated with decreased quality of life and worse illness perceptions, which is most likely caused by symptoms of dyspepsia and reflux. These symptoms should be adequately treated, and patients may be in need of extra support and specific information about their oesophageal adenocarcinoma risk.

Impactfactor *3.477*

Clinical Course of Nodular Regenerative Hyperplasia in Thiopurine Treated Inflammatory Bowel Disease Patients

Simsek M, Meijer B, Ramsoekh D, Bouma G, van der Wouden EJ, den Hartog B, de Vries AC, Hoentjen F, Dijkstra G, de Boer SY, Jansen JM, van der Meulen AE, Beukers R, Brink MA, Steinhauser T, Oldenburg B, **Gilissen LP**, Naber TH, Verhagen MA, de Boer NKH, Mulder CJJ Dutch Initiative on Crohn and Colitis (ICC)

Clin Gastroenterol Hepatol. 2018 Jun 1. pii: S1542-3565(18)30495-6. [Epub ahead of print]

Geen abstract beschikbaar

Impactfactor *7.683*

Comparison of MRI and colonoscopy in determining tumor height in rectal cancer

Jacobs L*, Meek DB, van Heukelom J, Bollen TL, Siersema PD, Smits AB, Tromp E, Los M, Weusten BL, van Lelyveld N

United European Gastroenterol J. 2018 Feb;6(1):131-137

Background and aim:

Endoscopy and magnetic resonance imaging (MRI) are used routinely in the diagnostic and preoperative work-up of rectal cancer. We aimed to compare colonoscopy and MRI in determining rectal tumor height.

Methods:

Between 2002 and 2012, all patients with rectal cancer with available MRIs and endoscopy reports were included. All MRIs were reassessed for tumor height by two abdominal radiologists. To obtain insight in techniques used for endoscopic determination of tumor height, a survey among regional endoscopists was conducted.

Results:

A total of 211 patients with rectal cancer were included. Tumor height was significantly lower when assessed by MRI than by endoscopy with a mean difference of 2.5?cm (95% CI: 2.1-2.8). Although the agreement between tumor height as measured by MRI and endoscopy was good (intraclass correlation coefficient (ICC) 0.7 (95% CI: 0.7-0.8)), the 95% limits of agreement varied from -3.0?cm to 8.0?cm. In 45 patients (21.3%), tumors were regarded as low by MRI and middle-high by endoscopy. MRI inter- and intraobserver agreements were excellent with an ICC of 0.8 (95% CI: 0.7-0.9) and 0.9 (95% CI: 0.9-1.0), respectively. The survey showed no consensus among endoscopists as to how to technically measure tumor height.

Conclusion:

This study showed large variability in rectal tumor height as measured by colonoscopy and MRI. Since MRI measurements showed excellent inter- and intraobserver agreement, we suggest using tumor height measurement by MRI for diagnostic purposes and treatment allocation.

Impactfactor *3.477*

*Ten tijde van publicatie verbonden aan: Department of Gastroenterology and Hepatology, St Antonius Hospital Nieuwegein, Nieuwegein

Detection of residual disease after neoadjuvant chemoradiotherapy for oesophageal cancer (preSANO): a prospective multicentre, diagnostic cohort study

Noordman BJ, Spaander MC, Valkema R, Wijnhoven BP, van Berge Henegouwen MI, Shapiro J, Biermann K, van der Gaast A, van Hillegersberg R, Hulshof MC, Krishnadath KK, Lagarde SM, Nieuwenhuijzen GA, Oostenbrug LE, Siersema PD, **Schoon EJ**, Sosef MN, Steyerberg EW, van Lanschot JJ; SANO study group.: **Curvers WL**, Creemers GJ, Roef MJ, van der Sangen MJ

Lancet Oncol. 2018 Jul;19(7):965-974

BACKGROUND:

After neoadjuvant chemoradiotherapy for oesophageal cancer, roughly half of the patients with squamous cell carcinoma and a quarter of those with adenocarcinoma have a pathological complete response of the primary tumour before surgery. Thus, the necessity of standard oesophagectomy after neoadjuvant chemoradiotherapy should be reconsidered for patients who respond sufficiently to neoadjuvant treatment. In this study, we aimed to establish the accuracy of detection of residual disease after neoadjuvant chemoradiotherapy with different diagnostic approaches, and the optimal combination of diagnostic techniques for clinical response evaluations.

METHODS:

The preSANO trial was a prospective, multicentre, diagnostic cohort study at six centres in the Netherlands. Eligible patients were aged 18 years or older, had histologically proven, resectable, squamous cell carcinoma or adenocarcinoma of the oesophagus or oesophagogastric junction, and were eligible for potential curative therapy with neoadjuvant chemoradiotherapy (five weekly cycles of carboplatin [area under the curve 2 mg/mL per min] plus paclitaxel [50 mg/m2 of body-surface area] combined with 41·4 Gy radiotherapy in 23 fractions) followed by oesophagectomy. 4-6 weeks after completion of neoadjuvant chemoradiotherapy, patients had oesophagogastroduodenoscopy with biopsies and endoscopic ultrasonography with measurement of maximum tumour thickness. Patients with histologically proven locoregional residual disease or no-pass during endoscopy and without distant metastases underwent immediate surgical resection. In the remaining patients a second clinical response evaluation was done (PET-CT, oesophagogastroduodenoscopy with biopsies, endoscopic ultrasonography with measurement of maximum tumour thickness, and fine-needle aspiration of suspicious lymph nodes), followed by surgery 12-14 weeks after completion of neoadjuvant chemoradiotherapy. The primary endpoint was the correlation between clinical response during clinical response evaluations and the final pathological response in resection specimens, as shown by the proportion of tumour regression grade (TRG) 3 or 4 (>10% residual carcinoma in the resection specimen) residual tumours that was missed during clinical response evaluations. This study was registered with the Netherlands Trial Register (NTR4834), and has been completed.

FINDINGS:

Between July 22, 2013, and Dec 28, 2016, 219 patients were included, 207 of whom were included in the analyses. Eight of 26 TRG3 or TRG4 tumours (31% [95% CI 17-50]) were missed by endoscopy with regular biopsies and fine-needle aspiration. Four of 41 TRG3 or TRG4 tumours (10% [95% CI 4-23]) were missed with bite-on-bite biopsies and fine-needle aspiration. Endoscopic ultrasonography with maximum tumour thickness measurement missed TRG3 or TRG4 residual tumours in 11 of 39 patients (28% [95% CI 17-44]). PET-CT missed six of 41 TRG3 or TRG4 tumours (15% [95% CI 7-28]). PET-CT detected interval distant histologically proven metastases in 18 (9%) of 190 patients (one squamous cell carcinoma, 17 adenocarcinomas).

INTERPRETATION:

After neoadjuvant chemoradiotherapy for oesophageal cancer, clinical response evaluation with endoscopic ultrasonography, bite-on-bite biopsies, and fine-needle aspiration of suspicious lymph nodes was adequate for detection of locoregional residual disease, with PET-CT for detection of interval metastases. Active surveillance with this combination of diagnostic modalities is now being assessed in a phase 3 randomised controlled trial (SANO trial; Netherlands Trial Register NTR6803).

Impactfactor 36.418

Double-Balloon Endoscopy after Incomplete Colonoscopy and Its Comparison with Computed Tomography Colonography

Hermans C, Zee DV, **Gilissen L**

Clin Endosc. 2018 Jan 51(1):66-71. Epub 2018 Jan 10

BACKGROUND/AIMS:

Because of the national screening program for colorectal carcinoma in The Netherlands, the number of colonoscopies has increased. In case of incomplete colonoscopy, computed tomography colonography (CTC) and double-balloon colonoscopy (DBc) are alternative options. This study evaluated cecal intubation rate and pathology detection rate in the previously unexplored part of the colon, complication rate of DBc, and CTC results after incomplete colonoscopy.

METHODS:
Retrospective observational study in a tertiary referral hospital regarding DBc and CTC reports from cases with incomplete colonoscopy.
RESULTS:
Sixty-three DBcs were performed after incomplete colonoscopy. Cecal intubation rate was 95%. Detection rate was 58% (5% carcinoma and 3% high-grade dysplastic adenoma). CTC preceded 54% of DBcs and 62% of CTC findings were confirmed. In 16%, a biopsy was taken, and in 60%, an intervention (mostly polypectomy) was performed. One major complication (1.5%) occurred, i.e., arterial bleeding due to polypectomy necessitating right hemicolectomy. CTC (n=213) showed a possible lesion in 35%, and could be confirmed by follow-up endoscopy or surgery in 65%.
CONCLUSIONS:
DBc is effective and safe for completion of colon inspection in incomplete colonoscopy. In patients with a high likelihood of pathology, DBc is preferred over CTC.

Impactfactor --

Endoscopic Botulinum Toxin for Gastroparesis: Results of a Retrospective Series

Fabiënne G. M. Smeets, **Denise Strijbos**, Daniel Keszthelyi, Chantal V. Hoge, Joanna W. Kruimel, José M. Conchillo and Ad A.M. Masclee

Gastrointest. Disord.2018 14 December 2018

Beneficial effects of pyloric botulinum toxin injection have been described in a subgroup of gastroparesis patients. Our aim is to evaluate whether clinical, manometric and/or scintigraphic parameters are able to predict treatment outcome. Forty patients (67% female, age 49 (36–56) years) with decompensated gastroparesis treated with botulinum toxin were included in this retrospective analysis. Objective parameters were high-resolution antroduodenal manometry, gastric emptying rate (scintigraphy), and weight change. Subjective treatment outcome was assessed with a Global Physician Assessment Scale. Binary logistic regression analysis was performed to identify predictors for treatment outcome. Fourteen patients (35%) were symptom-responders, and 65% of patients were short-term weight-responders. For both subjective and objective treatment outcome, no differences were found in manometric and scintigraphic variables between responders and non-responders. Neither clinical nor manometric or scintigraphic variables could predict subjective and objective treatment outcome. In conclusion, symptom improvement is achieved in a subgroup of gastroparesis patients treated with endoscopic pyloric botulinum toxin. Although the majority of patients were able to maintain their baseline weight at short-term follow-up, a substantial group of patients needed nutritional interventions on long-term follow-up. However, none of the demographic, clinical, scintigraphic, or antroduodenal manometry variables were able to predict either subjective or objective treatment outcome

Impactfactor --

Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial

van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, Bollen TL, Bosscha K, Bouwense SA, Bruno MJ, Cappendijk VC, Consten EC, Dejong CH, van Eijck CH, Erkelens WG, van Goor H, van Grevenstein WMU, Haveman JW, Hofker SH, Jansen JM, Laméris JS, van Lienden KP, Meijssen MA, Mulder CJ, Nieuwenhuijs VB, Poley JW, Quispel R, de Ridder RJ, Römkens TE, Scheepers JJ, Schepers NJ, Schwartz MP, Seerden T, Spanier BWM, Straathof JWA, Strijker M, Timmer R, Venneman NG, Vleggaar FP, Voermans RP, Witteman BJ, Gooszen HG, Dijkgraaf MG, Fockens P; Dutch Pancreatitis Study Group.: **Schoon EJ**

Lancet. 2018 Jan 6 391(10115):51-58. Epub 2017 Nov 3

BACKGROUND:
Infected necrotising pancreatitis is a potentially lethal disease and an indication for invasive intervention. The surgical step-up approach is the standard treatment. A promising alternative is the endoscopic step-up approach. We compared both approaches to see whether the endoscopic step-up approach was superior to the surgical step-up approach in terms of clinical and economic outcomes.
METHODS:
In this multicentre, randomised, superiority trial, we recruited adult patients with infected necrotising pancreatitis and an indication for invasive intervention from 19 hospitals in the Netherlands. Patients were randomly assigned to either the endoscopic or the surgical step-up approach. The endoscopic approach consisted of endoscopic ultrasound-guided transluminal drainage followed, if necessary, by endoscopic necrosectomy. The surgical approach consisted of percutaneous catheter drainage followed, if necessary, by video-assisted retroperitoneal debridement. The primary endpoint was a composite of major complications or death during 6-month follow-up. Analyses were by intention to treat. This trial is registered with the ISRCTN registry, number ISRCTN09186711.
FINDINGS:
Between Sept 20, 2011, and Jan 29, 2015, we screened 418 patients with pancreatic or extrapancreatic necrosis, of which 98 patients were enrolled and randomly assigned to the endoscopic step-up approach (n=51) or the surgical step-up approach (n=47). The primary endpoint occurred in 22 (43%) of 51 patients in the endoscopy group and in 21 (45%) of 47 patients in the surgery group (risk ratio [RR] 0·97, 95% CI 0·62-1·51; p=0·88). Mortality did not differ

between groups (nine [18%] patients in the endoscopy group vs six [13%] patients in the surgery group; RR 1·38, 95% CI 0·53-3·59, p=0·50), nor did any of the major complications included in the primary endpoint.
INTERPRETATION:
In patients with infected necrotising pancreatitis, the endoscopic step-up approach was not superior to the surgical step-up approach in reducing major complications or death. The rate of pancreatic fistulas and length of hospital stay were lower in the endoscopy group. The outcome of this trial will probably result in a shift to the endoscopic step-up approach as treatment preference.

Impactfactor 53.254

Endoscopic ultrasound measurements for detection of residual disease after neoadjuvant chemoradiotherapy for esophageal cancer

van der Bogt RD, Noordman BJ, Krishnadath KK, Roumans CAM, **Schoon EJ**, Oostenbrug LE, Siersema PD, Vleggaar FP, van Lanschot JJB, Spaander MCW

Endoscopy. 2018 Nov 29. [Epub ahead of print]

BACKGROUND:
Endoscopic ultrasound (EUS) measurements of residual thickness and residual area have been suggested to correlate with histopathological residual tumor after neoadjuvant chemoradiotherapy (nCRT) for esophageal cancer. This study assessed the predictive value of EUS-based measurements using tumor thickness and tumor area before nCRT, and residual thickness and residual area 6 and 12 weeks after completion of nCRT for detection of residual disease.
METHODS:
This was a substudy of the diagnostic multicenter preSANO trial. The primary end point of the current study was the percentage of tumor regression grade (TRG) 3?-?4 (>?10?% vital tumor cells) residual disease that was detected using EUS-based measurements. Associations of absolute measurements of residual thickness/area and proportional change compared with baseline were evaluated. In the case of a statistically significant association, optimal cut-offs to distinguish TRG3?-?4 residual disease from TRG1 (no vital tumor cells) were determined using Youden's J index.
RESULTS:
138 patients were included. Residual thickness and residual area were statistically significantly associated with TRG3?-?4 residual disease 12 weeks after completion of nCRT (odds ratio 1.36, P?<?0.01 and 1.64, P?=?0.02, respectively). The cut-off for residual thickness was 4.5?mm, which correctly detected 87?% of TRG3?-?4 residual disease and 52?% of TRG1. The cut-off for residual area was 0.92?cm2, which detected 89?% of TRG3?-?4 residual disease and 40?% of TRG1.
CONCLUSIONS:
EUS measurements of residual thickness and residual area adequately detected TRG3?-?4 residual disease with a sensitivity of almost 90?% 12 weeks after completion of nCRT. Hence, residual thickness and residual area may aid in the restaging of esophageal cancer after nCRT.

Impactfactor 6.629

Influence of Helicobacter pylori infection on gastrointestinal symptoms and complications in bariatric surgery patients: a review and meta-analysis

Smelt HJM, Smulders JF, **Gilissen LPL**, Said M, Ugale S, Pouwels S

Surg Obes Relat Dis. 2018 Oct;14(10):1645-1657

BACKGROUND:
Numerous papers have discussed the importance of preoperative detection and eradication of Helicobacter pylori (HP) in bariatric patients.
OBJECTIVES:
This systematic review specifically focuses on the influence of HP infection on clinical symptoms, complications, and abnormal endoscopic findings in postbariatric patients.
METHODS:
A systematic search on the influence of HP infection on postoperative complications in bariatric surgery was conducted. The methodologic quality of the included studies was rated using the Newcastle-Ottawa rating scale. The agreement between the reviewers was assessed with Cohen's kappa. The included studies were assessed into 2 groups, studies with and without eradication therapy preoperatively.
RESULTS:
A total of 21 studies were included with a methodologic quality ranging from poor to good. The agreement between the reviewers, assessed with the Cohen's kappa, was .70. Overall, tendency in the included studies was that HP infection was associated with an increased risk for developing marginal ulcers and postoperative complications. A meta-analysis on the incidence of marginal ulcers and overall postoperative complications was conducted and showed, respectively, an odds ratio of .508 (.031-8.346) and 2.863 (.262-31.268).
CONCLUSIONS:
HP is frequently found in patients before and after bariatric and metabolic surgery. We assessed whether, according

to the current literature, HP increases the risk for developing postoperative complications after surgery. This meta-analysis shows that a methodologically good study should be performed to clarify the role of HP in bariatric patients and the question of whether HP should be eradicated before surgery.

Impactfactor 3.900

Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial

Noordman BJ, Wijnhoven BPL, Lagarde SM, Boonstra JJ, Coene PPLO, Dekker JWT, Doukas M, van der Gaast A, Heisterkamp J, Kouwenhoven EA, Nieuwenhuijzen GAP, Pierie JEN, Rosman C, van Sandick JW, van der Sangen MJC, Sosef MN, Spaander MCW, Valkema R, van der Zaag ES, Steyerberg EW, van Lanschot JJB SANO-study group.: Creemers GJ, **Schoon EJ**, Wyndaele D

BMC Cancer. 2018 Feb 6 18(1):142

BACKGROUND:
Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard treatment for locally advanced oesophageal cancer. With this treatment, 29% of patients have a pathologically complete response in the resection specimen. This provides the rationale for investigating an active surveillance approach. The aim of this study is to assess the (cost-)effectiveness of active surveillance vs. standard oesophagectomy after nCRT for oesophageal cancer.
METHODS:
This is a phase-III multi-centre, stepped-wedge cluster randomised controlled trial. A total of 300 patients with clinically complete response (cCR, i.e. no local or disseminated disease proven by histology) after nCRT will be randomised to show non-inferiority of active surveillance to standard oesophagectomy (non-inferiority margin 15%, intra-correlation coefficient 0.02, power 80%, 2-sided a 0.05, 12% drop-out). Patients will undergo a first clinical response evaluation (CRE-I) 4-6 weeks after nCRT, consisting of endoscopy with bite-on-bite biopsies of the primary tumour site and other suspected lesions. Clinically complete responders will undergo a second CRE (CRE-II), 6-8 weeks after CRE-I. CRE-II will include 18F-FDG-PET-CT, followed by endoscopy with bite-on-bite biopsies and ultra-endosonography plus fine needle aspiration of suspected lymph nodes and/or PET- positive lesions. Patients with cCR at CRE-II will be assigned to oesophagectomy (first phase) or active surveillance (second phase of the study). The duration of the first phase is determined randomly over the 12 centres, i.e., stepped-wedge cluster design. Patients in the active surveillance arm will undergo diagnostic evaluations similar to CRE-II at 6/9/12/16/20/24/30/36/48 and 60 months after nCRT. In this arm, oesophagectomy will be offered only to patients in whom locoregional regrowth is highly suspected or proven, without distant dissemination. The main study parameter is overall survival; secondary endpoints include percentage of patients who do not undergo surgery, quality of life, clinical irresectability (cT4b) rate, radical resection rate, postoperative complications, progression-free survival, distant dissemination rate, and cost-effectiveness. We hypothesise that active surveillance leads to non-inferior survival, improved quality of life and a reduction in costs, compared to standard oesophagectomy.
DISCUSSION:
If active surveillance and surgery as needed after nCRT leads to non-inferior survival compared to standard oesophagectomy, this organ-sparing approach can be implemented as a standard of care.

Impactfactor 3.288

Novel Developments in Endoscopic Mucosal Imaging

van der Sommen F, **Curvers WL**, Nagengast WB

Gastroenterology. 2018 May 154(7):1876-1886. Epub 2018 Feb 17

Endoscopic techniques such as high-definition and optical-chromoendoscopy have had enormous impact on endoscopy practice. Since these techniques allow assessment of most subtle morphological mucosal abnormalities, further improvements in endoscopic practice lay in increasing the detection efficacy of endoscopists. Several new developments could assist in this. First, web based training tools could improve the skills of the endoscopist for enhancing the detection and classification of lesions. Secondly, incorporation of computer aided detection will be the next step to raise endoscopic quality of the captured data. These systems will aid the endoscopist in interpreting the increasing amount of visual information in endoscopic images providing real-time objective second reading. In addition, developments in the field of molecular imaging open opportunities to add functional imaging data, visualizing biological parameters, of the gastrointestinal tract to white-light morphology imaging. For the successful implementation of abovementioned techniques, a true multi-disciplinary approach is of vital importance.

Impactfactor 20.773

Percutaneous endoscopic colostomy for adults with chronic constipation: Retrospective case series of 12 patients

Strijbos D, Keszthelyi D, Masclee AAM, **Gilissen LPL**

Neurogastroenterol Motil. 2018 May 30(5):e13270. Epub 2017 Dec 18

BACKGROUND:
Percutaneous endoscopic colostomy (PEC) is a technique derived from percutaneous endoscopic gastrostomy.

When conservative treatment of chronic obstipation fails, colon irrigation via PEC seems less invasive than surgical interventions. However, previous studies have noted high complication rates of PEC, mostly related to infections. Our aim was to report our experiences with PEC in patients with chronic refractory constipation.
METHODS:
Retrospective analysis of all patients who underwent PEC for refractory constipation in our secondary referral hospital between 2009 and 2016.
KEY RESULTS:
Twelve patients received a PEC for chronic, refractory constipation. Short-term efficacy for relief of constipation symptoms was good in 8 patients and moderate in 4 patients. Two patients had the PEC removed because of spontaneous improvement of constipation. Three patients, who initially noticed a positive effect, preferred an ileostomy over PEC after 1-5 years. One PEC was removed because of an abscess. Long-term efficacy is 50%: 6 patients still use their PEC after 3.3 years of follow-up. No mortality occurred.
CONCLUSIONS AND INTERFERENCES:
PEC offers a technically easily feasible and safe treatment option for patients with chronic constipation not responding to conventional therapy. Long-term efficacy of PEC in our patients is 50%.

Impactfactor *3.842*

Performance measures for endoscopy services: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative

Valori R, Cortas G, de Lange T, Balfaqih OS, de Pater M, Eisendrath P, Falt P, Koruk I, Ono A, Rustemovic N, **Schoon E**, Veitch A, Senore C, Bellisario C, Minozzi S, Bennett C, Bretthauer M, Dinis-Ribeiro M, Domagk D, Hassan C, Kaminski MF, Rees CJ, Spada C, Bisschops R, Rutter M

Endoscopy. 2018 Dec;50(12):1186-1204

The European Society of Gastrointestinal Endoscopy (ESGE) and United European Gastroenterology present a list of key performance measures for endoscopy services. We recommend that these performance measures be adopted by all endoscopy services across Europe. The measures include those related to the leadership, organization, and delivery of the service, as well as those associated with the patient journey. Each measure includes a recommendation for a minimum and target standard for endoscopy services to achieve. We recommend that all stakeholders in endoscopy take note of these ESGE endoscopy services performance measures to accelerate their adoption and implementation. Stakeholders include patients and their advocacy groups; service leaders; staff, including endoscopists; professional societies; payers; and regulators.

Impactfactor *6.629*

Predictive features for early cancer detection in Barrett's esophagus using Volumetric Laser Endomicroscopy

van der Sommen F, Klomp SR, Swager AF, Zinger S, **Curvers WL**, Bergman JJGHM, **Schoon EJ**, de With PHN

Comput Med Imaging Graph. 2018 Jul 67:9-20. Epub 2018 Apr 13

The incidence of Barrett cancer is increasing rapidly and current screening protocols often miss the disease at an early, treatable stage. Volumetric Laser Endomicroscopy (VLE) is a promising new tool for finding this type of cancer early, capturing a full circumferential scan of Barrett's Esophagus (BE), up to 3-mm depth. However, the interpretation of these VLE scans can be complicated, due to the large amount of cross-sectional images and the subtle grayscale variations. Therefore, algorithms for automated analysis of VLE data can offer a valuable contribution to its overall interpretation. In this study, we broadly investigate the potential of Computer-Aided Detection (CADe) for the identification of early Barrett's cancer using VLE. We employ a histopathologically validated set of ex-vivo VLE images for evaluating and comparing a considerable set of widely-used image features and machine learning algorithms. In addition, we show that incorporating clinical knowledge in feature design, leads to a superior classification performance and additional benefits, such as low complexity and fast computation time. Furthermore, we identify an optimal tissue depth for classification of 0.5-1.0?mm, and propose an extension to the evaluated features that exploits this phenomenon, improving their predictive properties for cancer detection in VLE data. Finally, we compare the performance of the CADe methods with the classification accuracy of two VLE experts. With a maximum Area Under the Curve (AUC) in the range of 0.90-0.93 for the evaluated features and machine learning methods versus an AUC of 0.81 for the medical experts, our experiments show that computer-aided methods can achieve a considerably better performance than trained human observers in the analysis of VLE data.

Impactfactor *--*

Randomised controlled trial of transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND Study)

Barendse RM, Musters GD, de Graaf EJR, van den Broek FJC, Consten ECJ, Doornebosch PG, Hardwick JC, de Hingh IHJT, Hoff C, Jansen JM, van Milligen de Wit AWM, van der Schelling GP, **Schoon EJ**, Schwartz MP, Weusten BLAM, Dijkgraaf MG, Fockens P, Bemelman WA, Dekker E; TREND Study group

Gut. 2018 May;67(5):837-846. Epub 2017 Jun 28

OBJECTIVE:
Non-randomised studies suggest that endoscopic mucosal resection (EMR) is equally effective in removing large rectal adenomas as transanal endoscopic microsurgery (TEM), but EMR might be more cost-effective and safer. This trial compares the clinical outcome and cost-effectiveness of TEM and EMR for large rectal adenomas.
DESIGN:
Patients with rectal adenomas =3?cm, without malignant features, were randomised (1:1) to EMR or TEM, allowing endoscopic removal of residual adenoma at 3 months. Unexpected malignancies were excluded postrandomisation. Primary outcomes were recurrence within 24 months (aiming to demonstrate non-inferiority of EMR, upper limit 10%) and the number of recurrence-free days alive and out of hospital.
RESULTS:
Two hundred and four patients were treated in 18 university and community hospitals. Twenty-seven (13%) had unexpected cancer and were excluded from further analysis. Overall recurrence rates were 15% after EMR and 11% after TEM; statistical non-inferiority was not reached. The numbers of recurrence-free days alive and out of hospital were similar (EMR 609±209, TEM 652±188, p=0.16). Complications occurred in 18% (EMR) versus 26% (TEM) (p=0.23), with major complications occurring in 1% (EMR) versus 8% (TEM) (p=0.064). Quality-adjusted life years were equal in both groups. EMR was approximately €3000 cheaper and therefore more cost-effective.
CONCLUSION:
Under the statistical assumptions of this study, non-inferiority of EMR could not be demonstrated. However, EMR may have potential as the primary method of choice due to a tendency of lower complication rates and a better cost-effectiveness ratio. The high rate of unexpected cancers should be dealt with in further studies.

Impactfactor *17.016*

Salvage endoscopic resection in patients with esophageal adenocarcinoma after chemoradiotherapy

Noordzij IC, Curvers WL, Huysentruyt CJ, Nieuwenhuijzen GA, Creemers GJ, van der Sangen MJ, **Schoon EJ**

Endosc Int Open. 2018 Sep;6(9):E1126-E1129

Background and study aims For early esophageal adenocarcinoma, endoscopic resection is an accepted curative treatment with an excellent long-term prognosis. Case series from Japan have reported endoscopic resection of residual esophageal squamous cell carcinoma after chemoradiotherapy. This is the first report describing endoscopic resection of residual esophageal adenocarcinoma after chemoradiotherapy. Two patients with advanced esophageal adenocarcinoma had been treated with chemoradiotherapy because comorbidity precluded esophageal resection. When residual tumor was observed endoscopically, complete remission was achieved by salvage endoscopic therapy alone or in combination with argon plasma coagulation (APC). Both patients achieved long-term sustained remission and died of non-tumor-related causes.

Impactfactor --

Simplified versus standard regimen for focal radiofrequency ablation of dysplastic Barrett's oesophagus: a multicentre randomised controlled trial

Pouw RE, Künzli HT, Bisschops R, Sondermeijer CM, Koch AD, Didden P, Gotink AW, **Schoon EJ, Curvers WL**, Bergman JJ, Weusten BL

Lancet Gastroenterol Hepatol. 2018 Aug;3(8):566-574

BACKGROUND:
For focal radiofrequency ablation of Barrett's oesophagus, a simplified regimen (3?×?15 J/cm2, without cleaning) has proven to be as effective as the standard regimen (2?×?15 J/cm2, followed by cleaning, followed by 2?×?15 J/cm2). However, this simplified regimen seemed to be associated with a higher stenosis rate. Therefore, we lowered the radiofrequency energy and hypothesised that this new simplified regimen would be as effective and safe as the standard regimen.
METHODS:
This randomised non-inferiority trial included patients with dysplastic Barrett's oesophagus or residual Barrett's oesophagus after endoscopic resection or circumferential radiofrequency ablation, in five European tertiary referral centres. Patients were randomly assigned (1:1) to the new simplified regimen (3?×?12 J/cm2, without cleaning) or the standard regimen, with variable block sizes of four, six, and eight patients, stratified by participating hospital. Focal radiofrequency ablation was done every 3 months, up to a maximum of three treatments, until all Barrett's oesophagus was eradicated. The primary outcome was complete endoscopic and histological regression of dysplasia and intestinal metaplasia after two focal radiofrequency ablation treatments, assessed in the intention-to-treat population. Non-inferiority was assessed on the basis of the difference between groups in the median percentage of Barrett's oesophagus surface regression, with a non-inferiority margin of -15%. This study is registered with www.trialregister.nl, number NTR4994, and is completed.
FINDINGS:
Between March 25, 2015, and July 25, 2016, 84 patients were randomly assigned to treatment: 44 to receive the simplified regimen and 40 to receive the standard regimen. One patient assigned to the simplified regimen and four assigned to the standard regimen were excluded because they weree found not to be eligible; therefore the final intention-to-treat population consisted of 43 patients in the simplified ablation group and 36 in the standard

ablation group. Complete endoscopic and histological regression of dysplasia and intestinal metaplasia after two focal radiofrequency ablation treatments was achieved in 32 (74%, 95% CI 59-87) patients treated with the simplified protocol, versus 30 (83%, 95% CI 67-94) patients treated with the standard protocol (p=0·34). Median Barrett's oesophagus surface regression after two focal radiofrequency ablation sessions was 98% (IQR 95-100) in the simplified regimen group and 100% (97-100) in the standard regimen group. The difference between medians was 2% (95% CI -0·562 to 3·162); thus the simplified regimen was deemed non-inferior to the standard regimen. Stenoses requiring dilatation were observed in four (9%) of 43 patients in the simplified regimen group and four (11%) of 36 in the standard regimen group. Post-procedural bleeding requiring repeat endoscopy occurred in one (2%) patient in the simplified ablation group and three (8%) patients in the standard ablation group. One patient (2%) in the simplified treatment group died 36 days after the second radiofrequency ablation procedure, due to an unknown cause.

INTERPRETATION:

Based on the results of this study, we conclude that the simplified regimen is the preferred regimen for focal radiofrequency ablation of Barrett's oesophagus.

Impactfactor --

The Amsterdam ReBus progressor cohort: identification of 165 Barrett's surveillance patients who progressed to early neoplasia and 723 nonprogressor patients

Duits LC, Klaver E, Bureo Gonzalez A, Boerwinkel DF, Ten Kate FJW, Offerhaus GJA, Meijer SL, Visser M, Seldenrijk CA, Krishnadath KK, **Schoon EJ**, Weusten BLAM, Mallant-Hent RC, Pouw RE, Bergman JJGHM

Dis Esophagus. 2018 Jun 4. [Epub ahead of print]

Patient selection is suboptimal in most studies focused on identifying biological markers for neoplastic progression in Barrett's esophagus (BE). This study aims to describe a stringently selected community-based case-control cohort of non-dysplastic BE (NDBE) patients who progressed to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) and BE patients who never progressed to be used for future biomarker studies. We identified all patients referred for endoscopic work-up of BE neoplasia at three tertiary referral centers for treatment of BE neoplasia between 2000 and 2013. We performed a detailed registration of any endoscopic surveillance history before neoplastic progression. Controls were selected from a retrospective BE surveillance registration in 10 community hospitals. A total of 887 patients were referred for endoscopic work-up of BE neoplasia. Based on predefined selection criteria, we identified 165 progressor patients (82% men; mean age 55 years ± 10.4) with a baseline endoscopy demonstrating NDBE > 2 years before neoplastic progression. Using the same predefined selection criteria, 723 nonprogressor patients (67% men; mean age 57 years ± 11.3) with >2 years of endoscopic surveillance were identified. Median length of the BE segment was 5 cm (IQR 4-7) in progressors and 4 cm (IQR 2-6) in controls. Median duration of surveillance was 89 months (IQR 54-139) in progressors and 76 months (IQR 47-116) in nonprogressors. Paraffin embedded biopsies are available for biomarker research in all patients. Ethical approval was obtained and material transfer agreements were signed with all 58 contributing pathology labs. This is the largest community-based case-control cohort of BE patients with and without progression to early neoplasia. The stringent selection criteria and the availability of paraffin embedded biopsy specimens make this a unique cohort for biomarker studies.

Impactfactor 2.702

The occurrence and characteristics of endoscopically unexpected malignant degeneration in large rectal adenomas

Bronzwaer MES, Musters GD, Barendse RM, Koens L, de Graaf EJR, Doornebosch PG, Schwartz MP, Consten ECJ, **Schoon EJ**, de Hingh IHJT, Tanis PJ, Dekker E, Fockens P TREND study group

Gastrointest Endosc. 2018 Mar 87(3):862-871.e1. Epub 2017 Oct 10

BACKGROUND AND AIMS: Large non-pedunculated rectal polyps are most commonly resected by endoscopic mucosal resection (EMR) or transanal endoscopic microsurgery (TEM). Despite pre-procedural diagnostics, unexpected rectal cancer is incidentally encountered within the resected specimen. This study aimed to compare the diagnostic assessment and procedural characteristics of lesions with and without unexpected submucosal invasion.

METHODS: A post-hoc analysis of a multicenter randomized trial (TREND study) was performed in which patients with a non-pedunculated rectal polyp of =3 cm without endoscopic suspicion of invasive growth were randomized between EMR and TEM.

RESULTS: Unexpected rectal cancer was detected in 13% (27/203) of patients; 15 after EMR and 12 after TEM. Most consisted of low-risk T1 cancers (78%, n = 18). There were no differences in the diagnostic assessment between lesions with and without unexpected submucosal invasion. Diagnostic biopsies revealed similar rates of high-grade dysplasia (28% [7/25] vs 18% [26/144]). When compared with EMR of adenomas, EMR procedures of unexpected cancers had a lower success rate of submucosal lifting (60% vs 93%, P < .001), were more often assessed as endoscopically incomplete (33% vs 10%, P = .01), and were more frequently terminated prematurely (60% vs 8%, P = .001).

CONCLUSIONS: Diagnostic assessment of large non-pedunculated rectal polyps revealed similar characteristics between unexpected cancers and adenomas. Unexpected cancers during EMR were non-lifting in 40%, endoscopically assessed as incomplete in 33%, and terminated prematurely in 60%. In treatment-naive patients, these factors should raise suspicion of malignancy and need discussion in a multidisciplinary team meeting for decision on further treatment strategies.

Impactfactor 7.204

Tolerability, Safety, and Outcomes of Neoadjuvant Chemoradiotherapy With Capecitabine for Patients Aged = 70 Years With Locally Advanced Rectal Cancer

Jacobs L*, van der Vlies E, Ten Bokkel Huinink D, Bloemendal H, Intven M, Smits AB, Weusten BLAM, Siersema PD, van Lelyveld N, Los M

Clin Colorectal Cancer. 2018 Sep;17(3):179-186. Epub 2018 Mar 8

INTRODUCTION:

In studies of colorectal cancer, the elderly have been frequently underrepresented because comorbid conditions and functional status often lead to study exclusion. For elderly patients with an indication for neoadjuvant chemoradiotherapy (nCRT), physicians usually decide using clinical factors whether nCRT should be offered. The aim of the present retrospective study was to assess the tolerability of nCRT with capecitabine and the surgical outcomes in patients aged = 70 years with locally advanced rectal cancer.

PATIENTS AND METHODS:

Data from 1372 rectal cancer patients diagnosed from 2002 to 2012 at 4 Dutch hospitals were used. Patients aged = 70 years were included if they had received nCRT, and their data were analyzed for treatment deviations, postoperative complications, mortality, disease-free survival (DFS), and overall survival (OS). The data were stratified into 3 age groups (ie, 70-74, 75-79, and = 80 years).

RESULTS:

We identified 447 patients aged = 70 years. Of these patients, 42 had received nCRT, and 37 (88%) had completed nCRT. Radiation dermatitis, fatigue, and diarrhea were reported in 62%, 57%, and 43% of the 42 patients, respectively. Of the 42 patients, 40 (95%) underwent surgery, 1 patient refused resection, and 1 patient died during nCRT of severe mucositis due to dihydropyrimidine dehydrogenase deficiency. The postoperative complication rate was 30%, and the 30-day mortality rate was 0%. A pathologic complete response was found in 7.5%. The 2- and 5-year DFS and OS rates were 58.5% and 40.7% and 81.0% and 58.2%, respectively.

CONCLUSION:

The results of the present multicenter study have shown that if selected on clinical factors, nCRT with capecitabine is safe and well tolerated in elderly patients. No negative effect on surgical outcome was measured, and the beneficial effect (pathologic complete response, DFS, and OS) seemed comparable to that for younger age groups. We believe that elderly patients should not be excluded from nCRT on the basis of age only.

Impactfactor 3.861

**Ten tijde van publicatie verbonden aan: Department of Gastroenterology and Hepatology, St Antonius Hospital Nieuwegein, Nieuwegein*

Mond en Kaakchirurgie

The effect of resorbable membranes on one-stage ridge augmentation in anterior single-tooth replacement: A randomized controlled clinical trial

Jonker BP, Wolvius EB, van der Tas JT, **Pijpe J**

Clin Oral Implants Res. 2018 Feb 29(2):235-247. Epub 2017 Dec 19

AIM:

To evaluate the effect of resorbable membranes on one-stage ridge augmentation procedures in small (2-4 mm) buccal bony dehiscences in anterior maxillary single-tooth replacement.

MATERIALS AND METHODS:

Patients with a buccal bony dehiscence after implant placement in the esthetic zone were randomly allocated to one-stage ridge augmentation with (M+) or without a membrane (M-). Second-phase surgery was performed after 8 weeks, and follow-up was performed 1, 6, and =12 months after loading. Outcomes included implant survival and success, complications, clinical and radiographic parameters, esthetic results and patient satisfaction.

RESULTS:

Fifty-two patients were randomized to one-stage ridge augmentation with (n = 25) or without use of a membrane (n = 27). No significant differences in implant survival and success have been observed. The risk of having a small mucosal dehiscence was more than six times higher in the M+ group than in the M- group (RR 6.24, 95% CI 0.81 to 48.21). At the last follow-up, the bleeding index (BI) was marginally higher in the M+ group (14/9/2/0) compared to the M- group (24/2/0/0) (U = 205, Z = -2.97, p = .003, r = .42). The median change in marginal bone level was statistically lower in the M+ group (0.06 mm) than the M- group (0.60 mm) at last follow-up (U = 120, Z = -2.73 a p = .006 r = .42). Total pink esthetic index (PES) and white esthetic score (WES) and combined PES/WES were not significantly different between treatment groups at more than 12 months after loading. Only the subcategory root convexity/soft tissue color scored significantly lower in the M+ group (1.5) compared to the M- group (2.0) at the last follow-up (U = 172, Z = -2.34, p = .019 r = .34). No differences were found in patient satisfaction.

CONCLUSION:

The use of a resorbable membrane in small buccal bony dehiscences in anterior maxillary single-tooth replacement resulted in less marginal bone loss, but showed more mucosal dehiscences, higher bleeding scores and lower scores on root convexity and soft tissue color after at least one year of loading. No effect was seen on implant survival and success, overall esthetic results, and patient satisfaction.

Impactfactor 4.305

Neurologie

A decrease in blood pressure is associated with unfavorable outcome in patients undergoing thrombectomy under general anesthesia

Treurniet KM, Berkhemer OA, Immink RV, Lingsma HF, Ward-van der Stam VM, Hollmann MW, Vuyk J, van Zwam WH, van der Lugt A, van Oostenbrugge RJ, Dippel DW, Coutinho JM, Roos YB, Marquering HA, Majoie CB; MR CLEAN investigators* : **Keizer K**, Tielbeek AV

J Neurointerv Surg. 2018 Feb;10(2):107-111

BACKGROUND: Up to two-thirds of patients are either dependent or dead 3 months after thrombectomy for acute ischemic stroke (AIS). Loss of cerebral autoregulation may render patients with AIS vulnerable to decreases in mean arterial pressure (MAP).

OBJECTIVE: To determine whether a fall in MAP during intervention under general anesthesia (GA) affects functional outcome.

METHODS: This subgroup analysis included patients from the MR CLEAN trial treated with thrombectomy under GA. The investigated variables were the difference between MAP at baseline and average MAP during GA (?MAP) as well as the difference between baseline MAP and the lowest MAP during GA (?LMAP). Their association with a shift towards better outcome on the modified Rankin Scale (mRS) after 90 days was determined using ordinal logistic regression with adjustment for prognostic baseline variables.

RESULTS: Sixty of the 85 patients treated under GA in MR CLEAN had sufficient anesthetic information available for the analysis. A greater ?MAP was associated with worse outcome (adjusted common OR (acOR) 0.95 per point mm Hg, 95% CI 0.92 to 0.99). An average MAP during GA 10 mm Hg lower than baseline MAP constituted a 1.67 times lower odds of a shift towards good outcome on the mRS. For ?LMAP this association was not significant (acOR 0.97 per mm Hg, 95% CI 0.94 to 1.00, p=0.09).

CONCLUSIONS: A decrease in MAP during intervention under GA compared with baseline is associated with worse outcome.

Impactfactor 3.524

Autism spectrum disorder: an early and frequent feature in cerebrotendinous xanthomatosis

Stelten BML*, Bonnot O, Huidekoper HH, van Spronsen FJ, van Hasselt PM, Kluijtmans LAJ, Wevers RA, Verrips A.

J Inherit Metab Dis. 2018 Jul;41(4):641-646. Epub 2017 Sep 11

BACKGROUND: Cerebrotendinous xanthomatosis (CTX) is an autosomal recessively inherited inborn error of metabolism (IEM) due to mutations in the CYP27A1 gene. The clinical picture ranges from being nearly asymptomatic in early childhood, up to severe disability at adult age. Infantile-onset diarrhea and juvenile-onset cataract are the earliest symptoms in childhood. In the current study, we evaluated the presence of autism spectrum disorder (ASD) in a large cohort of CTX patients.

METHODS: We performed a retrospective patient file study in 77 genetically confirmed Dutch CTX patients to determine the frequency of ASD. In addition, we compared plasma cholestanol levels in CTX patients with and without a diagnosis of ASD and tried to establish a relation between CYP27A1 genotype and ASD.

RESULTS: In our CTX cohort, 10 patients (13%; nine pediatric and one adult) with ASD were identified. At the time of diagnosis of ASD, most patients only exhibited symptoms of diarrhea and/or intellectual disability without signs of cataract or neurological symptoms. No correlation was found between the presence of ASD and the level of cholestanol or CYP27A1 genotype. The behavioral problems stabilized or improved after treatment initiation with chenodeoxycholic acid (CDCA) in all pediatric patients.

CONCLUSIONS:

We conclude that ASD is an early and probably underestimated frequent feature in CTX. Metabolic screening for CTX should be performed in patients with ASD when accompanied by diarrhea, intellectual disability, juvenile cataract, and/or neurological involvement. Early recognition allows for earlier initiation of specific treatment and will improve clinical outcome. Our results add CTX to the list of treatable IEMs associated with ASD.

Impactfactor 4.092

**Ten tijde van publicatie verbonden aan: Department of Neurology, Canisius Wilhelmina Hospital, Nijmegen*

Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data

Campbell BCV, van Zwam WH, Goyal M, Menon BK, Dippel DWJ, Demchuk AM, Bracard S, White P, Dávalos A, Majoie CBLM, van der Lugt A, Ford GA, de la Ossa NP, Kelly M, Bourcier R, Donnan GA, Roos YBWEM, Bang OY, Nogueira RG, Devlin TG, van den Berg LA, Clarençon F, Burns P, Carpenter J, Berkhemer OA, Yavagal DR, Pereira VM, Ducrocq X, Dixit A, Quesada H, Epstein J, Davis SM, Jansen O, Rubiera M, Urra X, Micard E, Lingsma HF, Naggara O, Brown S, Guillemin F, Muir KW, van Oostenbrugge RJ, Saver JL, Jovin TG, Hill MD, Mitchell PJ; HERMES collaborators: **Keizer K**, Tielbeek AV

Lancet Neurol. 2018 Jan 17(1):47-53. . Epub 2017 Dec 16

BACKGROUND: General anaesthesia (GA) during endovascular thrombectomy has been associated with worse patient outcomes in observational studies compared with patients treated without GA. We assessed functional

outcome in ischaemic stroke patients with large vessel anterior circulation occlusion undergoing endovascular thrombectomy under GA, versus thrombectomy not under GA (with or without sedation) versus standard care (ie, no thrombectomy), stratified by the use of GA versus standard care.

METHODS: For this meta-analysis, patient-level data were pooled from all patients included in randomised trials in PuMed published between Jan 1, 2010, and May 31, 2017, that compared endovascular thrombectomy predominantly done with stent retrievers with standard care in anterior circulation ischaemic stroke patients (HERMES Collaboration). The primary outcome was functional outcome assessed by ordinal analysis of the modified Rankin scale (mRS) at 90 days in the GA and non-GA subgroups of patients treated with endovascular therapy versus those patients treated with standard care, adjusted for baseline prognostic variables. To account for between-trial variance we used mixed-effects modelling with a random effect for trials incorporated in all models. Bias was assessed using the Cochrane method. The meta-analysis was prospectively designed, but not registered.

FINDINGS: Seven trials were identified by our search; of 1764 patients included in these trials, 871 were allocated to endovascular thrombectomy and 893 were assigned standard care. After exclusion of 74 patients (72 did not undergo the procedure and two had missing data on anaesthetic strategy), 236 (30%) of 797 patients who had endovascular procedures were treated under GA. At baseline, patients receiving GA were younger and had a shorter delay between stroke onset and randomisation but they had similar pre-treatment clinical severity compared with patients who did not have GA. Endovascular thrombectomy improved functional outcome at 3 months both in patients who had GA (adjusted common odds ratio (cOR) 1·52, 95% CI 1·09-2·11, p=0·014) and in those who did not have GA (adjusted cOR 2·33, 95% CI 1·75-3·10, p<0·0001) versus standard care. However, outcomes were significantly better for patients who did not receive GA versus those who received GA (covariate-adjusted cOR 1·53, 95% CI 1·14-2·04, p=0·0044). The risk of bias and variability between studies was assessed to be low.

INTERPRETATION: Worse outcomes after endovascular thrombectomy were associated with GA, after adjustment for baseline prognostic variables. These data support avoidance of GA whenever possible. The procedure did, however, remain effective versus standard care in patients treated under GA, indicating that treatment should not be withheld in those who require anaesthesia for medical reasons.

Impactfactor *27.138*

Movement disorders in cerebrotendinous xanthomatosis.

Stelten BML, van de Warrenburg BPC, Wevers RA, Verrips A

Parkinsonism Relat Disord. 2018 Jul 19. pii: S1353-8020(18)30310-9. [Epub ahead of print]

Cerebrotendinous xanthomatosis (CTX) is an inborn error of cholesterol and bile acid metabolism, leading to neuropsychiatric and systemic manifestations. Movement disorders have rarely been reported in CTX, while a detailed appreciation of the full phenotypic spectrum is required in order to prevent underdiagnosis of this disease. This review focuses on the frequency of more unusual, non-ataxia and non-spasticity movement disorders reported in CTX. In total, 39 articles were reviewed, describing 55 CTX patients with a movement disorder. Additionally, we report on seven patients with parkinsonism out of our Dutch cohort of 79 (77 genetically proven) CTX patients. Mean age at onset of the movement disorder was 40?±?12 years (median 40, range 13-62 years). Movement disorders can be considered a late disease manifestation. Parkinsonism was the most frequently reported movement disorder, followed by dystonia, myoclonus and postural tremor. Movement disorders were found to be mixed in 23% of patients and were usually part of a complex clinical picture, rather than a prominent symptom. Still, in 18% of the cases, a movement disorder was the presenting symptom. Unusual movement disorders represent a rare clinical feature in CTX, but CTX should be considered in the differential diagnosis of these movement disorders, particularly in case of early onset, and when associated with other neurological features (especially cognitive impairment, pyramidal and cerebellar signs) and/or with systemic features (such as diarrhoea, cataract and tendon xanthomas). CTX is a treatable disorder, stressing the importance of considering CTX as a potential cause of movement disorders.

Impactfactor *4.721*

Neurodegeneration With Brain Iron Accumulation: A Novel Mutation in the Ceruloplasmin Gene

Stelten BML, van Ommen W, **Keizer K**

JAMA Neurol. 2018 Oct 29. [Epub ahead of print]

Geen abstract beschikbaar

Impactfactor *11.460*

Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomised, phase 3 study

Kappos L, Bar-Or A , Cree BAC, Fox RJ, Giovannoni G, Gold R, Vermersch P, Arnold DL, Arnould S, Scherz T, Wolf C, Wallström E, Dahlke F; EXPAND Clinical Investigator: **Hengstman GJ**

Lancet. 2018 Mar 31;391(10127):1263-1273

BACKGROUND:

No treatment has consistently shown efficacy in slowing disability progression in patients with secondary

progressive multiple sclerosis (SPMS). We assessed the effect of siponimod, a selective sphingosine 1-phosphate (S1P) receptor1,5 modulator, on disability progression in patients with SPMS.

METHODS:

This event-driven and exposure-driven, double-blind, phase 3 trial was done at 292 hospital clinics and specialised multiple sclerosis centres in 31 countries. Using interactive response technology to assign numbers linked to treatment arms, patients (age 18-60 years) with SPMS and an Expanded Disability Status Scale score of 3·0-6·5 were randomly assigned (2:1) to once daily oral siponimod 2 mg or placebo for up to 3 years or until the occurrence of a prespecified number of confirmed disability progression (CDP) events. The primary endpoint was time to 3-month CDP. Efficacy was assessed for the full analysis set (ie, all randomly assigned and treated patients); safety was assessed for the safety set. This trial is registered with ClinicalTrials.gov, number NCT01665144.

FINDINGS:

1651 patients were randomly assigned between Feb 5, 2013, and June 2, 2015 (1105 to the siponimod group, and 546 to the placebo group). One patient did not sign the consent form, and five patients did not receive study drug, all of whom were in the siponimod group. 1645 patients were included in the analyses (1099 in the siponimod group and 546 in the placebo). At baseline, the mean time since first multiple sclerosis symptoms was 16·8 years (SD 8·3), and the mean time since conversion to SPMS was 3·8 years (SD 3·5); 1055 (64%) patients had not relapsed in the previous 2 years, and 918 (56%) of 1651 needed walking assistance. 903 (82%) patients receiving siponimod and 424 (78%) patients receiving placebo completed the study. 288 (26%) of 1096 patients receiving siponimod and 173 (32%) of 545 patients receiving placebo had 3-month CDP (hazard ratio 0·79, 95% CI 0·65-0·95; relative risk reduction 21%; p=0·013). Adverse events occurred in 975 (89%) of 1099 patients receiving siponimod versus 445 (82%) of 546 patients receiving placebo; serious adverse events were reported for 197 (18%) patients in the siponimod group versus 83 (15%) patients in the placebo group. Lymphopenia, increased liver transaminase concentration, bradycardia and bradyarrhythmia at treatment initiation, macular oedema, hypertension, varicella zoster reactivation, and convulsions occurred more frequently with siponimod than with placebo. Initial dose titration mitigated cardiac first-dose effects. Frequencies of infections, malignancies, and fatalities did not differ between groups.

INTERPRETATION:

Siponimod reduced the risk of disability progression with a safety profile similar to that of other S1P modulators and is likely to be a useful treatment for SPMS.

Impactfactor 53.254

The capability set for work - correlates of sustainable employability in workers with multiple sclerosis

van Gorp DA, van der Klink JJ, Abma FI, Jongen PJ, van Lieshout I, Arnoldus EP, Beenakker EA, Bos HM, van Eijk JJ, Fermont J, Frequin ST, de Gans K, **Hengstman GJ**, Hupperts RM, Mostert JP, Pop PH, Verhagen WI, Zemel D, Heerings MAP, Reneman MF, Middelkoop HA, Visser LH, van der Hiele K

Health Qual Life Outcomes. 2018 Jun 1;16(1):113

BACKGROUND:

The aim of this study was to examine whether work capabilities differ between workers with Multiple Sclerosis (MS) and workers from the general population. The second aim was to investigate whether the capability set was related to work and health outcomes.

METHODS:

A total of 163 workers with MS from the MS@Work study and 163 workers from the general population were matched for gender, age, educational level and working hours. All participants completed online questionnaires on demographics, health and work functioning. The Capability Set for Work Questionnaire was used to explore whether a set of seven work values is considered valuable (A), is enabled in the work context (B), and can be achieved by the individual (C). When all three criteria are met a work value can be considered part of the individual's 'capability set'.

RESULTS:

Group differences and relationships with work and health outcomes were examined. Despite lower physical work functioning (U?=?4250, p?=?0.001), lower work ability (U?=?10591, p?=?0.006) and worse self-reported health (U?=?9091, p?=?0.001) workers with MS had a larger capability set (U?=?9649, p?=?0.001) than the general population. In workers with MS, a larger capability set was associated with better flexible work functioning (r?=?0.30), work ability (r?=?0.25), self-rated health (r?=?0.25); and with less absenteeism (r?=?-?0.26), presenteeism (r?=?-?0.31), cognitive/neuropsychiatric impairment (r?=?-?0.35), depression (r?=?-?0.43), anxiety (r?=?-?0.31) and Fatigue (r?=?-?0.34).

CONCLUSIONS:

Workers with MS have a larger capability set than workers from the general population. In workers with MS a larger capability set was associated with better work and health outcomes.

Impactfactor 2.278

Nucleaire Geneeskunde

Dutch Economic Value of Radium-223 in Metastatic Castration-Resistant Prostate Cancer

Peters ML, de Meijer C, **Wyndaele D**, Noordzij W, Leliveld-Kors AM, van den Bosch J, van den Berg PH, Baka A, Gaultney JG

Appl Health Econ Health Policy. 2018 Feb 16(1):133-143

Erratum in: Appl Health Econ Health Policy. 2018 Jan 4

BACKGROUND:

The treatment of metastatic castration-resistant prostate cancer has changed with the introduction of radium-223, cabazitaxel, abiraterone and enzalutamide. To assess value for money, their cost effectiveness in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel from the Dutch societal perspective was investigated.

METHODS:

A cost-effectiveness analysis was conducted using efficacy, symptomatic skeletal-related event and safety data obtained from indirect treatment comparisons. Missing skeletal-related event data for cabazitaxel were conservatively assumed to be identical to radium-223. A Markov model combined these clinical inputs with Dutch-specific resource use and costs for metastatic castration-resistant prostate cancer treatment from a societal perspective. Total quality-adjusted life-years and costs in 2017 euros were calculated over a 5-year (lifetime) time horizon.

RESULTS:

Radium-223 resulted in €6092 and €4465 lower costs and 0.02 and 0.01 higher quality-adjusted life-years compared with abiraterone and cabazitaxel, respectively, demonstrating dominance of radium-223. Sensitivity analyses reveal a 64% (54%) chance of radium-223 being cost effective compared with abiraterone (cabazitaxel) at the informal €80,000 willingness-to-pay threshold. Compared with enzalutamide, radium-223 resulted in slightly lower quality-adjusted life-years (-0.06) and €7390 lower costs, revealing a 61% chance of radium-223 being cost effective compared with enzalutamide. The lower costs of radium-223 compared with abiraterone and enzalutamide are driven by lower drug costs and prevention of expensive skeletal-related events. Compared with cabazitaxel, the lower costs of radium-223 are driven by lower costs of the drug, administration and adverse events.

CONCLUSION:

Radium-223 may be a less costly treatment strategy offering similar gains in health benefits compared with abiraterone, cabazitaxel and enzalutamide in patients with metastatic castration-resistant prostate cancer previously treated with docetaxel from the Dutch societal perspective.

Impactfactor 1.885

Evaluation of the most commonly used (semi-)quantitative parameters of 18F-FDG PET/CT to detect malignant transformation of neurofibromas in neurofibromatosis type 1

Brinkman M, **Jentjens S**, Boone K, Anten M, Stumpel CT, Nelemans PJ, van Kroonenburgh MJ

Nucl Med Commun. 2018 Nov;39(11):961-968

In patients with neurofibromatosis type 1, transformation of neurofibromas into a malignant peripheral nerve sheath tumor (MPNST) is a severe complication of the disease. Fluorine-18-fluorodeoxyglucose PET/computed tomography (PET/CT) is a viable option for detecting malignant tumors in neurofibromatosis type 1 patients. The aim of this review was to assess the diagnostic performance of the most frequently used parameters of PET/CT in detecting MPNST. An extensive computer search was performed using the Cochrane Library, Pubmed, and Medline/Embase databases. Two reviewers independently extracted data of relevant studies and assessed the methodological quality (QUADAS-2). The diagnostic performance of PET/CT parameters in individual studies was determined by calculating a diagnostic odds ratio (DOR) using the absolute numbers of true-positive, true-negative, false-positive, and false-negative test results. A total of eight studies were included, of which three evaluated the standardized uptake value as a diagnostic parameter, two assessed the tumor-to-liver (T/L) ratio, and three articles described both parameters. The cut-off values for maximum standardized uptake value (SUVmax) ranged from 3.2 to 4.5; for the T/L ratio, the cut-off values were between 1.0 and 4.3. The sensitivity and specificity ranged from 90 to 100% and from 80 to 100%, respectively (SUVmax). T/L ratios were associated with 92-100% sensitivity and 72-94% specificity. The corresponding DORs ranged from 57 to 145 (SUVmax) and 35 to 655 (T/L ratio). Both the SUV and the T/L ratio are associated with high sensitivity combined with acceptable specificity in detecting MPNST. There is a tendency toward higher DORs using the T/L ratio, but the number of studies is limited.

Impactfactor 1.495

Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial

Noordman BJ, Wijnhoven BPL, Lagarde SM, Boonstra JJ, Coene PPLO, Dekker JWT, Doukas M, van der Gaast A, Heisterkamp J, Kouwenhoven EA, Nieuwenhuijzen GAP, Pierie JEN, Rosman C, van Sandick JW, van der Sangen MJC, Sosef MN, Spaander MCW, Valkema R, van der Zaag ES, Steyerberg EW, van Lanschot JJB SANO-study group.: Creemers GJ, Schoon EJ, **Wyndaele D**

BMC Cancer. 2018 Feb 6 18(1):142

BACKGROUND:
Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard treatment for locally advanced oesophageal cancer. With this treatment, 29% of patients have a pathologically complete response in the resection specimen. This provides the rationale for investigating an active surveillance approach. The aim of this study is to assess the (cost-)effectiveness of active surveillance vs. standard oesophagectomy after nCRT for oesophageal cancer.
METHODS:
This is a phase-III multi-centre, stepped-wedge cluster randomised controlled trial. A total of 300 patients with clinically complete response (cCR, i.e. no local or disseminated disease proven by histology) after nCRT will be randomised to show non-inferiority of active surveillance to standard oesophagectomy (non-inferiority margin 15%, intra-correlation coefficient 0.02, power 80%, 2-sided a 0.05, 12% drop-out). Patients will undergo a first clinical response evaluation (CRE-I) 4-6 weeks after nCRT, consisting of endoscopy with bite-on-bite biopsies of the primary tumour site and other suspected lesions. Clinically complete responders will undergo a second CRE (CRE-II), 6-8 weeks after CRE-I. CRE-II will include 18F-FDG-PET-CT, followed by endoscopy with bite-on-bite biopsies and ultra-endosonography plus fine needle aspiration of suspected lymph nodes and/or PET- positive lesions. Patients with cCR at CRE-II will be assigned to oesophagectomy (first phase) or active surveillance (second phase of the study). The duration of the first phase is determined randomly over the 12 centres, i.e., stepped-wedge cluster design. Patients in the active surveillance arm will undergo diagnostic evaluations similar to CRE-II at 6/9/12/16/20/24/30/36/48 and 60 months after nCRT. In this arm, oesophagectomy will be offered only to patients in whom locoregional regrowth is highly suspected or proven, without distant dissemination. The main study parameter is overall survival; secondary endpoints include percentage of patients who do not undergo surgery, quality of life, clinical irresectability (cT4b) rate, radical resection rate, postoperative complications, progression-free survival, distant dissemination rate, and cost-effectiveness. We hypothesise that active surveillance leads to non-inferior survival, improved quality of life and a reduction in costs, compared to standard oesophagectomy.
DISCUSSION:
If active surveillance and surgery as needed after nCRT leads to non-inferior survival compared to standard oesophagectomy, this organ-sparing approach can be implemented as a standard of care.

Impactfactor *3.288*

Taalstoornissen bij dementie deel?1: primair progressieve afasie

Peter van Domburg, Femke Deguelle, Yvonne Raaijmakers, Susan Slot, **Sander Jentjens**

Neuropraxis, 2018;22(1):2-15

Primair progressieve afasie (PPA) is een klinisch syndroom dat wordt gedefinieerd door geïsoleerde progressieve taalstoornissen, die reeds meerdere jaren bestaan alvorens zich dementie ontwikkelt, meestal uit het spectrum van frontotemporale lobaire degeneratie (FTLD). Wat PPA bijzonder maakt, is dat er sprake is van een neurodegeneratief proces in een selectief functioneel cerebraal (taal)netwerk. Het onderzoek naar PPA heeft niet alleen nieuwe kennis opgeleverd over het ontstaan en het vroege beloop van dementie, maar ook inzichten in de functionele neuroanatomie van taalnetwerken en de neurolinguïstiek. In het eerste deel van deze bijdrage wordt een overzicht gegeven van de subtypen van PPA en hun mogelijke etiologie. Verder bevat het artikel een handreiking voor de beoordeling en behandeling in de algemene klinische praktijk, op basis van literatuuronderzoek en eigen ervaring.

Impactfactor --

Thyroid Gland 18F-FDG Uptake in Neurofibromatosis Type 1

van Lierop ZYGJ, **Jentjens S**, Anten MHME, Wierts R, Stumpel CT, Havekes B, van Kroonenburgh MJPG

Eur Thyroid J. 2018 Jun;7(3):155-161. Epub 2018 Jun 5

Purpose:
To investigate thyroid gland characteristics on 18F-FDG positron emission tomography/computed tomography (PET/CT) imaging in patients with neurofibromatosis type 1 (NF1).
Subjects and Methods:
Thyroid gland characteristics of patients with a clinical diagnosis of NF1 who underwent 18F-FDG PET/CT imaging for the first time to distinguish benign neurofibroma from malignant peripheral nerve sheath tumor (MPNST) at our institution (n = 69) were compared to PET/CT imaging of sarcoidosis (n = 25) and early stage lung cancer (T1N0M0 tumors, n = 15) patients.
Results:
Two NF1 patients (3%) showed a diffuse 18F-FDG uptake in the thyroid gland, 2 patients (3%) had an irregular uptake, and 7 patients (10%) had a focal uptake. Among the sarcoidosis patients, 1 showed a diffuse uptake (4%) and 1 had an irregular uptake (4%). In the early stage lung cancer group, 1 patient showed a diffuse uptake (7%) and 1 had a focal uptake (7%). NF1 patients had larger mean thyroid volume and mean SUVmax compared to sarcoidosis patients but not compared to early stage lung cancer patients. Four NF1 patients were diagnosed with multinodular goiter, 2 patients were diagnosed with benign chronic lymphocytic thyroiditis, 1 patient had metastasis to the thyroid, and 1 patient had medullary thyroid cancer.

Conclusion:

Even though NF1 patients did not show an increased risk of thyroid incidentaloma on PET/CT compared to previous studies on non-thyroid cancer patients, the incidence shows that awareness of possible thyroid disease is important.

Impactfactor --

Onderwijs en Onderzoek

A software-based tool for video motion tracking in the surgical skills assessment landscape

Ganni S, Botden SMBI, Chmarra M, Goossens RHM, **Jakimowicz JJ**

Surg Endosc. 2018 Jun 32(6):2994-2999. Epub 2018 Jan 16

BACKGROUND:
The use of motion tracking has been proved to provide an objective assessment in surgical skills training. Current systems, however, require the use of additional equipment or specialised laparoscopic instruments and cameras to extract the data. The aim of this study was to determine the possibility of using a software-based solution to extract the data.
METHODS:
6 expert and 23 novice participants performed a basic laparoscopic cholecystectomy procedure in the operating room. The recorded videos were analysed using Kinovea 0.8.15 and the following parameters calculated the path length, average instrument movement and number of sudden or extreme movements.
RESULTS:
The analysed data showed that experts had significantly shorter path length (median 127 cm vs. 187 cm, p?=?0.01), smaller average movements (median 0.40 cm vs. 0.32 cm, p?=?0.002) and fewer sudden movements (median 14.00 vs. 21.61, p?=?0.001) than their novice counterparts.
CONCLUSION:
The use of software-based video motion tracking of laparoscopic cholecystectomy is a simple and viable method enabling objective assessment of surgical performance. It provides clear discrimination between expert and novice performance.

Impactfactor 3.117

Cancer risk perception in relation to associated symptoms in Barrett's patients: A cross sectional study on quality of life

van der Ende-van Loon MC, Rosmolen WD, **Houterman S**, Schoon EJ, Curvers WL

United European Gastroenterol J. 2018 Nov;6(9):1316-1322

Background:
Barrett's oesophagus affects patients' quality of life and may be a psychological burden due to the threat of developing an oesophageal adenocarcinoma.
Objective:
Assessing the oesophageal adenocarcinoma risk perceived by non-dysplastic Barrett's oesophagus patients and its association with quality of life, illness perception and reflux symptoms.
Methods:
This cross-sectional questionnaire study included 158 Barrett's oesophagus non-dysplastic patients aged 18-75 years. Based on their annual and lifetime oesophageal adenocarcinoma risk estimations measured with the Magnifier Scale, patients were classified as overestimating or underestimating. Associations between the groups where assed on demographics, reflux symptoms and results of the Outcomes Study Short-Form-36 (SF-36) and the Brief Illness Perception Questionnaire (B-IPQ).
Results:
The annual oesophageal adenocarcinoma risk was overestimated by 41%. Overestimating patients had lower means on the SF-36 domains: bodily pain (annual p?=?0.007 and lifetime p?=?0.014), general health (annual p?=?0.011 and lifetime p?=?0.014), vitality (annual p?=?0.030), physical functioning (lifetime p?=?0.028), worse illness perception (total score p?=?0.001) and significantly more reflux symptoms.
Conclusions:
Overestimation of the oesophageal adenocarcinoma risk by Barrett's oesophagus patients was associated with decreased quality of life and worse illness perceptions, which is most likely caused by symptoms of dyspepsia and reflux. These symptoms should be adequately treated, and patients may be in need of extra support and specific information about their oesophageal adenocarcinoma risk.

Impactfactor 3.477

Comparison of ultrasound guidance with palpation and direct visualisation for peripheral vein cannulation in adult patients: a systematic review and meta-analysis

van Loon FH, Buise MP, Claassen JJ, **Dierick-van Daele AT**, Bouwman AR

Br J Anaesth. 2018 Aug;121(2):358-366

BACKGROUND:
Peripheral vein cannulation is a routine and straightforward invasive procedure, although i.v. access can be difficult to obtain. To increase the success rate of inserting an i.v. catheter, many devices have been proposed, including ultrasonography. The objective of this study was to compare ultrasound guidance with the traditional approach of palpation and direct visualisation for peripehral vein cannulation. The primary outcome was successful peripheral i.v. cannulation.
METHODS:
Database search was performed on PubMed, Clinical Key, CINAHL, Cochrane Library of Clinical Trials, and Trip

Database (from January 2000 to December 2017). Random-effect meta-analysis was performed to determine the pooled odds ratio for success in peripheral i.v. cannulation.
RESULTS:
After database review and eligibility screening, eight studies were included in the final analysis, with a total of 1660 patients. The success rate in the ultrasound group was 81% (n=855), and was 70% (n=805) in the control group, resulting in a pooled odds ratio for success upon ultrasound-guided peripheral i.v. cannulation of 2.49 (95% confidence interval 1.37-4.52, P=0.003). Furthermore, the ultrasound-guided technique reduced the number of punctures and time needed to achieve i.v. access, and increased the level of patient satisfaction, although it did not result in a decreased number of complications.
CONCLUSIONS:
Ultrasound guidance increases the success rate of peripheral i.v. cannulation, especially in patients with known or predicted difficult i.v. access.

Impactfactor 6.499

Defining and Measuring a Standard Set of Patient-Relevant Outcomes in Coronary Artery Disease

Daeter EJ, Timmermans MJ, Hirsch A, Lipsic E, **Houterman S**; Meetbaar Beter advisory board, van Veghel D, van der Nat PB

Am J Cardiol. 2018 Jun 15;121(12):1477-1488

Systematic outcome measurement enables to continuously improve treatment results and stimulates dissemination of best practices. For patients with coronary artery disease, no examples yet exist of standard sets of patient-relevant outcome measures that have already been fully implemented at a large scale in clinical care. The aim of this paper is twofold: (1) to share the standard set of outcome measures as developed by Meetbaar Beter, and (2) to show how the standard set is presented and published to support improvement of cardiac care. A step-wise approach was followed by an expert panel to construct a standard set of outcome measures. This resulted in a comprehensive set of relevant outcome measures, comprising 4 generic and 11 treatment-specific outcomes. Both short-term and long-term outcomes measures up to 5 years of follow-up were included. Relevant initial conditions were selected to enable case-mix adjustment. The standard set has been implemented in 21 hospitals across the Netherlands. The results and experiences have been used to fine-tune the set in 4 reporting cycles in 2012 to 2016, using an annual maintenance cycle. Currently about 83,000 percutaneous coronary interventions and 30,000 coronary artery bypass graftings are included in the dataset, covering the majority of all percutaneous coronary interventions and coronary artery bypass graftings in the Netherlands. In conclusion, Meetbaar Beter has defined and implemented a comprehensive set of patient-relevant outcome measures for coronary artery disease, and the variation of the results among the centers indicates that there are sufficient opportunities to further improve cardiac care in the Netherlands.

Impactfactor 3.171

Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium: The REDUCE Randomized Clinical Trial

van den Boogaard M, Slooter AJ, Brüggemann RJ, Schoonhoven L,, Beishuizen A, Vermeijden JW, Pretorius D, de Koning J, Simons KS, Dennesen PJW, Van der Voort PH, **Houterman S**, van der Hoeven JG, Pickkers P; REDUCE Study Investigators, van der Woude, Besselink A, Hofstra LS, Spronk PE, van den Bergh W, Donker DW, Fuchs M, Karakus A, Koeman M, van Duijnhoven M, Hannink G

JAMA. 2018 Feb 20;319(7):680-690

Importance:
Results of studies on use of prophylactic haloperidol in critically ill adults are inconclusive, especially in patients at high risk of delirium.
Objective:
To determine whether prophylactic use of haloperidol improves survival among critically ill adults at high risk of delirium, which was defined as an anticipated intensive care unit (ICU) stay of at least 2 days.
Design, Setting, and Participants:
Randomized, double-blind, placebo-controlled investigator-driven study involving 1789 critically ill adults treated at 21 ICUs, at which nonpharmacological interventions for delirium prevention are routinely used in the Netherlands. Patients without delirium whose expected ICU stay was at least a day were included. Recruitment was from July 2013 to December 2016 and follow-up was conducted at 90 days with the final follow-up on March 1, 2017.
Interventions:
Patients received prophylactic treatment 3 times daily intravenously either 1 mg (n?=?350) or 2 mg (n?=?732) of haloperidol or placebo (n?=?707), consisting of 0.9% sodium chloride.
Main Outcome and Measures:
The primary outcome was the number of days that patients survived in 28 days. There were 15 secondary outcomes, including delirium incidence, 28-day delirium-free and coma-free days, duration of mechanical

ventilation, and ICU and hospital length of stay.
Results:
All 1789 randomized patients (mean, age 66.6 years [SD, 12.6]; 1099 men [61.4%]) completed the study. The 1-mg haloperidol group was prematurely stopped because of futility. There was no difference in the median days patients survived in 28 days, 28 days in the 2-mg haloperidol group vs 28 days in the placebo group, for a difference of 0 days (95% CI, 0-0; P?=?.93) and a hazard ratio of 1.003 (95% CI, 0.78-1.30, P=.82). All of the 15 secondary outcomes were not statistically different. These included delirium incidence (mean difference, 1.5%, 95% CI, -3.6% to 6.7%), delirium-free and coma-free days (mean difference, 0 days, 95% CI, 0-0 days), and duration of mechanical ventilation, ICU, and hospital length of stay (mean difference, 0 days, 95% CI, 0-0 days for all 3 measures). The number of reported adverse effects did not differ between groups (2 [0.3%] for the 2-mg haloperidol group vs 1 [0.1%] for the placebo group).
Conclusions and Relevance:
Among critically ill adults at high risk of delirium, the use of prophylactic haloperidol compared with placebo did not improve survival at 28 days. These findings do not support the use of prophylactic haloperidol for reducing mortality in critically ill adults.

Impactfactor 47.661

External validation of a prediction model to select the best day-three embryo for transfer in in vitro fertilization or intracytoplasmatic sperm injection procedures

Blank C, Duijf IT, Slappendel E, Mischi M, **Houterman S**, Maas JW, de Sutter P, Schoot BC
Fertil Steril. 2018 Oct;110(5):917-924

OBJECTIVE:
To evaluate the multivariate embryo selection model by van Loendersloot et al. (2014) (VL) in a different geographical context.
DESIGN:
This is a retrospective external validation study of a 5-year cohort of women undergoing in vitro fertilization or intracytoplasmatic sperm injection.
SETTING:
Two outpatient fertility clinics.
PATIENT(S):
A total of 1,197 women who underwent 1,610 fresh in vitro fertilization or intracytoplasmatic sperm injection cycles with single embryo transfer were included.
INTERVENTION(S):
None.
MAIN OUTCOME MEASURE(S):
The area under the receiver operating characteristics curve for diagnostic efficacy was used to assess the discriminative value of the model. Calibration for testing the validity of the VL model was performed using the Hosmer-Lemeshow goodness-of-fit test and a calibration plot.
RESULT(S):
Three hundred thirty-three patients (21%) achieved a viable pregnancy of at least 11 weeks. The area under the receiver operating characteristics curve using the VL model was 0.68. No significant difference between the predicted implantation rate and the observed implantation rates was showed using the Hosmer-Lemeshow (X2= 6.70). The calibration plot showed an intercept of the regression line of 0.34 and the estimated slope was 0.7
COCLUSION:
The investigated VL model was able to distinguish between higher and lower implantation potential of embryos in our clinical setting.

Impactfactor 4.803

Impact of brachytherapy technique (2D versus 3D) on outcome following radiotherapy of cervical cancer

Derks K, Steenhuijsen JLG, van den Berg HA, **Houterman S**, Cnossen J, van Haaren P, De Jaeger K
J Contemp Brachytherapy. 2018 Feb 10(1):17-25. Epub 2018 Feb 22

Purpose:
The purpose of this study was to analyze the effect of 2D conventional brachytherapy (CBT) compared to 3D MRI-guided brachytherapy (IGBT) with and without the use of interstitial needles on local control, overall survival, and toxicity in patients treated for cervical cancer with radiation or chemoradiation.
Material and methods:
A retrospective analysis was performed of biopsy-proven FIGO IB-IVA cervical cancer patients, treated with primary radiation or chemoradiation, followed by brachytherapy (BT) between January 1997 and July 2016. Endpoints were local control, overall survival, and toxicity.
Results:
Of 126 patients included, 35 have been treated with CBT, 31 with IGBT without needles (IC), and 60 with IGBT with needles (ICIS). External beam radiotherapy (EBRT) had mostly been delivered concurrently with chemotherapy (weekly cisplatin).

Overall local control was 93% after 1 year, and 88% after 3 years. Overall 3-year survival was 75%, and 5-year survival was 66%. The 3D technique (IGBT cohorts) showed a trend for an improved local control and overall survival (p = 0.05) compared to the 2D technique (CBT cohort). A decrease in toxicity was observed from 17% (2D cohort) to 12% (3D cohort). The use of interstitial needles was associated with a higher high-risk clinical target volume (HR-CTV) dose (11.3 Gy vs. 9.9 Gy) and a lower D2cc bladder dose (10.9 Gy vs. 14.7 Gy, both p < 0.01).
Conclusions:
In cervical cancer treatment, the use of a 3D brachytherapy technique (MRI-guided with or without interstitial needles) showed a trend towards an increased local control and improved overall survival with reduced toxicity, compared to the conventional 2D brachytherapy technique. The use of interstitial needles allowed dose sculpting, resulting in delivery of higher doses to the HR-CTV, while reducing radiation doses to organs at risk, such as the bladder.
Impactfactor --

Impact of Sex on the Outcome of Isolated Aortic Valve Replacement and the Role of Different Preoperative Profiles

Ter Woorst JF, Hoff AHT, van Straten AHM, **Houterman S**, Soliman-Hamad MA
J Cardiothorac Vasc Anesth. 2018 Aug 24. pii: S1053-0770(18)30842-5. [Epub ahead of print]

OBJECTIVE:
The aim of this study was to compare the patient profiles and outcomes of men and women undergoing isolated aortic valve replacement.
DESIGN:
Patient data were analyzed retrospectively.
SETTING:
This single-center study was performed at Catharina Hospital in Eindhoven, the Netherlands.
PARTICIPANTS:
The study comprised 2,362 patients, of whom 1,040 (44%) were women and 1,322 were men (56%).
INTERVENTIONS:
Isolated aortic valve replacement was performed between January 1998 and December 2016.
MEASUREMENTS AND MAIN RESULTS:
The mean follow-up was 8.3 ± 5.1 years. Women were relatively older (69.9 years v 64.6 years; p < 0.001); more of them were underweight, obese, and diabetic; and they had lower hemoglobin values and worse renal function than did men. However, fewer women than men experienced chronic obstructive pulmonary disease, aortic regurgitation, left ventricular dysfunction, and endocarditis. Early mortality did not differ significantly between men and women (p?=?0.238). Overall survival was worse in women (p < 0.001). After correction for potential risk factors, female sex was not associated with worse survival. During the study period, the mean age of patients undergoing aortic valve replacement increased. In addition, the mean age at the time of death increased, following the trend of national statistics.
CONCLUSIONS:
Although women undergoing aortic valve replacement have relatively more risk factors than do men, early mortality in women is not significantly higher than in men. Overall survival is worse in women than in men; however, after adjustment for preoperative risk factors, there is no difference in overall survival between women and men.

Impactfactor 1.574

Opportunistic salpingectomy in women undergoing hysterectomy: Results from the HYSTUB randomised controlled trial

Van Lieshout LAM, Pijlman B, Vos MC, de Groot MJM, **Houterman S**, Coppus SFPJ, Harmsen MG, Vandenput I, Piek JMJ
Maturitas. 2018 Jan 107:1-6. Epub 2017 Oct 3

OBJECTIVE:
To evaluate whether opportunistic salpingectomy in premenopausal women undergoing hysterectomy for benign indications is both hormonally and surgically safe, compared with hysterectomy without salpingectomy.
STUDY DESIGN:
In this multicentre randomised controlled trial, women were randomised to undergo either hysterectomy with opportunistic bilateral salpingectomy (intervention group) or standard hysterectomy with preservation of the Fallopian tubes (control group).
MAIN OUTCOME MEASURES:
The primary outcome was the difference in serum anti-Müllerian hormone concentration (?AMH), measured pre-surgery and 6 months post-surgery. Secondary outcomes were surgical outcomes and duration of hospital stay. The sample size was powered at 50 participants per group (n=100) to compare ?AMH after hysterectomy with salpingectomy to ?AMH after standard hysterectomy.
RESULTS:
Between March 2013 and December 2016, 104 women, aged 30-55 years, were randomly allocated to

hysterectomy with opportunistic bilateral salpingectomy (n=52) or standard hysterectomy (n=52). The baseline characteristics did not differ between the two groups. The median ?AMH was -0.14pmol/L (IQR -1.47-0.95) in the intervention group and 0.00pmol/L (IQR -1.05-0.80) in the control group (p=0.49). The addition of salpingectomy did not impair surgical results and it did not affect duration of hospital stay.
CONCLUSION:
Addition of opportunistic bilateral salpingectomy during hysterectomy did not result in a larger effect on ovarian reserve when compared with hysterectomy alone, neither did it affect surgical outcomes. Therefore, opportunistic salpingectomy seems to be a safe procedure in premenopausal women undergoing hysterectomy for benign gynaecological conditions

Impactfactor *3.315*

Pain upon inserting a peripheral intravenous catheter: Size does not matter

van Loon FH, Puijn LA, van Aarle WH, **Dierick-van Daele AT**, Bouwman AR

J Vasc Access. 2018 May;19(3):258-265

BAGROUND: Approximately 1.2 billion peripheral intravenous catheters are inserted across the world annually. It is known that intravenous cannulation may be a painful procedure, which affects cognitive abilities by increasing anxiety and discomfort.
AIM: We hypothesized that inserting a smaller sized peripheral intravenous catheter has a lower level of pain sensation compared to a larger sized catheter.
METHODS: This observational, cross-sectional study was conducted between May and October 2016, in which surgical patients, aged 18 years or older, were eligible to participate. Experienced anesthesiologists and nurse anesthetists routinely obtained peripheral intravenous access according to the standards of care. The primary outcome was pain (verbal numeric rating scale, 0-10) upon intravenous cannulation.
RESULTS: A total of 1063 patients were included and they were divided into four groups: group 1, 22 gauge (N = 29); group 2, 20 gauge (N = 447); group 3, 18 gauge (N = 531); and group 4, sized over 18 gauge (N = 56). Inserting an 18-gauged peripheral intravenous catheter resulted in the lowest pain score (3.2 ± 2.0). As a result of the multivariate linear analysis, five factors were significantly associated with pain upon inserting a peripheral intravenous catheter (sex, American Society of Anesthesiology classification, a patients risk profile on the A-DIVA scale, site of cannulation on the extremity, and whether or not the attempt was successful); however, the size of the inserted peripheral intravenous catheter had no significant relation to the primary outcome.
CONCLUSION: Inserting a smaller sized peripheral intravenous catheter did not result in a lower pain sensation. Moreover, to prevent pain upon inserting a peripheral intravenous catheter, an unsuccessful attempt must be avoided.

Impactfactor *1.306*

Real-time location systems in nursing homes: state of the art and future applications

C.E. Oude Weernink, E. Felix, P.J.E.M. Verkuijlen, **A.T.M. Dierick-van Daele**, J.K. Kazak, J. van Hoof

Journal of Enabling Technologies, 2018; Vol. 12 Issue: 2, pp.45-56

Purpose
In the domain of healthcare, both process efficiency and the quality of care can be improved through the use of dedicated pervasive technologies. Among these applications are so-called real-time location systems (RTLS). Such systems are designed to determine and monitor the location of assets and people in real time through the use of wireless sensor networks. Numerous commercially available RTLS are used in hospital settings. The nursing home is a relatively unexplored context for the application of RTLS and offers opportunities and challenges for future applications. The paper aims to discuss these issues.
Design/methodology/approach
This paper sets out to provide an overview of general applications and technologies of RTLS. Thereafter, it describes the specific healthcare applications of RTLS, including asset tracking, patient tracking and personnel tracking. These overviews are followed by a forecast of the implementation of RTLS in nursing homes in terms of opportunities and challenges.
Findings
By comparing the nursing home to the hospital, the RTLS applications for the nursing home context that are most promising are asset tracking of expensive goods owned by the nursing home in order to facilitate workflow and maximise financial resources, and asset tracking of personal belongings that may get lost due to dementia.
Originality/value
This paper is the first to provide an overview of potential application of RTLS technologies for nursing homes. The paper described a number of potential problem areas that can be addressed by RTLS.

Impactfactor --

"Reflection-Before-Practice" Improves Self-Assessment and End-Performance in Laparoscopic Surgical Skills Training

Ganni S, Botden SMBI, Schaap DP, Verhoeven BH, Goossens RHM, Jakimowicz JJ

J Surg Educ. 2018 Mar - Apr;75(2):527-533. Epub 2017 Aug 17

OBJECTIVE:
To establish whether a systematized approach to self-assessment in a laparoscopic surgical skills course improves accordance between expert- and self-assessment.
DESIGN:
A systematic training course in self-assessment using Competency Assessment Tool was introduced into the normal course of evaluation within a Laparoscopic Surgical Skills training course for the test group (n = 30). Differences between these and a control group (n = 30) who did not receive the additional training were assessed.
SETTING:
Catharina Hospital, Eindhoven, The Netherlands (n = 27), and GSL Medical College, Rajahmundry, India (n = 33).
PARTICIPANTS:
Sixty postgraduate year 2 and 3 surgical residents who attended the 2-day Laparoscopic Surgical Skills grade 1 level 1 curriculum were invited to participate.
RESULTS:
The test group (n = 30) showed better accordance between expert- and self-assessment (difference of 1.5, standard deviation [SD] = 0.2 versus 3.83, SD = 0.6, p = 0.009) as well as half the number (7 versus 14) of cases of overreporting. Furthermore, the test group also showed higher overall mean performance (mean = 38.1, SD = 0.7 versus mean = 31.8, SD = 1.0, p < 0.001) than the control group (n = 30). The systematic approach to self-assessment can be viewed as responsible for this and can be seen as "reflection-before-practice" within the framework of reflective practice as defined by Donald Schon.
CONCLUSION:
Our results suggest that "reflection-before-practice" in implementing self-assessment is an important step in the development of surgical skills, yielding both better understanding of one's strengths and weaknesses and also improving overall performance.

Impactfactor 2.302

Review on Factors Influencing Physician Guideline Adherence in Cardiology

Hoorn CJGM, Crijns HJGM, Dierick-van Daele ATM, Dekker LRC

Cardiol Rev. 2018 Apr 9. [Epub ahead of print]

Cardiovascular disease is the most common cause of death in Western countries. Physician adherence to guidelines is often suboptimal, resulting in impaired patient outcome and prognosis. Multiple studies have been conducted to evaluate patterns and the influencing factors of patient adherence, but little is known about factors influencing physician guideline adherence. This review aims to identify factors influencing physician guideline adherence relevant to cardiology and to provide insights and suggestions for future improvement. Physician adherence was measured as adherence to standard local medical practice and applicable guidelines. Female gender and older age had a negative effect on physician guideline adherence. In addition, independent of the type of heart disease, physicians without cardiologic specialization were linked to physician noncompliance. Also, guideline adherence in primary care centers was at a lower level compared to secondary or tertiary care centers. The importance of guideline adherence increases as patients age, and complex diseases and comorbidity arise. Appropriate resources and interventions, taking important factors for nonadherence in account, are necessary to improve guideline adoption and adherence in every level of the chain. This in turn should improve patient outcome.

Impactfactor 1.951

Operatiekamers

The RAQET Study: the Effect of Eating a Popsicle Directly After Bariatric Surgery on the Quality of Patient Recovery; a Randomised Controlled Trial

Pouwels S, **Stepaniak PS**, Buise MP, Bouwman RA, Nienhuijs SW

Indian J Surg. 2018 Jun;80(3):245-251

Quality of recovery could be influenced positively if there is less postoperative sore throat (POST). Eating a popsicle might attenuate this sore throat. Especially for bariatric surgery, early recovery is important. Adding popsicles to the postoperative protocol could be beneficial. Our hypothesis is that offering a popsicle in the recovery room to patients after bariatric surgery will decrease POST and will increase quality of postoperative recovery. Patients undergoing elective bariatric surgery, between the 23 February 2015 and 3 April, were randomised to either the popsicle group or control group. Primary endpoint was the incidence of POST and secondly if a reduction in POST influences quality of recovery at the first day postoperative measured with the Bariatric Quality Of Recovery (BQoR) questionnaire. One hundred and thirty-three patients were assessed for eligibility. For the final analysis, 44 patients in the intervention and 65 in the control group were available. Eating a popsicle after bariatric surgery had no significant effect on the incidence of POST. Significant effects (in favour of the popsicle group) were seen in muscle pain score ($p = 0.047$) and sore mouth score ($p = 0.012$). Popsicle intragroup analysis revealed that eating the whole popsicle (compared to partially eating the popsicle) has positive effects on nausea ($p = 0.059$), feeling cold ($p = 0.008$), and mean total comfort score ($p = 0.011$). Of the patients who became nauseous and/or had to vomit because of the popsicle, $n = 4$ had more severe pain ($p = 0.04$) and the mean pain score was higher ($p = 0.09$). The present study demonstrates that offering a popsicle early during recovery after bariatric surgery is feasible without adverse effects, although eating popsicle did not reduce postoperative sore throat. There are possible beneficial effects, such as reduced muscle pains and less sore mouth, that may enhance the quality of recovery. More research is necessary to further substantiate the effect of eating popsicles on the quality of recovery in this patient population.

Impactfactor 0.509

Orthopedie

Gait kinetics in children with clubfeet treated surgically or with the Ponseti method: A meta-analysis

Tuinsma AB, Vanwanseele B, van Oorschot L, Kars HJ, Grin L, Reijman M, **Besselaar AT**, **van der Steen M**

Gait Posture. 2018 Oct;66:94-100. Epub 2018 Aug 13

BACKGROUND:
Currently, the Ponseti method is the gold standard for treatment of clubfeet. For long-term functional evaluation of this method, gait analysis can be performed. Previous studies have assessed gait differences between Ponseti treated clubfeet and healthy controls.
RESEARCH QUESTION/PURPOSE:
The aims of this systematic review were to compare the gait kinetics of Ponseti treated clubfeet with healthy controls and to compare the gait kinetics between clubfoot patients treated with the Ponseti method or surgically.
METHODS:
A systematic search was performed in Embase, Medline Ovid, Web of Science, Scopus, Cochrane, Cinahl ebsco, and Google scholar, for studies reporting on gait kinetics in children with clubfeet treated with the Ponseti method. Studies were excluded if they only used EMG or pedobarography. Data were extracted and a risk of bias was assessed. Meta-analyses and qualitative analyses were performed.
RESULTS:
Nine studies were included, of which five were included in the meta-analyses. The meta-analyses showed that ankle plantarflexor moment (95% CI -0.25 to -0.19) and ankle power (95% CI -0.89 to -0.60, were significantly lower in the Ponseti treated clubfeet compared to the healthy controls. No significant difference was found in ankle dorsiflexor and plantarflexor moment, and ankle power between clubfeet treated with surgery compared to the Ponseti method.
SIGNIFICANCE:
Differences in gait kinetics are present when comparing Ponseti treated clubfeet with healthy controls. However, there is no significant difference between surgically and Ponseti treated clubfeet. These results give more insight in the possibilities of improving the gait pattern of patients treated for clubfeet.

Impactfactor 2.273

Identification and treatment of residual and relapsed idiopathic clubfoot in 88 children

Stouten JH, **Besselaar AT, van der Steen MC**

Acta Orthop. 2018 Aug;89(4):448-453

Background and purpose - The Ponseti treatment is successful in idiopathic clubfoot. However, approximately 11-48% of all clubfeet maintain residual deformities or relapse. Early treatment, which possibly reduces the necessity for additional surgery, requires early identification of these problematic clubfeet. We identify deformities of residual/relapsed clubfeet and the treatments applied to tackle these deformities in a large tertiary clubfoot treatment center. Patients and methods - Retrospective chart review of patients who visited our clinic between 2012 and 2015 focused on demographics, deformities of the residual/relapsed clubfoot, and applied treatment. Residual deformities were defined as deformities that were never fully corrected and needed additional treatment. We defined relapse as any deformity of the clubfoot reoccurring, after initial successful treatment, with necessity for additional treatment. Results - We identified 33 patients with residual and 55 patients with relapsed clubfeet. In both groups decreased dorsal flexion and adduction were the most often registered deformities. Furthermore, often equinus/decreased dorsiflexion, active supination, and varus occurred. In more than half, typical profiles of combined deformities were found. Relapses occurred at all stages of treatment and follow-up; half of the residual or relapsed clubfeet were identified before the end of the bracing period. In half of the patients, additional treatment consisted of the Ponseti treatment, one-quarter also required adaptation of the brace protocol, and one-quarter needed additional surgery. The Ponseti treatment was mainly reapplied if feet presented with relapses or residues until the age of 5. Interpretation - Practitioners should especially be aware of equinus/decreased dorsiflexion, adduction, and active supination as a sign of a residual or relapsed clubfoot. Due to the heterogeneous profiles of these clubfeet, treatment strategy should be based on a step-by step approach including recasting, bracing, and if necessary surgical intervention.

Impactfactor 3.076

Incidence of congenital idiopathic clubfoot in the Netherlands

Besselaar AT, Kamp MC, Reijman M, **van der Steen M**

J Pediatr Orthop B. 2018 Nov;27(6):563-567

The incidence of clubfoot patients is an important factor for centralization of care. Medical records of 21 accredited clubfoot centers were selected using the diagnosis treatment codes and checked to confirm diagnosis. All idiopathic clubfoot cases born during 2013-2014 were analyzed with respect to sex, affected foot, regional distribution, and seasonal variation. Among the 346?522 live births, 377 idiopathic clubfoot cases were registered. The incidence of the congenital idiopathic clubfoot in the Netherlands during 2013 and 2014 was 1.09 per 1000 live births, indicating that every year, ~200 children with one or two clubfeet are born in the Netherlands. On the basis of this finding, we can start to refine clubfoot care.

Impactfactor 0.610

Influence of cast change interval in the Ponseti method: A systematic review

Giesberts RB, **van der Steen MC**, Maathuis PG, **Besselaar AT**, Hekman EE, Verkerke GJ

PLoS One. 2018 Jun 22;13(6):e0199540

BACKGROUND:
Clubfeet are commonly treated using the Ponseti method. This method involves weekly manipulation and casting which gradually corrects the position of the foot. However, the reasons for following a weekly interval are not clear.
QUESTION / PURPOSE:
The aim is to investigate the influence of the cast change interval on treatment outcomes in the Ponseti method.
METHODS:
We performed a systematic review of comparative studies in which the cast change interval was varied. Scientific databases were searched for relevant publications, screened for eligibility and assessed for a risk of bias. A 'best evidence' synthesis tool was used to synthesize the results of the included studies and draw conclusions from relevant clinical outcomes.
RESULTS:
Nine papers matched the inclusion criteria, which provided data of 587 subjects who had a total of 870 clubfeet. There is strong evidence for a positive relation between cast change interval and treatment duration. However, there is no evidence for any relation between the cast change interval and the required number of casts, tenotomy rate, required surgery or failure rate.
CONCLUSIONS:
Accelerated versions are as effective and safe as the traditional Ponseti method. However, more research is needed to assess the long-term results and to identify an optimal cast change interval.

Impactfactor 2.766

Long-term follow-up after bilateral percutaneous epiphysiodesis around the knee to reduce excessive predicted final height

Goedegebuure WJ, Jonkers F, Boot AM, Bakker-van Waarde WM, van Tellingen V, Heeg M, Odink RJ, van Douveren F, **Besselaar AT, van der Steen MC**

Arch Dis Child. 2018 Mar;103(3):219-223. Epub 2017 Oct 13

CONTEXT:
Percutaneous epiphysiodesis (PE) around the knee to reduce predicted excessive final height. Studies until now included small numbers of patients and short follow-up periods.
OBJECTIVE AND DESIGN:
This Dutch multicentre, long-term, retrospective, follow-up study aimed to assess adult height (AH), complications, knee function and patient satisfaction after PE. The primary hypothesis was that PE around the knee in constitutionally tall boys and girls is an effective treatment for reducing final height with low complication rates and a high level of patient satisfaction.
PARTICIPANTS:
77 treated adolescents and 60 comparisons.
INTERVENTION:
Percutaneous epiphysiodesis.
OUTCOME:
AH, complications, knee function, satisfaction.
RESULTS:
In the PE-treated group, final height was 7.0?cm (±6.3?cm) lower than predicted in boys and 5.9?cm (±3.7?cm) lower than predicted in girls. Short-term complications in file search were seen in 5.1% (three infections, one temporary nerve injury), one requiring reoperation. Long-term complications in file search were seen in 2.6% (axis deformity 1.3%, prominent head of fibula 1.3%). No significant difference in knee function was found between treated cases and comparisons. Satisfaction was high in both the comparison and PE groups; most patients in the PE group recommended PE as the treatment for close relatives with tall stature.
CONCLUSION:
PE is safe and effective in children with predicted excessive AH. There was no difference in patient satisfaction between the PE and comparison group. Careful and detailed counselling is needed before embarking on treatment.

Impactfactor 3.258

Measurement properties of the OARSI core set of performance-based measures for hip osteoarthritis: a prospective cohort study on reliability construct validity and responsiveness in 90 hip osteo-arthritis patients

Tolk JJ, Janssen RPA, Prinsen CSAC, **van der Steen MMC**, Bierma Zeinstra SMA, Reijman M

Acta Orthop. 2018 Nov 19:1-6. [Epub ahead of print]

Background and purpose - Improvement of physical function is one of the main treatment goals in severe hip osteoarthritis (OA) patients. The Osteoarthritis Research Society International (OARSI) has identified a core set of performance-based tests to assess the construct physical function: 30-s chair stand test (30-s CST), 4x10-meter fast-paced walk test (40 m FPWT), and a stair-climb test. Despite this recommendation, available evidence on the

measurement properties is limited. We evaluated the reliability, validity, and responsiveness of these performance-based measures in patients with hip OA scheduled for total hip arthroplasty (THA). Patients and methods - Baseline and 12-month follow-up measurements were prospectively obtained in 90 end-stage hip OA patients who underwent THA. As there is no gold standard for comparison, the hypothesis testing method was used for construct validity and responsiveness analysis. A test can be assumed valid if =75% of predefined hypotheses are confirmed. A subgroup (n = 30) underwent test-retest measurements for reliability analysis. The Oxford Hip Score, Hip injury and Osteoarthritis Outcome Score-Physical Function Short Form, pain during activity score, and muscle strength were used as comparator instruments. Results - Test-retest reliability was appropriate; intraclass correlation coefficient values exceeded 0.70 for all 3 tests. None of the performance-based measures reached 75% hypothesis confirmation for the construct validity or responsiveness analysis. Interpretation - The performance-based tests have good reliability in the assessment of physical function. Construct validity and responsiveness, using patient-reported measures and muscle strength as comparator instruments, could not be confirmed. Therefore, our findings do not justify their use for clinical practice.

Impactfactor 3.076

Quantifying joint stiffness in clubfoot patients

van der Steen MC, Andrei PA, van Rietbergen , Ito K, **Besselaar AT**

Clin Biomech (Bristol, Avon). 2018 Oct 27;60:185-190

BACKGROUND:

In clinical practice, clubfeet feel stiffer compared to healthy feet. Furthermore, the clinical impression is that stiffer clubfeet have a higher tendency to relapse. Until now, no objective measure has been available to determine the stiffness of clubfeet. The goal of the current project was to objectively quantify ankle and subtalar joint stiffness in clubfeet patients and to compare this stiffness between clubfeet patients and healthy controls using a newly developed measurement device.

METHODS:

The newly developed Torque-Displacement-Handpiece in combination with an adjusted Abduction Dorsiflexion Mechanism clubfoot-brace, made it possible to move a foot over two rotational axis, while continuously capturing the applied torque and the achieved angulation. Based on this information, stiffness of the ankle and subtalar joint were assessed for 11 clubfoot patients with 17 clubfeet and 11 healthy subjects with 22 healthy feet.

FINDINGS:

With the Torque-Displacement-Handpiece measuring device it was possible to measure torque, angulation and stiffness in a reliable and precise manner. Clubfoot patients showed less angulation and a higher stiffness for measurements over the ADM subtalar axis compared to controls. After adjusting for shoe size, the stiffness for measurements over the ADM tibiotalar axis was also significantly higher in clubfeet than controls.

INTERPRETATION:

Overall, these results indicate that clubfoot patients have a higher ankle and subtalar joint stiffness in the affected joint compared to healthy controls. In the future, the Torque-Displacement-Handpiece could be used to monitor stiffness of clubfeet during treatment, and as such, play a potential role in the early detection of relapsing clubfeet.

Impactfactor 2.584

Should the Extended Lateral Approach Remain Part of Standard Treatment in Displaced Intra-articular Calcaneal Fractures?

Jansen SC, Bransen J, van Montfort G, **Besselaar AT**, van der Veen AH

J Foot Ankle Surg. 2018 Nov - Dec;57(6):1120-1124

The aim of this study was to evaluate the results of open reduction and internal fixation through the extended lateral approach (ELA) in displaced intra-articular calcaneal fractures and to determine whether this approach should remain part of standard therapy. This retrospective cohort study included 60 patients with 64 displaced intra-articular calcaneal fractures who underwent surgical treatment through the ELA. Outcome measures were the visual analog scale foot and ankle (VAS FA), the American Orthopedic Foot and Ankle Society (AOFAS) score, surgical site infections (SSIs), and reoperations. We determined the AOFAS score for 40 patients with 42 fractures, and 42 patients with 44 fractures completed the VAS FA questionnaire. The mean VAS FA score was 61.0 ± 23.4 and the median AOFAS score was 83 (range 33 to 100), with 55% good to excellent scores. We found 10.9% superficial SSIs successfully treated with antibiotics. In 4.7% of patients a deep SSI was diagnosed, wherefore premature implant removal was necessary. Patients with an SSI did not have significantly lower VAS FA or AOFAS scores than did patients without an SSI (p = .318 and p = .766, respectively). Implant removal in absence of SSIs was necessary in 17 patients because of pain, and 3 patients needed secondary arthrodesis because of persistent pain. We concluded that the ELA proved to be a safe procedure, and moreover the most common complications did not influence the long-term outcomes of patients. However, recent literature demonstrates that less invasive techniques seem to exceed the ELA with respect to wound complications.

Impactfactor 1.138

Pamm

Betere overleving na een Staphylococcus aureus-bacteriëmie bij betrokkenheid van het antibioticateam en bundelaanpak?

M. van den Hurk, J. Fonville, H.S.M. Ammerlaan, C. Miedema, S. Sanders, **I Overdevest**

TVI : tijdschrift voor infectieziekten, 2018;13(1):3-10

Geen abstract beschikbaar

Impactfactor --

Improved diagnostic stratification of digitised Barrett's oesophagus biopsies by p53 immunohistochemical staining

van der Wel MJ, Duits LC, Pouw RE, Seldenrijk CA, Offerhaus GJ, Visser M, Ten Kate FJ, Biermann K, Brosens LA, Doukas M, **Huysentruyt C**, Karrenbeld A, Kats-Ugurlu G, van der Laan JS, **van Lijnschoten GI**, Moll FC, Ooms AH, van der Valk H, Tijssen JG, Bergman JJ, Meijer SL

Histopathology. 2018 May;72(6):1015-1023

AIMS:

Interobserver agreement for dysplasia in Barrett's oesophagus (BO) is low, and guidelines advise expert review of dysplastic cases. The aim of this study was to assess the added value of p53 immunohistochemistry (IHC) for the homogeneity within a group of dedicated gastrointestinal (GI) pathologists.

METHODS AND RESULTS:

Sixty-single haematoxylin and eosin (HE) slide referral BO cases [20 low-grade dysplasia (LGD); 20 high-grade dysplasia (HGD); and 20 non-dysplastic BO reference cases] were digitalised and independently assessed twice in random order by 10 dedicated GI pathologists. After a 'wash-out' period, cases were reassessed with the addition of a corresponding p53 IHC slide. Outcomes were: (i) proportion of 'indefinite for dysplasia' (IND) diagnoses; (ii) interobserver agreement; and (iii) diagnostic accuracy as compared with a consensus 'gold standard' diagnosis defined at an earlier stage by five core expert BO pathologists after their assessment of this case set. Addition of p53 IHC decreased the mean proportion of IND diagnoses from 10 of 60 to eight of 60 (P = 0.071). Mean interobserver agreement increased significantly from 0.45 to 0.57 (P = 0.0021). The mean diagnostic accuracy increased significantly from 72% to 82% (P = 0.0072) after p53 IHC addition.

CONCLUSION:

Addition of p53 IHC significantly improves the histological assessment of BO biopsies, even within a group of dedicated GI pathologists. It decreases the proportion of IND diagnoses, and increases interobserver agreement and diagnostic accuracy. This justifies the use of accessory p53 IHC within our upcoming national digital review panel for BO biopsy cases.

Impactfactor *3.267*

Preliminary results of a cohort study of induction chemotherapy-based treatment for locally recurrent rectal cancer

van Zoggel DMGI, Bosman SJ, Kusters M, Nieuwenhuijzen GAP, Cnossen JS, Creemers GJ, **van Lijnschoten G**, Rutten HJT.

Br J Surg. 2018 Mar;105(4):447-452.Epub 2017 Nov 23

BACKGROUND: A significant number of patients treated for locally recurrent rectal cancer have local or systemic failure, especially after incomplete surgical resection. Neoadjuvant treatment regimens in patients who have already undergone preoperative (chemo)radiotherapy for the primary tumour are limited. The objective of the present study was to evaluate the influence of a neoadjuvant regimen incorporating induction chemotherapy (ICT) in patients with locally recurrent rectal cancer who had preoperative (chemo)radiotherapy for the primary cancer or An Earlier Local reccurence.

METHODS: Patients were treated with a sequential neoadjuvant regimen including three or four cycles of 5-fluorouracil and oxaliplatin-containing chemotherapy. When no progressive disease was found at evaluation, neoadjuvant treatment was continued with chemoradiation therapy (CRRT) using 30?Gy with concomitant capecitabine. If there was a response to ICT, the patient was advised to continue with systemic chemotherapy after CRRT as consolidation chemotherapy while waiting for resection. These patients were compared with patients who received CRRT alone in the same time interval.

RESULTS: Of 58 patients who had ICT, 32 (55 per cent) had surgery with clear resection margins, of whom ten (17 per cent) exhibited a pathological complete response (pCR). The remaining 26 patients had 23 R1 and three R2 resections. In 71 patients who received CRRT, a similar rate of R0 (35 patients) and R1 (36) resection was found (P?=?0·506), but only three patients (4 per cent) had a pCR (P?=?0·015).

CONCLUSION: The incorporation of ICT in neoadjuvant regimens for locally recurrent rectal cancer is a promising strategy.

Impactfactor *5.433*

Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer

Schaap DP, Ogura A, Nederend J, Maas M, Cnossen JS, Creemers GJ, **van Lijnschoten I**, Nieuwenhuijzen GA, Rutten HJ, Kusters M

Br J Surg. 2018 Dec;105(13):1844-1852

BACKGROUND:
Lateral nodal disease in rectal cancer remains a subject of debate and is treated differently in the East and the West. The predictive value of lateral lymph node and MRI-detected extramural vascular invasion (mrEMVI) features on oncological outcomes was assessed in this study.
METHODS:
In this retrospective cohort study, data on patients with cT3-4 rectal cancer within 8?cm from the anal verge were considered over a 5-year period (2009-2013). Lateral lymph node size, malignant features and mrEMVI features were evaluated and related to oncological outcomes.
RESULTS:
In total, 192 patients were studied, of whom 30 (15·6 per cent) underwent short-course radiotherapy and 145 (75·5 per cent) received chemoradiotherapy. A lateral lymph node short-axis size of 10?mm or more was associated with a significantly higher 5-year lateral/presacral local recurrence rate of 37 per cent, compared with 7·7 per cent in nodes smaller than 10?mm (P?=?0·041). Enlarged nodes did not result in a higher 5-year rate of distant metastasis (23 per cent versus 27·7 per cent in nodes smaller than 10?mm; P?=?0·563). However, mrEMVI positivity was related to more metastatic disease (5-year rate 43 versus 26·3 per cent in the mrEMVI-negative group; P?=?0·014), but not with increased lateral/presacral recurrence. mrEMVI occurred in 46·6 per cent of patients with nodes smaller than 10?mm, compared with 29 per cent in patients with nodes of 10?mm or larger (P?=?0·267).
CONCLUSION:
Although lateral nodal disease is more a local problem, mrEMVI mainly predicts distant recurrence. The results of this study showed an unacceptably high local recurrence rate in patients with a short axis of 10?mm or more, despite neoadjuvant (chemo)radiotherapy

Impactfactor 5.433

Review: Pathology and Its Clinical Relevance of Mucinous Appendiceal Neoplasms and Pseudomyxoma Peritonei

Legué LM, Creemers GJ, de Hingh IHJT, Lemmens VEPP, **Huysentruyt CJ**

Clin Colorectal Cancer. 2018 Dec 6. pii: S1533-0028(18)30467-5. [Epub ahead of print]

Until recently, many classifications existed for the terminology and histopathologic classification of appendiceal mucinous neoplasms, mucinous appendiceal adenocarcinomas, and pseudomyxoma peritonei (PMP). A major accomplishment was achieved by consensus-based histopathologic classifications on behalf of the Peritoneal Surface Oncology Group International regarding mucinous appendiceal tumours and PMP. As different classifications were used over the years and also owing to the rare nature of these tumors, many clinicians are not familiar with the terminology and the impact on patient management. Hence, an overview concerning mucinous appendiceal neoplasms, mucinous appendiceal adenocarcinomas, and PMP is provided to serve as an introduction into the basic morphology of these tumors with tentative recommendations for management.

Impactfactor 3.861

Safety and effectiveness of SGM-101 a fluorescent antibody targeting carcinoembryonic antigen for intraoperative detection of colorectal cancer: a dose-escalation pilot study

Boogerd LSF, Hoogstins CES, Schaap DP, Kusters M, Handgraaf HJM, van der Valk MJM, Hilling DE, Holman FA, Peeters KCMJ, Mieog JSD, van de Velde CJH, Farina-Sarasqueta A, **van Lijnschoten I**, Framery B, Pèlegrin A, Gutowski M, Nienhuijs SW, de Hingh IHJT, Nieuwenhuijzen GAP, Rutten HJT, Cailler F, Burggraaf J, et al

Lancet Gastroenterol Hepatol. 2018 Mar 3(3):181-191. Epub 2018 Jan 30

BACKGROUND:
Tumour-targeted fluorescence imaging has the potential to advance current practice of oncological surgery by selectively highlighting malignant tissue during surgery. Carcinoembryonic antigen (CEA) is overexpressed in 90% of colorectal cancers and is a promising target for colorectal cancer imaging. We aimed to assess the tolerability of SGM-101, a fluorescent anti-CEA monoclonal antibody, and to investigate the feasibility to detect colorectal cancer with intraoperative fluorescence imaging.
METHODS:
We did an open-label, pilot study in two medical centres in the Netherlands. In the dose-escalation cohort, we included patients (aged =18 years) with primary colorectal cancer with increased serum CEA concentrations (upper limit of normal of =3 ng/mL) since diagnosis, who were scheduled for open or laparoscopic tumour resection. In the expansion cohort, we included patients (aged =18 years) with recurrent or peritoneal metastases of colorectal cancer, with increasing serum concentrations of CEA since diagnosis, who were scheduled for open surgical resection. We did not mask patients, investigators, or anyone from the health-care team. We assigned patients using a 3?+?3 dose design to 5 mg, 7·5 mg, or 10 mg of SGM-101 in the dose-escalation cohort. In the expansion

cohort, patients received a dose that was considered optimal at that moment of the study but not higher than the dose used in the dose-escalation cohort. SGM-101 was administered intravenously for 30 min to patients 2 or 4 days before surgery. Intraoperative imaging was done to identify near-infrared fluorescent lesions, which were resected and assessed for fluorescence. The primary outcome was tolerability and safety of SGM-101, assessed before administration and continued up to 12 h after dosing, on the day of surgery, the first postoperative day, and follow-up visits at the day of discharge and the first outpatient clinic visit. Secondary outcomes were effectiveness of SGM-101 for detection of colorectal cancer, assessed by tumour-to-background ratios (TBR); concordance between fluorescent signal and tumour status of resected tissue; and diagnostic accuracy in both cohorts. This trial is registered with the Nederlands Trial Register, number NTR5673, and ClinicalTrials.gov, number NCT02973672.

FINDINGS:

Between January, 2016, and February, 2017, 26 patients (nine in the dose-escalation cohort and 17 in the expansion cohort) were included in this study. SGM-101 did not cause any treatment-related adverse events, although three possibly related mild adverse events were reported in three (33%) of nine patients in the dose-escalation cohort and five were reported in three (18%) of 17 patients in the expansion cohort. Five moderate adverse events were reported in three (18%) patients in the expansion cohort, but they were deemed unrelated to SGM-101. No changes in vital signs, electrocardiogram, or laboratory results were found after administration of the maximum dose of 10 mg of SGM-101 in both cohorts. A dose of 10 mg, administered 4 days before surgery, showed the highest TBR (mean TBR 6·10 [SD 0·42] in the dose-escalation cohort). In the expansion cohort, 19 (43%) of 43 lesions were detected using fluorescence imaging and were not clinically suspected before fluorescent detection, which changed the treatment strategy in six (35%) of 17 patients. Sensitivity was 98%, specificity was 62%, and accuracy of fluorescence intensity was 84% in the expansion cohort.

INTERPRETATION:

This study presents the first clinical use of CEA-targeted detection of colorectal cancer and shows that SGM-101 is safe and can influence clinical decision making during the surgical procedure for patients with colorectal cancer.

Impactfactor --

Salvage endoscopic resection in patients with esophageal adenocarcinoma after chemoradiotherapy

Noordzij IC, Curvers WL, **Huysentruyt CJ**, Nieuwenhuijzen GA, Creemers GJ, van der Sangen MJ, Schoon EJ

Endosc Int Open. 2018 Sep;6(9):E1126-E1129

Background and study aims For early esophageal adenocarcinoma, endoscopic resection is an accepted curative treatment with an excellent long-term prognosis. Case series from Japan have reported endoscopic resection of residual esophageal squamous cell carcinoma after chemoradiotherapy. This is the first report describing endoscopic resection of residual esophageal adenocarcinoma after chemoradiotherapy. Two patients with advanced esophageal adenocarcinoma had been treated with chemoradiotherapy because comorbidity precluded esophageal resection. When residual tumor was observed endoscopically, complete remission was achieved by salvage endoscopic therapy alone or in combination with argon plasma coagulation (APC). Both patients achieved long-term sustained remission and died of non-tumor-related causes.

Impactfactor --

The Dutch Pancreas Biobank Within the Parelsnoer Institute: A Nationwide Biobank of Pancreatic and Periampullary Diseases

Strijker M, Gerritsen A, van Hilst J, Bijlsma MF, Bonsing BA, Brosens LA, Bruno MJ, van Dam RM, Dijk F, van Eijck CH, Farina Sarasqueta A, Fockens P, Gerhards MF, Groot Koerkamp B, van der Harst E, de Hingh IH, van Hooft JE, **Huysentruyt CJ**, Kazemier G, Klaase JM, van Laarhoven CJ, van Laarhoven HW, Liem MS, de Meijer VE, van Rijssen LB, van Santvoort HC, Suker M, Verhagen JH, Verheij J, Verspaget HW, Wennink RA, Wilmink JW, Molenaar IQ, Boermeester MA, Busch OR, Besselink MG; Dutch Pancreatitis Study Group and Dutch Pancreatic Cancer Group

Pancreas. 2018 Apr;47(4):495-501

OBJECTIVES:

Large biobanks with uniform collection of biomaterials and associated clinical data are essential for translational research. The Netherlands has traditionally been well organized in multicenter clinical research on pancreatic diseases, including the nationwide multidisciplinary Dutch Pancreatic Cancer Group and Dutch Pancreatitis Study Group. To enable high-quality translational research on pancreatic and periampullary diseases, these groups established the Dutch Pancreas Biobank.

METHODS:

The Dutch Pancreas Biobank is part of the Parelsnoer Institute and involves all 8 Dutch university medical centers and 5 nonacademic hospitals. Adult patients undergoing pancreatic surgery (all indications) are eligible for inclusion. Preoperative blood samples, tumor tissue from resected specimens, pancreatic cyst fluid, and follow-up blood samples are collected. Clinical parameters are collected in conjunction with the mandatory Dutch Pancreatic Cancer Audit.

RESULTS:

Between January 2015 and May 2017, 488 patients were included in the first 5 participating centers: 4 university

medical centers and 1 nonacademic hospital. Over 2500 samples were collected: 1308 preoperative blood samples, 864 tissue samples, and 366 follow-up blood samples.

CONCLUSIONS:

Prospective collection of biomaterials and associated clinical data has started in the Dutch Pancreas Biobank. Subsequent translational research will aim to improve treatment decisions based on disease characteristics.

Impactfactor 2.958

The Value of (18)F-FDG PET/CT in Diagnosis and During Follow-up in 273 Patients with Chronic Q Fever

Kouijzer IJE, Kampschreur LM, Wever PC, Hoekstra C, van Kasteren MEE, de Jager-Leclercq MGL, Nabuurs-Franssen MH, **Wegdam-Blans MCA**, Ammerlaan HSM, Buijs J, Geus-Oei LF, Oyen WJG, Bleeker-Rovers CP

J Nucl Med. 2018 Jan 59(1):127-133. Epub 2017 May 25

In 1%-5% of all acute Q fever infections, chronic Q fever develops, mostly manifesting as endocarditis, infected aneurysms, or infected vascular prostheses. In this study, we investigated the diagnostic value of 18F-FDG PET/CT in chronic Q fever at diagnosis and during follow-up. Methods: All adult Dutch patients suspected of chronic Q fever who were diagnosed since 2007 were retrospectively included until March 2015, when at least one 18F-FDG PET/CT scan was obtained. Clinical data and results from 18F-FDG PET/CT at diagnosis and during follow-up were collected. 18F-FDG PET/CT scans were prospectively reevaluated by 3 nuclear medicine physicians using a structured scoring system. Results: In total, 273 patients with possible, probable, or proven chronic Q fever were included. Of all 18F-FDG PET/CT scans performed at diagnosis, 13.5% led to a change in diagnosis. Q fever-related mortality rate in patients with and without vascular infection based on 18F-FDG PET/CT was 23.8% and 2.1%, respectively (P = 0.001). When 18F-FDG PET/CT was added as a major criterion to the modified Duke criteria, 17 patients (1.9-fold increase) had definite endocarditis. At diagnosis, 19.6% of 18F-FDG PET/CT scans led to treatment modification. During follow-up, 57.3% of 18F-FDG PET/CT scans resulted in treatment modification. Conclusion:18F-FDG PET/CT is a valuable technique in diagnosis of chronic Q fever and during follow-up, often leading to a change in diagnosis or treatment modification and providing important prognostic information on patient survival.

Impactfactor 7.439

Plastische Chirurgie

De Implementatie van de FACE-Qhuidkankermodule in Nederland

Brouwer P, Westra I, Ottenhof MJ, **Hoogbergen MM**, Mouës-Vink

Ned. Tijdschr. Plast. Chir. 2018 (9):1, 39-41

Excisie van huidkanker in het gelaat kan mutilerend zijn. Het sluiten van resterende defecten na excisie kent dan ook vele uitdagingen. Werden er in 1973 nog 4000 nieuwe gevallen van basaalcelcarcinomen (BCC's) gediagnosticeerd, stond de teller in 2014 reeds op 37.700. Van alle BCC's bevindt ongeveer 60% zich in het hoofdhalsgebied. Er is onderzoek gedaan naar effectiviteit van excisies maar niet naar de tevredenheid van de patiënt. De FACE-Q is een 'patient reported outcome measure' (PROM) die ons in staat stelt om lichamelijke klachten, tevredenheid met uiterlijk, gezondheidsgerelateerde levenskwaliteit en psychologisch welzijn te meten. Dit met als doel om te komen tot een patient-centered-model, waarbij shared decision-making leidt tot de keuze voor de juiste behandeling. Het Catharina Ziekenhuis Eindhoven (CZE) en het Medisch Centrum Leeuwarden (MCL) bundelen de krachten in het verzamelen van data en nodigen andere behandelcentra uit zich aan te sluiten bij dit project.

Impactfactor --

Development of the BODY-Q Chest Module Evaluating Outcomes following Chest Contouring Surgery

Klassen AF, Kaur M, Poulsen L, Fielding C, Geerards D, van de Grift TC, **Hoogbergen M**, Juhl CB, Lorenzen MM, McEvenue G, McLean H, Moliver C, Mullender MG, Panchapakesan V, Repo JP, Rose M, Sørensen JA, Støving RK, Pusic AL

Plast Reconstr Surg. 2018 Dec 142(6):1600-1608

BACKGROUND:

Plastic surgery to improve chest appearance is becoming increasingly popular. The BODY-Q is a patient-reported outcome instrument designed for weight loss and/or body contouring. In this article, the authors describe the development of a new module for masculinizing chest contouring surgery.

METHODS:

Qualitative methods were used to develop the BODY-Q Chest Module, which was subsequently field-tested in Canada, the United States, The Netherlands, and Denmark between June of 2016 and June of 2017. Participants were aged 16 years or older and seen for gynecomastia, weight loss, or transman chest surgery. Data were collected using either a Web-based application or paper questionnaire. Rasch measurement theory analysis was performed.

RESULTS:

The sample included 739 participants (i.e., 174 gynecomastia, 224 weight loss, and 341 gender-affirming). Rasch measurement theory analysis refined a 10-item chest scale and a five-item nipple scale. All items had ordered thresholds and good item fit, and scales evidenced reliability [i.e., person separation index and Cronbach alpha values were 0.95 and 0.98 (chest scale) and 0.87 and 0.94 (nipple scale), respectively]. Scores for both scales correlated more strongly with similar (satisfaction with the body) versus dissimilar (psychological and social function) BODY-Q scales. The mean scores for the chest and nipple scales were significantly higher ($p < 0.001$ on independent samples t tests) in participants who were postoperative compared with preoperative.

CONCLUSION:

This new BODY-Q Chest Module is a clinically meaningful and scientifically sound patient-reported outcome instrument that can be used to measure outcomes for masculinizing chest contouring surgery.

Impactfactor *3.475*

The kinetics and mechanism of bone morphogenetic protein 2 release from calcium phosphate-based implant-coatings

Liu Y, **Schouten C**, Boerman O, Wu G, Jansen JA, Hunziker EB

J Biomed Mater Res A. 2018 Sep 106(9):2363-2371

Biomimetically deposited calcium phosphate-based coatings of prostheses can serve as a vehicle for the targeted delivery of growth factors to the local implant environment. Based on indirect evidence in previous studies we hypothesize that such agents are liberated gradually from the coating via a cell-mediated degradation. In the present study, we tested this hypothesis by investigating the release mechanism and its kinetics by use of a radiolabeled osteogenic agent (131 I-BMP-2) under conditions in which native cell populations with a coating-degradative potential were either absent or present. The release of 131 I-BMP-2 was monitored for 5 weeks, either in vitro or after implantation at an ectopic (subcutaneous) site in rats in vivo. Only from implants that bore a coating-incorporated depot of bone morphogenetic protein 2 (BMP-2) was the agent released slowly and steadily over 5 weeks, that is, 50% of the loaded dose was liberated in vivo (5 to 10% weekly), as against 14.6% in vitro (less than 1% weekly). The coatings bearing an incorporated depot of BMP-2 underwent significant cell-mediated degradation, whereas under cell-free conditions no degradation occurred, and the spontaneous release of BMP-2 was negligible. Our findings confirm this carrier system to be a suitable vehicle for the sustained and cell-mediated delivery of BMP-2.

Impactfactor *3.231*

Trends on Axillary Surgery in Nondistant Metastatic Breast Cancer Patients Treated Between 2011 and 2015: A Dutch Population-based Study in the ACOSOG-Z0011 and AMAROS Era

Poodt IG, Spronk PE, Vugts G, van Dalen T, Peeters MT, Rots ML, Kuijer A, Nieuwenhuijzen GA, Schipper RJ

Ann Surg. 2018 Dec;268(6):1084-1090

OBJECTIVES:

To evaluate patterns of care in axillary surgery for Dutch clinical T1-4N0M0 (cT1-4N0M0) breast cancer patients and to assess the effect of the American College for Surgeons Oncology Group (ACOSOG)-Z0011 and After Mapping of the Axilla: Radiotherapy Or Surgery (AMAROS) trial on axillary surgery patterns in Dutch cT1-2N0M0 sentinel node positive breast cancer patients.

BACKGROUND:

Since publication of the ACOSOG-Z0011 and AMAROS trial, omitting a completion axillary lymph node dissection (cALND) in sentinel node positive breast cancer patients is proposed in selected patients.

METHODS:

Data were obtained from the nationwide Nationaal Borstkanker Overleg Nederland breast cancer audit. Descriptive analyses were used to demonstrate trends in axillary surgery. Multivariable logistic regression analyses were used to identify factors associated with the omission of cALND in cT1-2N0M0 sentinel node-positive breast cancer patients.

RESULTS:

Between 2011 and 2015 in cT1-4N0M0 breast cancer patients, the use of sentinel lymph node biopsy as definitive axillary staging increased from 72% to 93%, and (c)ALND as definitive axillary staging decreased from 24% to 6% ($P < 0.001$). The use of cALND decreased from 75% to 17% in cT1-2N0 sentinel node-positive patients ($P < 0.001$). Earlier year of diagnosis, lower age, primary mastectomy, invasive lobular subtype, increasing tumor grade, and treatment in a nonteaching hospital were associated with a lower probability of omitting cALND ($P < 0.001$).

CONCLUSIONS:

This study shows a trend towards less extensive axillary surgery in Dutch cT1-T4N0M0 breast cancer patients; illustrated by an overall increase of sentinel lymph node biopsy and decrease in cALND. Despite this trend, particularly noticed in cT1-2N0 sentinel node-positive patients after publication of the ACOSOG-Z0011 and AMAROS trial, variations in patterns of care in axillary surgery are still present.

Impactfactor 1.536

Trocar port scar quality in morbidly obese patients after bariatric surgery

de Vries CEE, Dekker AC, van Veen RN, **van der Zeeuw FT**, Coblijn UK, Brölmann FE, van Wagensveld BA

Surg Obes Relat Dis. 2018 May;14(5):616-622. Epub 2018 Feb 7

BACKGROUND:

Patient satisfaction of scar quality and their influence on health-related quality of life (HRQoL) have never been investigated in morbidly obese patients.

OBJECTIVES:

Our objectives were (1) to assess scar quality 1 year post laparoscopic bariatric surgery by means of the Patient and Observer Scar Assessment Scale (POSAS), and (2) to examine the influence of patients' perception of scar quality on patients' HRQoL.

SETTING:

A large Bariatric Center of Excellence in the Netherlands.

METHODS:

This was a descriptive pilot study of patients who underwent primary laparoscopic bariatric surgery. One year after surgery, patients and 2 observers completed the POSAS. HRQoL was assessed by using the RAND-36. Agreement of POSAS scores between patients and observers was calculated with intraclass correlation coefficient. Correlations between POSAS scores and HRQoL scores were calculated with Spearman's rho.

RESULTS:

A total of 50 patients were included. Patients scored their scar quality worse than observers (21 versus 15-16), particularly on visual parameters (4-5 versus 2-3). Patients and observers showed poor agreement on all POSAS items (intraclass correlation coefficient = .16-.32). No significant correlations were detected between POSAS and HRQoL scores.

CONCLUSION:

While patient scar quality satisfaction was relatively low after bariatric surgery, these outcomes were not correlated with HRQoL. Bariatric surgeons should be aware that patients could have a different view on scar quality compared with them. This realization is important to manage patient expectations regarding scar quality after bariatric surgery. Effective communication may improve patient satisfaction as an outcome.

Impactfactor 3.900

Psychologie

A prospective cohort study assessing differences in cosmetic appreciation of lateralization while smiling in patients with a peripheral facial palsy

Luijmes RE, Beurskens CHG, Pouwels S, Ingels KJAO

Laterality. 2018 Jul;23(4):381-390. Epub 2017 Apr 26

We investigated the differences in cosmetic appreciation of patients with a left and a right peripheral facial palsy (PFP) while smiling. Smiling pictures of patients with a facial palsy with House-Brackmann II-VI were reversed as a mirror image and offered as a pair of pictures, together with the true image. Twenty-six patients with a PFP and 24 medical professionals familiar with facial palsy were asked to choose the most attractive photograph. Patients rated their own pictures. Medical professionals preferred pictures of patients with a right and left PFP in, respectively, a mean of 43.00?±?12.25% and 57.00?±?12.28% (p?=?.005). Patients with a right PFP chose their mirror and true image in 65% and 35% in smiling pictures (p?=?.01). Patients with a left PFP facial palsy chose their mirror and true image in 58% and 42% in smiling pictures (p?=?.02). The House-Brackmann score and age of the patients did not influence preferences of medical professionals and patients. We have found that medical professionals have a significant preference for pictures of patients with a left PFP. Patients with a left PFP and right PFP significantly prefer their mirror image in smiling pictures.

Impactfactor *1.388*

Radiologie

A decrease in blood pressure is associated with unfavorable outcome in patients undergoing thrombectomy under general anesthesia

Treurniet KM, Berkhemer OA, Immink RV, Lingsma HF, Ward-van der Stam VM, Hollmann MW, Vuyk J, van Zwam WH, van der Lugt A, van Oostenbrugge RJ, Dippel DW, Coutinho JM, Roos YB, Marquering HA1, Majoie CB; MR CLEAN investigators* : Keizer K, **Tielbeek AV**

J Neurointerv Surg. 2018 Feb;10(2):107-111

BACKGROUND:
Up to two-thirds of patients are either dependent or dead 3 months after thrombectomy for acute ischemic stroke (AIS). Loss of cerebral autoregulation may render patients with AIS vulnerable to decreases in mean arterial pressure (MAP).
OBJECTIVE:
To determine whether a fall in MAP during intervention under general anesthesia (GA) affects functional outcome.
METHODS:
This subgroup analysis included patients from the MR CLEAN trial treated with thrombectomy under GA. The investigated variables were the difference between MAP at baseline and average MAP during GA (?MAP) as well as the difference between baseline MAP and the lowest MAP during GA (?LMAP). Their association with a shift towards better outcome on the modified Rankin Scale (mRS) after 90 days was determined using ordinal logistic regression with adjustment for prognostic baseline variables.
RESULTS:
Sixty of the 85 patients treated under GA in MR CLEAN had sufficient anesthetic information available for the analysis. A greater ?MAP was associated with worse outcome (adjusted common OR (acOR) 0.95 per point mm Hg, 95% CI 0.92 to 0.99). An average MAP during GA 10 mm Hg lower than baseline MAP constituted a 1.67 times lower odds of a shift towards good outcome on the mRS. For ?LMAP this association was not significant (acOR 0.97 per mm Hg, 95% CI 0.94 to 1.00, p=0.09).
CONCLUSIONS:
A decrease in MAP during intervention under GA compared with baseline is associated with worse outcome.

Impactfactor 3.524

Diagnosing internal herniation after laparoscopic Roux-en-Y gastric bypass: usefulness of systematically reviewing CT scans using ten signs

Ederveen JC, van Berckel MMG, **Jol S**, Nienhuijs SW, **Nederend J**

Eur Radiol. 2018 Sep 28(9):3583-3590. Epub 2018 Mar 2

OBJECTIVES:
To evaluate if systematically reviewing CT scans using ten signs leads to a better accuracy in diagnosing internal herniation (IH), compared to the original report. Also, the difference in accuracy was analysed between experience levels.
METHODS:
Patients were retrospectively included if they had undergone laparoscopic gastric bypass surgery between 2011 and 2014, and if additional radiological examination was performed for suspected IH between 2011 and 2016. Out of 1475 patients who had undergone laparoscopic gastric bypass surgery, 183 patients had one or more additional radiological examinations. A total of 245 CT scans were performed. All were reassessed by an abdominal radiologist, a radiology resident and intern. Assessment was done using ten signs from previous literature. Overall suspicion of IH was graded using a 5-point Likert scale. Accuracy was calculated using two-way contingency tables. Interobserver agreement was calculated using Fleiss' kappa.
RESULTS:
After 70 reoperations an IH was diagnosed in 48.6% (34/70). There was an increase in specificity for diagnosing IH with reoperation as reference from 52.8% (19/36; 95% CI 35.7-69.2%) in the original report to 86.1% (31/36; 95% CI 74.8-97.4%) for the radiologist (p = 0.002), 77.8% (28/36; 95% CI 64.2-91.4%) for the resident (p = 0.026) and 77.8% (28/36; 95% CI 64.2-91.4%) for the intern (p = 0.026). Interobserver agreement was good.
CONCLUSIONS:
Systematically reviewing CT scans using a list of ten CT signs can improve specificity and thereby reduce unnecessary reoperations, especially in a high pre-test probability population. The tool can be easily taught to less experienced readers.
KEY POINTS:
• Computed tomography is useful to diagnose internal herniation(IH) after gastric bypass surgery • Ten signs are described to improve CT diagnosis of IH • Systematically reviewing CT scans improves specificity • There is no difference in experience levels when using these ten signs.

Impactfactor 2.843

Double-Balloon Endoscopy after Incomplete Colonoscopy and Its Comparison with Computed Tomography Colonography

Hermans C, **uwDV**, Gilissen L

Clin Endosc. 2018 Jan 51(1):66-71. Epub 2018 Jan 10

BACKGROUND/AIMS:
Because of the national screening program for colorectal carcinoma in The Netherlands, the number of colonoscopies has increased. In case of incomplete colonoscopy, computed tomography colonography (CTC) and double-balloon colonoscopy (DBc) are alternative options. This study evaluated cecal intubation rate and pathology detection rate in the previously unexplored part of the colon, complication rate of DBc, and CTC results after incomplete colonoscopy.
METHODS:
Retrospective observational study in a tertiary referral hospital regarding DBc and CTC reports from cases with incomplete colonoscopy.
RESULTS:
Sixty-three DBcs were performed after incomplete colonoscopy. Cecal intubation rate was 95%. Detection rate was 58% (5% carcinoma and 3% high-grade dysplastic adenoma). CTC preceded 54% of DBcs and 62% of CTC findings were confirmed. In 16%, a biopsy was taken, and in 60%, an intervention (mostly polypectomy) was performed. One major complication (1.5%) occurred, i.e., arterial bleeding due to polypectomy necessitating right hemicolectomy. CTC (n=213) showed a possible lesion in 35%, and could be confirmed by follow-up endoscopy or surgery in 65%.
CONCLUSIONS:
DBc is effective and safe for completion of colon inspection in incomplete colonoscopy. In patients with a high likelihood of pathology, DBc is preferred over CTC.

Impactfactor --

Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data

Campbell BCV, van Zwam WH, Goyal M, Menon BK, Dippel DWJ, Demchuk AM, Bracard S, White P, Dávalos A, Majoie CBLM, van der Lugt A, Ford GA, de la Ossa NP, Kelly M, Bourcier R, Donnan GA, Roos YBWEM, Bang OY, Nogueira RG, Devlin TG, van den Berg LA, Clarençon F, Burns P, Carpenter J, Berkhemer OA, Yavagal DR, Pereira VM, Ducrocq X, Dixit A, Quesada H, Epstein J, Davis SM, Jansen O, Rubiera M, Urra X, Micard E, Lingsma HF, Naggara O, Brown S, Guillemin F, Muir KW, van Oostenbrugge RJ, Saver JL, Jovin TG, Hill MD, Mitchell PJ; HERMES collaborators: Keizer K, **Tielbeek AV**

Lancet Neurol. 2018 Jan 17(1):47-53. . Epub 2017 Dec 16

BACKGROUND:
General anaesthesia (GA) during endovascular thrombectomy has been associated with worse patient outcomes in observational studies compared with patients treated without GA. We assessed functional outcome in ischaemic stroke patients with large vessel anterior circulation occlusion undergoing endovascular thrombectomy under GA, versus thrombectomy not under GA (with or without sedation) versus standard care (ie, no thrombectomy), stratified by the use of GA versus standard care.
METHODS:
For this meta-analysis, patient-level data were pooled from all patients included in randomised trials in PuMed published between Jan 1, 2010, and May 31, 2017, that compared endovascular thrombectomy predominantly done with stent retrievers with standard care in anterior circulation ischaemic stroke patients (HERMES Collaboration). The primary outcome was functional outcome assessed by ordinal analysis of the modified Rankin scale (mRS) at 90 days in the GA and non-GA subgroups of patients treated with endovascular therapy versus those patients treated with standard care, adjusted for baseline prognostic variables. To account for between-trial variance we used mixed-effects modelling with a random effect for trials incorporated in all models. Bias was assessed using the Cochrane method. The meta-analysis was prospectively designed, but not registered.
FINDINGS:
Seven trials were identified by our search; of 1764 patients included in these trials, 871 were allocated to endovascular thrombectomy and 893 were assigned standard care. After exclusion of 74 patients (72 did not undergo the procedure and two had missing data on anaesthetic strategy), 236 (30%) of 797 patients who had endovascular procedures were treated under GA. At baseline, patients receiving GA were younger and had a shorter delay between stroke onset and randomisation but they had similar pre-treatment clinical severity compared with patients who did not have GA. Endovascular thrombectomy improved functional outcome at 3 months both in patients who had GA (adjusted common odds ratio (cOR) 1·52, 95% CI 1·09-2·11, p=0·014) and in those who did not have GA (adjusted cOR 2·33, 95% CI 1·75-3·10, p<0·0001) versus standard care. However, outcomes were significantly better for patients who did not receive GA versus those who received GA (covariate-adjusted cOR 1·53, 95% CI 1·14-2·04, p=0·0044). The risk of bias and variability between studies was assessed to be low.
INTERPRETATION:
Worse outcomes after endovascular thrombectomy were associated with GA, after adjustment for baseline

prognostic variables. These data support avoidance of GA whenever possible. The procedure did, however, remain effective versus standard care in patients treated under GA, indicating that treatment should not be withheld in those who require anaesthesia for medical reasons.

Impactfactor 27.138

Frequency and characteristics of additionally detected ipsilateral breast lesions following recall at screening mammography

Lameijer J, Coolen AM, **Nederend J**, Voogd AC, Tjan-Heijnen VC, Duijm LE

Breast. 2018 Aug 28;42:94-101

PURPOSE:
To determine the frequency and outcome of additionally detected ipsilateral breast abnormalities following recall at screening mammography.
METHODS AND MATERIALS:
We included a consecutive series of 130,338 screening mammograms obtained between January 1, 2014 and January 1, 2016. During 2-year follow-up, clinical data were collected of all recalls. Women with a bilateral recall (115) and women recalled for multiple lesions in one breast (165) were excluded from the analyses. Screening outcome parameters were determined for recalled women with or without evaluation of additional ipsilateral breast abnormalities following recall.
RESULTS:
A total of 3995 women were recalled (recall rate, 3.1%). In 258 (6.4%) of these women, another lesion was detected in the ipsilateral breast than the one for which she had been recalled. Biopsy was more frequently performed of additionally detected ipsilateral lesions than of recalled lesions (55.8% (144/258)) versus 39.7% (1375/3457), (p?<?0.001)). The proportion of malignancy in recalled lesions and additionally detected lesions was comparable (21.5% (743/3457) versus 19.0% (49/258), p?=?0.34). Of all 144 biopsies of additionally detected ipsilateral lesions, 9 revealed a synchronous tumour in addition to a malignant recalled lesion, and 33 biopsies revealed multicentric or multifocal tumours. In 5 women, the recalled lesion turned out to be benign, whereas the additional lesion in a different quadrant was malignant at biopsy. A total of 97 biopsies showed benign findings.
CONCLUSION:
A substantial proportion of women are analyzed for additional ipsilateral breast lesions following recall. These lesions are more frequently biopsied than recalled lesions, but have a comparable probability of being malignant. The majority of additionally detected cancerous lesions are part of multifocal or multicentric malignancies.

Impactfactor 2.951

Frequency and characteristics of contralateral breast abnormalities following recall at screening mammography

Lameijer JRC, Coolen AM, Voogd AC, Strobbe LJ, Louwman MWJ, Venderink D, Tjan-Heijnen VC, Duijm LEM

Eur Radiol. 2018 Oct 28(10):4205-4214. Epub 2018 Apr 17

Erratum in: Eur Radiol. 2018 Jun 25

PURPOSE:
To determine the frequency and characteristics of contralateral, non-recalled breast abnormalities following recall at screening mammography.
METHODS: We included a series of 130,338 screening mammograms performed between 1 January 2014 and 1 January 2016. During the 1-year follow-up, clinical data were collected for all recalls. Screening outcome was determined for recalled women with or without evaluation of contralateral breast abnormalities.
RESULTS: Of 3,995 recalls (recall rate 3.1%), 129 women (3.2%) underwent assessment of a contralateral, non-recalled breast abnormality. Most lesions were detected at clinical mammography and/or breast tomosynthesis (101 women, 78.3%). The biopsy rate was similar for recalled lesions and contralateral, non-recalled lesions, but the positive predictive value of biopsy was higher for recalled lesions (p = 0.01). A comparable proportion of the recalled lesions and contralateral, non-recalled lesions were malignant (p = 0.1). The proportion of ductal carcinoma in situ was similar for both groups, as well as invasive cancer characteristics and type of surgical treatment.
CONCLUSIONS: About 3% of recalled women underwent evaluation of contralateral, non-recalled breast lesions. Evaluation of the contralateral breast after recall is important as we found that 15.5% of contralateral, non-recalled lesions were malignant. Contralateral cancers and screen-detected cancers show similar characteristics, stage and surgical treatment.
KEY POINTS: • 3% of recalled women underwent evaluation of contralateral, non-recalled lesions • One out of seven contralateral, non-recalled lesions was malignant • A contralateral cancer was diagnosed in 0.5% of recalls • Screen-detected cancers and non-recalled, contralateral cancers showed similar histological characteristics • Tumour stage and surgical treatment were similar for both groups.

Impactfactor 2.843

Incidence and tumour characteristics of bilateral and unilateral interval breast cancers at screening mammography

van Bommel RMG, Voogd AC, **Nederend J, Setz-Pels W**, Louwman MWJ, Strobbe LJ, Venderink D, Tjan-Heijnen VCG, Duijm LEM

Breast. 2018 Apr 38:101-106. Epub 2018 Jan 4

BACKGROUND:
Detected by screening mammography, bilateral breast cancer has a different pathological profile compared to unilateral breast cancer. We investigated the incidence of bilateral interval breast cancers and compared their characteristics with those of unilateral interval breast cancers.
METHODS:
We included all 468,720 screening mammograms of women who underwent biennial screening mammography in the South of the Netherlands between January 2005 and January 2015. We collected breast imaging reports, biopsy results and surgical reports of all referred women and of all women who presented with interval breast cancer. The tumour with the highest tumour stage (index cancer) was used for comparison with unilateral interval cancers.
RESULTS:
A total of 753 interval cancers were detected, of which 24 (3.2%) were bilateral. Among the invasive interval cancers, bilateral cancers more frequently showed a lobular histology than unilateral cancers (37.5% (9/24) vs. 16.1% (111/691), P = .01). There is a trend towards a larger proportion of bilateral than unilateral interval cancers graded 1 (45.8% (11/24) vs. 27.8% (192/691), P = .08). There were no other statistically significant differences in tumour characteristics. Also, the proportion of interval cancers showing significant mammographic abnormalities at the latest screen was comparable for unilateral and bilateral interval cancers (23.0% vs. 25.0%, P = .9).
DISCUSSION:
Bilateral interval cancers comprise a small proportion of all interval cancers. Except of a higher proportion of invasive lobular cancers and a more favourable histological grade of invasive cancers, tumour characteristics are comparable for bilateral and unilateral interval breast cancers.

Impactfactor *2.951*

Incorporation of the technologist's opinion for arbitration of discrepant assessments among radiologists at screening mammography

Coolen AM, **Lameijer JR**, Voogd AC, Strobbe LJ, Louwman MW, Tjan-Heijnen VC, Duijm LE

Breast Cancer Res Treat. 2018 Aug;171(1):143-149

PURPOSE:
We determined whether the addition of the technologist's opinion may be helpful in deciding if discordant readings at blinded double reading should be recalled.
METHODS:
A consecutive series of 99,013 digital screening mammograms, obtained between July 2013 and January 2015, were included. All mammograms were first interpreted by a technologist and then double read in a blinded fashion by a team of 13 screening radiologists. All concordant and discordant positive readings among radiologists were recalled.
RESULTS:
Out of 3562 recalls, 998 women were recalled after a discordant reading. Of these women, 337 (33.8%) had a positive technologist assessment, of which 40 (11.9%) were diagnosed with breast cancer. Sixty women with a negative technologist assessment (60/661, 9.1%) were diagnosed with breast cancer (p?=?0.16). Recall rate would have decreased with technologist arbitration (3.6% vs. 2.9%, p?<?0.001). Cancer detection rate decreased with 8.5%, from 7.1/1000 screens to 6.5/1000 screens (p?=?0.10). Among women with a positive technologist assessment, the probability of breast cancer was highest in case of suspicious microcalcifications and lowest for suspicious masses (30.4% (17/56) versus 7.0% (16/212), p?<?0.001). Breast cancers were diagnosed in all groups of mammographic abnormalities, except in women with a suspicious asymmetry and a negative technologist assessment.
CONCLUSIONS:
Assessment by a technologist does not provide a significant discriminating ability in case of a discordant radiologist reading and, taking into account the decrease in cancer detection rate, does not appear to be a suitable arbitration strategy for discordant recalls at blinded double reading.

Impactfactor *3.605*

Neurodegeneration With Brain Iron Accumulation: A Novel Mutation in the Ceruloplasmin Gene

Stelten BML, **van Ommen W**, Keizer K

JAMA Neurol. 2018 Oct 29. doi: [Epub ahead of print]

Geen abstract beschikbaar

Impactfactor 11.460

Predictive value of abdominal CT in evaluating internal herniation after bariatric laparoscopic Roux-en-Y gastric bypass

Ederveen JC, van Berckel MMG, Nienhuijs SW, Weber RJP, **Nederend J**

Br J Surg. 2018 Nov 105(12):1623-1629. Epub 2018 Jun 4

BACKGROUND:
Internal herniation, a serious complication after bariatric surgery, is challenging to diagnose. The aim of this study was to determine the accuracy of abdominal CT in diagnosing internal herniation.
METHODS:
The study included consecutive patients who had undergone laparoscopic gastric bypass surgery between 1 January 2011 and 1 January 2015 at a bariatric centre of excellence. To select patients suspected of having internal herniation, reports of abdominal CT and reoperations up to 1 January 2017 were screened. CT was presumed negative for internal herniation if no follow-up CT or reoperation was performed within 90?days after the initial CT, or no internal herniation was found during reoperation. The accuracy of abdominal CT in diagnosing internal herniation was calculated using two-way contingency tables.
RESULTS:
A total of 1475 patients were included (84·7 per cent women, mean age 46·5?years, median initial BMI 41·8?kg/m2). CT and/or reoperation was performed in 192 patients (13·0 per cent) in whom internal herniation was suspected. Internal herniation was proven laparoscopically in 37 of these patients. The incidence of internal herniation was 2·5 per cent. An analysis by complaint included a total of 265 episodes, for which 247 CT scans were undertaken. CT was not used to investigate 18 episodes, but internal herniation was encountered in one-third of these during reoperation. Combining the follow-up and intraoperative findings, the accuracy of CT for internal herniation had a sensitivity of 83·8 (95 per cent c.i. 67·3 to 93·2) per cent, a specificity of 87·1 (81·7 to 91·2) per cent, a positive predictive value of 53·4 (40·0 to 66·5) per cent and a negative predictive value of 96·8 (92·9 to 98·7) per cent.
CONCLUSION:
Abdominal CT is an important tool in diagnosing internal herniation, with a high specificity and a high negative predictive value.

Impactfactor 5.433

Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer

Schaap DP, Ogura A, **Nederend J**, Maas M, Cnossen JS, Creemers GJ, van Lijnschoten I, Nieuwenhuijzen GA, Rutten HJ, Kusters M

Br J Surg. 2018 Dec;105(13):1844-1852

BACKGROUND:
Lateral nodal disease in rectal cancer remains a subject of debate and is treated differently in the East and the West. The predictive value of lateral lymph node and MRI-detected extramural vascular invasion (mrEMVI) features on oncological outcomes was assessed in this study.
METHODS:
In this retrospective cohort study, data on patients with cT3-4 rectal cancer within 8?cm from the anal verge were considered over a 5-year period (2009-2013). Lateral lymph node size, malignant features and mrEMVI features were evaluated and related to oncological outcomes.
RESULTS:
In total, 192 patients were studied, of whom 30 (15·6 per cent) underwent short-course radiotherapy and 145 (75·5 per cent) received chemoradiotherapy. A lateral lymph node short-axis size of 10?mm or more was associated with a significantly higher 5-year lateral/presacral local recurrence rate of 37 per cent, compared with 7·7 per cent in nodes smaller than 10?mm (P?=?0·041). Enlarged nodes did not result in a higher 5-year rate of distant metastasis (23 per cent versus 27·7 per cent in nodes smaller than 10?mm; P?=?0·563). However, mrEMVI positivity was related to more metastatic disease (5-year rate 43 versus 26·3 per cent in the mrEMVI-negative group; P?=?0·014), but not with increased lateral/presacral recurrence. mrEMVI occurred in 46·6 per cent of patients with nodes smaller than 10?mm, compared with 29 per cent in patients with nodes of 10?mm or larger (P?=?0·267).
CONCLUSION:
Although lateral nodal disease is more a local problem, mrEMVI mainly predicts distant recurrence. The results of this study showed an unacceptably high local recurrence rate in patients with a short axis of 10?mm or more, despite neoadjuvant (chemo)radiotherapy

Impactfactor 5.433

Quality assurance of four-dimensional computed tomography in a multicentre trial of stereotactic body radiotherapy of centrally located lung tumours

Marie Lambrecht, Jan-Jakob Sonke, Ursula Nestle,, Heike Peulen, Damien C. Weber, Marcel Verheij, Coen W. Hurkmans

Physics and Imaging in Radiation Oncology 2018;8:57-62

Background and Purpose:
Extensive radiation therapy quality assurance (RTQA) programs are needed when advanced radiotherapy treatments are used. As part of the RTQA four dimensional computed tomography (4DCT)imaging performance needs to be assessed. Here we present the RTQA data related to 4DCT proceduresused within the context of stereotactic bodyradiotherapy(SBRT) of centrally located lungtumours .It provides an overview of the 4DCT acquisition methods and achievable accuracy of imaging lung tumour volumes.
Materials and Methods:
3DCT and 4DCT images were acquired from a CIRS phantom with spheres of 7.5 and 12.5 mm radius using the institutional scan protocols. Regular asymmetric tumour motion was simulated with varying amplitude sandperiods. Target volumes were reconstructed using auto-contouring with scanner specificthresholds. Volume and amplitudes deviations were assessed.
Results:
Although acquisition parameters were rather homogeneous over the eleven institutions analysed, volumedeviationswereobserved.Averagevolumedeviationsforthe12.5mmspherewere15%(-4%to69%)at
end of inspiration, 2% (-2% to 9.0%) at end of expiration and 12% (0% to 36%) at mid-ventilation. For the 7.5mm sphere deviations were 13% (-99% to 65%), 16% (-34% to 66%) and 1% (-13% to 20%), respectively. The amplitude deviation was generally within 2mm although underestimations up to 6mm were observed.
Conclusions:
The expiration phase was the most accurate phase to define the tumour volume and should be preferred for GTV delineation of tumours exhibiting large motion causing motion artefacts when using mid-ventilation or tracking techniques. The large variation found among the institutions indicated that further improvements in 4DCT imaging were possible. Recommendations for 4DCT QA have been formulated.

Impactfactor --

Radiotherapy quality assurance of SBRT for patients with centrally located lung tumours within the multicentre phase II EORTC Lungtech trial: Benchmark case results

Marie Lambrecht , Enrico Clementel, Jan-Jacob Sonke, Ursula Nestle, Sonja Adeba, Mathias Guckenberger, Nicolaus Andratschke, Damien C. Weber, Marcel Verheij, Coen W. Hurkmans

Radiotherapy and Oncology 2018; 23 oct, online 21 dec 2018

Purpose
To report on the benchmark case (BC) study performed in the context of the European Organisation for Research and Treatment of Cancer prospective multicentre Lungtech trial of SBRT for patients with inoperable centrally located lung tumours.
Methods and materials
Target volume and organs at risk (OARs) delineations first needed to be acceptable before the treatment plan was reviewed. Retrospectively, Dice similarity coefficients of the OARs and the target volumes were calculated and a set of gold standard contours adapted for each institution margins was applied on the accepted dose submissions to evaluate the influence of acceptable delineation variations on dosimetry.
Results
Twenty-five institutions participated. Five BCs were accepted at the first attempt. Twenty institutions had to revise their delineation at least once and seven had to revise their planning once. The V60 Gy dose coverage improved significantly (p?=?0.05) between the first and final submissions from median (range) 94.8% (22.5–97.8) to 95.3% (70.5–99.3). The median Dice coefficient varied significantly between OARs: The lowest values were found for the brachial plexus 0.25 (0.01–0.54) and the highest for the spinal cord 0.89 (0.71–0.95). The mean PTV Dice coefficient was 0.82 (0.48–0.92). Applying the gold standard contours, only one institution remained compliant with the dose coverage criteria with V60 Gy median (range) of 83.4% (54.2–93.9).
Conclusions
Clinical guidelines and radiotherapy protocols are not a substitute for timely radiotherapy quality assurance procedures, which improve dose coverage significantly. Delineation remains the main source of BC rejection and plan review without first reviewing delineation may not be efficient. Our results show that delineation variations seem to have a larger influence on PTV coverage than variations in planning and irradiation techniques and thus suggest that dose tolerance criteria should preferably take into account the accuracy of delineation.

Impactfactor *4.942*

The impact of radiological retroperitoneal lymphadenopathy on survival after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases

van der Werf LR, Wassenaar E, de Niet A, Lalezari F, Braam HJ, van Ramshorst B, **Nederend J**, de Hingh IHJT, Kok NFM, Aalbers AGJ.

Eur J Surg Oncol. 2018 Nov 1. pii: S0748-7983(18)31986-3. [Epub ahead of print]

OBJECTIVES:
To investigate the impact of retroperitoneal lymphadenopathy (RPLP) on pre-operative CT scan on overall survival

(OS) and disease-free survival (DFS) after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) for peritoneal metastases (PM) of colorectal cancer.

BACKGROUND:

In patients with PM enlarged retroperitoneal lymph nodes (RPLP) are usually considered extra-regional lymph node metastases and therefore these patients may be excluded from CRS-HIPEC. This is a clinical dilemma since it is often hard to obtain histology from these nodes.

METHODS:

In this multicenter, retrospective study all consecutive patients with colorectal PM treated with CRS-HIPEC between 2004 and 2013 were included. The preoperative CT-scan was re-analyzed for the presence of RPLP based on the radiological appearance of enlarged lymph nodes. Outcomes were OS and DFS. Kaplan-Meier methods and Cox regression modeling were used to analyze the impact of RPLP on OS and DFS.

RESULTS:

In 25 of 401 patients (6.1%) RPLP was observed on the preoperative CT-scan. Patient, tumor and surgical characteristics did not statistically significantly differ between groups with and without RPLP. After a median follow-up of 46 months, the one-, three- and five-year survival was 80%, 59%, 38% and 90%, 50%, 36% in the group with and without RPLP respectively. Median OS (47 vs. 35 months, logrank: p?=?0.70) and median DFS (14 vs. 15 months, logrank: p?=?0.81) did not statistically significantly differ between groups. In multivariable analysis, RPLP did not significantly influence survival.

CONCLUSION:

Enlarged retroperitoneal lymph nodes on a pre-operative CT-scan should not automatically exclude patients from CRS-HIPEC.

Impactfactor 3.688

The incidence of negative intraoperative findings after unsuccessful hydrostatic reduction of ileocolic intussusception in children: A retrospective analysis

Kanglie MMNP, de Graaf N, Beije F, Brouwers EMJ, Theuns-Valks SDM, **Jansen FH**, de Roy van Zuidewijn DBW, Verhoeven B, van Rijn RR, Bakx R Dutch Intussusception Group

J Pediatr Surg. 2018 Jun 1. pii: S0022-3468(18)30332-4. [Epub ahead of print]

BACKGROUND:

There is a lack of studies addressing the occurrence of negative intraoperative findings (that is the absence of intussusception) after an unsuccessful hydrostatic reduction of an ileocolic intussusception. The aim of this study is to determine the incidence of negative intraoperative findings after unsuccessful hydrostatic reduction of ileocolic intussusception.

METHODS:

We conducted a multicentre retrospective study of all children aged 0-18?years treated for ileocolic intussusception from January 1, 2010 to December 31, 2015 in 9 Dutch hospitals. Primary outcome measure was the percentage of children without an intussusception during surgical exploration after unsuccessful hydrostatic reduction.

RESULTS:

In the study period 436 patients were diagnosed with an ileocolic intussusception. Of these, 408 patients underwent hydrostatic reduction of an ileocolic intussusception. 112 patients (27.5%) underwent surgery after an unsuccessful hydrostatic reduction. In 13 (11.6%) patients no intraoperative evidence of intussusception was found. Patients who underwent surgical intervention after unsuccessful hydrostatic reduction were significantly younger than patients who had a successful hydrostatic reduction; there was no gender difference.

CONCLUSION:

A substantial number of children (11.6%) underwent a laparotomy after unsuccessful hydrostatic reduction in whom no intussusception was found intraoperatively. We suggest initiating laparoscopy instead of laparotomy when surgery is necessary.

LEVEL OF EVIDENCE:

Level II.

Impactfactor 2.128

Tumour characteristics of bilateral screen-detected cancers and bilateral interval cancers in women participating at biennial screening mammography

van Bommel R, **Lameijer JR**, Voogd AC, **Nederend J**, Louwman MWJ, **Setz-Pels W**, Strobbe LJ, Tjan-Heijnen VC, Duijm LE

Eur J Radiol. 2018 Nov;108:215-221

BACKGROUND:

Unilateral interval breast cancers show less favourable prognostic features than unilateral screen-detected cancers, but data on tumour characteristics of bilateral interval cancers in a systematically screened population are sparse. Therefore, we compared tumour characteristics of bilateral interval cancers with those of bilateral screen-detected cancers.

METHODS:
We included all 468,720 screening mammograms of women who underwent biennial screening mammography in the South of the Netherlands between January 2005 and January 2015. We collected breast imaging reports, biopsy results and surgical reports of all recalled women and of all women who presented with interval breast cancer. In women with synchronous bilateral breast screen-detected cancers and interval cancers showed similar characteristics, except for a larger proportion of T-stage 2 or worse (T2+) cancers among interval cancers (16/24 (66.7%) versus 23/58 (39.7%) (P?=?0.03). Index cancer, the tumour with the highest tumour stage was defined as the index cancer. For comparison of data between both groups Fisher exact test and Chi-square test were used.
RESULTS:
Synchronous bilateral cancer was diagnosed in 2.2% of screen-detected cancers (64/2947) and in 3.2% of interval cancers (24/753) (P?=?0.1). Index tumours of bilateral cancers, compared to contralateral cancers, were less frequently stage T1 in both bilateral screen-detected cancers and bilateral interval cancers (35/64 (60.3%) versus 40/64 (88.9%) (P?=?0.001) and 8/24 (33.3%) versus 18/24 (85.7%) (P?<?0.001), respectively). In bilateral screen-detected cancers, contralateral cancers were more often stage 1a-c (P?<?0.001) compared to index cancers. In bilateral index cancers, index cancers were more often of the lobular subtype (P?<?0.001).
CONCLUSION:
Index cancers of bilateral screen-detected cancers and bilateral interval cancers show significant differences in tumour size, whereas nodal status, receptor status and final surgical treatment are comparable. In bilateral screen-detected cancer, index cancers had a significantly higher tumour stage. In bilateral screen-detected cancer, index cancers were more often the ductal invasive subtype compared to contralateral cancers.

Impactfactor *2.843*

Vertebroplasty versus sham procedure for painful acute osteoporotic vertebral compression fractures (VERTOS IV): randomised sham controlled clinical trial

Firanescu CE, de Vries J, Lodder P, Venmans A, Schoemaker MC, Smeet AJ, Donga E, Juttmann JR, Klazen CAH, Elgersma OEH, **Jansen FH, Tielbeek AV**, Boukrab I, Schonenberg K, van Rooij WJJ, Hirsch JA, Lohle PNM

BMJ. 2018 May 9 361:k1551

Erratum in: BMJ. 2018 Jul 4 362:k2937

OBJECTIVE:
To assess whether percutaneous vertebroplasty results in more pain relief than a sham procedure in patients with acute osteoporotic compression fractures of the vertebral body.
DESIGN: Randomised, double blind, sham controlled clinical trial.
SETTING: Four community hospitals in the Netherlands, 2011-15.
PARTICIPANTS:
180 participants requiring treatment for acute osteoporotic vertebral compression fractures were randomised to either vertebroplasty (n=91) or a sham procedure (n=89).
INTERVENTIONS:
Participants received local subcutaneous lidocaine (lignocaine) and bupivacaine at each pedicle. The vertebroplasty group also received cementation,which was simulated in the sham procedure group.
MAIN OUTCOME MEASURES:
Main outcome measure was mean reduction in visual analogue scale (VAS) scores at one day, one week, and one, three, six, and 12 months. Clinically significant pain relief was defined as a decrease of 1.5 points in VAS scores from baseline. Secondary outcome measures were the differences between groups for changes in the quality of life for osteoporosis and Roland-Morris disability questionnaire scores during 12 months' follow-up.
RESULTS:
The mean reduction in VAS score was statistically significant in the vertebroplasty and sham procedure groups at all follow-up points after the procedure compared with baseline. The mean difference in VAS scores between groups was 0.20 (95% confidence interval -0.53 to 0.94) at baseline, -0.43 (-1.17 to 0.31) at one day, -0.11 (-0.85 to 0.63) at one week, 0.41 (-0.33 to 1.15) at one month, 0.21 (-0.54 to 0.96) at three months, 0.39 (-0.37 to 1.15) at six months, and 0.45 (-0.37 to 1.24) at 12 months. These changes in VAS scores did not, however, differ statistically significantly between the groups during 12 months' follow-up. The results for secondary outcomes were not statistically significant. Use of analgesics (non-opioids, weak opioids, strong opioids) decreased statistically significantly in both groups at all time points, with no statistically significant differences between groups. Two adverse events occurred in the vertebroplasty group: one respiratory insufficiency and one vasovagal reaction.
CONCLUSIONS:
Percutaneous vertebroplasty did not result in statistically significantly greater pain relief than a sham procedure during 12 months' follow-up among patients with acute osteoporotic vertebral compression fractures.

Impactfactor *23.259*

Radiotherapie

Comparison of 36 Gy, 20 Gy, or No Radiation Therapy After 6 Cycles of EBVP Chemotherapy and Complete Remission in Early-Stage Hodgkin Lymphoma Without Risk Factors: Results of the EORT-GELA H9-F Intergroup Randomized Trial

Thomas J, Fermé C, Noordijk EM, Morschhauser F, Girinsky T, Gaillard I, Lugtenburg PJ, André M, **Lybeert MLM**, Stamatoullas A, Beijert M, Hélias P, Eghbali H, Gabarre J, van der Maazen RWM, Jaubert J, Bouabdallah K, Boulat O, Roesink JM, Christian B, Ong F, Bordessoule D, Tertian G, Gonzalez H, Vranovsky A, Quittet P, Tirelli U, de Jong D, Audouin J, Aleman BMP, Henry-Amar M.

Int J Radiat Oncol Biol Phys. 2018 Apr 1;100(5):1133-1145

PURPOSE:

While patients with early-stage Hodgkin lymphoma (HL) have an excellent outcome with combined treatment, the radiation therapy (RT) dose and treatment with chemotherapy alone remain questionable. This noninferiority trial evaluates the feasibility of reducing the dose or omitting RT after chemotherapy.

METHODS AND MATERIALS:

Patients with untreated supradiaphragmatic HL without risk factors (age = 50 years, 4 to 5 nodal areas involved, mediastinum-thoracic ratio = 0.35, and erythrocyte sedimentation rate = 50 mm in first hour without B symptoms or erythrocyte sedimentation rate = 30 mm in first hour with B symptoms) were eligible for the trial. Patients in complete remission after chemotherapy were randomized to no RT, low-dose RT (20 Gy in 10 fractions), or standard-dose involved-field RT (36 Gy in 18 fractions). The limit of noninferiority was 10% for the difference between 5-year relapse-free survival (RFS) estimates. From September 1998 to May 2004, 783 patients received 6 cycles of epirubicin, bleomycin, vinblastine, and prednisone; 592 achieved complete remission or unconfirmed complete remission, of whom 578 were randomized to receive 36 Gy (n=239), 20 Gy of involved-field RT (n=209), or no RT (n=130).

RESULTS:

Randomization to the no-RT arm was prematurely stopped (=20% rate of inacceptable events: toxicity, treatment modification, early relapse, or death). Results in the 20-Gy arm (5-year RFS, 84.2%) were not inferior to those in the 36-Gy arm (5-year RFS, 88.6%) (difference, 4.4%; 90% confidence interval [CI] -1.2% to 9.9%). A difference of 16.5% (90% CI 8.0%-25.0%) in 5-year RFS estimates was observed between the no-RT arm (69.8%) and the 36-Gy arm (86.3%); the hazard ratio was 2.55 (95% CI 1.44-4.53; P<.001). The 5-year overall survival estimates ranged from 97% to 99%.

CONCLUSIONS:

In adult patients with early-stage HL without risk factors in complete remission after epirubicin, bleomycin, vinblastine, and prednisone chemotherapy, the RT dose may be limited to 20 Gy without compromising disease control. Omitting RT in these patients may jeopardize the treatment outcome.

Impactfactor 5.554

Effect of Neoadjuvant Chemoradiotherapy on Health-Related Quality of Life in Esophageal or Junctional Cancer: Results From the Randomized CROSS Trial

Noordman BJ, Verdam MGE, Lagarde SM, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, van Laarhoven HWM, Nieuwenhuijzen GAP, Hospers GAP, Bonenkamp JJ, Cuesta MA, Blaisse RJB, Busch OR, Ten Kate FJW, Creemers GM, Punt CJA, Plukker JTM, Verheul HMW, Spillenaar Bilgen EJ, van Dekken H, **van der Sangen MJC**, et al

J Clin Oncol. 2018 Jan 20 36(3):268-275. Epub 2017 Nov 21

Purpose To compare pre-agreed health-related quality of life (HRQOL) domains in patients with esophageal or junctional cancer who received neoadjuvant chemoradiotherapy (nCRT) followed by surgery or surgery alone. Secondary aims were to examine the effect of nCRT on HRQOL before surgery and the effect of surgery on HRQOL. Patients and Methods Patients were randomly assigned to nCRT (carboplatin plus paclitaxel with concurrent 41.4-Gy radiotherapy) followed by surgery or surgery alone. HRQOL was measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30) and -Oesophageal Cancer Module (QLQ-OES24) questionnaires pretreatment and at 3, 6, 9, and 12 months postoperatively. The nCRT group also received preoperative questionnaires. Physical functioning (PF; QLQ-C30) and eating problems (EA; QLQ-OES24) were chosen as predefined primary end points. Predefined secondary end points were global QOL (GQOL; QLQ-C30), fatigue (FA; QLQ-C30), and emotional problems (EM; QLQ-OES24). Results A total of 363 patients were analyzed. No statistically significant differences in postoperative HRQOL were found between treatment groups. In the nCRT group, PF, EA, GQOL, FA, and EM scores deteriorated 1 week after nCRT (Cohen's d: -0.93, P < .001; 0.47, P < .001; -0.84, P < .001; 1.45, P < .001; and 0.32, P = .001, respectively). In both treatment groups, all end points declined 3 months postoperatively compared with baseline (Cohen's d: -1.00, 0.33, -0.47, -0.34, and 0.33, respectively; all P < .001), followed by a continuous gradual improvement. EA, GQOL, and EM were restored to baseline levels during follow-up, whereas PF and FA remained impaired 1 year postoperatively (Cohen's d: 0.52 and -0.53, respectively; both P < .001). Conclusion Although HRQOL declined during nCRT, no effect of nCRT was apparent on postoperative HRQOL compared with surgery alone. In addition to the improvement in survival, these

findings support the view that nCRT according to the Chemoradiotherapy for Esophageal Cancer Followed by Surgery Study-regimen can be regarded as a standard of care.

Impactfactor *26.303*

Efficacy of Anastrozole after Tamoxifen in Early Breast Cancer Patients with Chemotherapy-Induced Ovarian Function Failure

van Hellemond IEG, Vriens IJH, Peer PGM, Swinkels ACP, Smorenburg CH, Seynaeve CM, **van der Sangen MJC**, Kroep JR, de Graaf H, Honkoop AH, Erdkamp FLG, van den Berkmortel FWPJ, de Boer M, de Roos WK, Linn SC, Imholz ALT, Tjan-Heijnen VCG

Int J Cancer. 2018 Dec 26. doi: [Epub ahead of print]

The DATA study (NCT00301457) compared 6 and 3 years of anastrozole in postmenopausal women with hormone receptor-positive early breast cancer after 2-3 years tamoxifen. Patients with chemotherapy-induced ovarian function failure (CIOFF) were also eligible, but could be at risk of ovarian function recovery (OFR). The current analysis compared the survival of women with CIOFF with definitely postmenopausal women and examined the influence of OFR on survival. Therefore, we selected patients from the DATA study aged 45-57 years at randomization who had received (neo)-adjuvant chemotherapy. They were classified by reversibility of postmenopausal status: possibly reversible in case of CIOFF (n=395) versus definitely postmenopausal (n=261). The former were monitored by E2 measurements for OFR. The occurrence of OFR was incorporated as a time-dependent covariate in a Cox-regression model for calculating the hazard ratio (HR). We used the landmark method to calculate residual 5-year survival rates. When comparing CIOFF women with definitely postmenopausal women, the survival was not different. Amongst CIOFF women with available E2 follow-up values (n= 329), experiencing OFR (n=39) had an unfavourable impact on distant recurrence-free survival (HR 2.27 (95% CI 0.98-5.25;P=0.05) and overall survival (HR 2.61 (95% CI 1.11-6.13;P=0.03)). After adjusting for tumor features, the HRs became 2.11 (95% CI 0.89-5.02;P=0.09) and 2.24 (95% CI 0.92-5.45;P=0.07) respectively. The residual 5-year rate for distant recurrence-free survival was 76.9% for women with OFR and 92.1% for women without OFR, and for 5-year overall survival 80.8% and 94.4%, respectively. Women with CIOFF receiving anastrozole may be at increased risk of disease recurrence if experiencing OFR.

Impactfactor *7.360*

High-precision Bladder Cancer Irradiation in the Elderly: Clinical Results for a Plan-of-the-day Integrated Boost Technique with Image Guidance Using Lipiodol Markers

Alexander J.W. Beulens, **Peter-Paul van der Toorn** , Michel J. de Wildt , Wout A. Scheepens

European Urology Oncology Available online 7 September 2018

Background

For most elderly patients with muscle-invasive bladder cancer (MIBC), surgery is not an option because of patient frailty. Conventional radiotherapy, with its high-dose irradiation of surrounding healthy tissues, remains the only curative treatment for this patient population.

Objective

To determine whether targeted radiotherapy with Lipiodol demarcation and plan-of-the-day integrated boost technique

(LPOD) is a viable curative treatment for elderly patients with MIBC.

Design, setting, and participants

Between September 2008 and September 2016 all MIBC patients in our hospital were screened for eligibility. We included patients with localised, unifocal T2–T4N0M0 grade 2–3 MIBC. Patients with a tumour volume >50% of the bladder wall surface, previous pelvic radiotherapy, and unilateral or bilateral hip prostheses were excluded. Intervention: Targeted radiotherapy using LPOD.

Outcome measurements and statistical analysis

Overall survival, urothelial cell cancer–specific survival (UCCSS), disease recurrence, and Radiation Therapy Oncology Group (RTOG) toxicity were measured. Statistical analyses included independent-sample t tests, ?2 tests, and Mann-Whitney U tests.

Results and limitations

A total of 44 patients (median age 80 yr) were included. Over median follow-up of 38 mo, one patient ceased treatment and 23 patients died. LPOD resulted in a 11.4% chance of local recurrence, high 3-yr UCCSS of 77%, RTOG grade >3 toxicity of 2.3–12.9%, and 3-yr overall survival of 49%.

Conclusions

LPOD is a feasible first-line treatment option for older patients with limited-volume T2–T4N0M0 grade 2–3 MIBC.

Impactfactor --

Impact of brachytherapy technique (2D versus 3D) on outcome following radiotherapy of cervical cancer

Derks K, Steenhuijsen JLG, **van den Berg HA**, Houterman S, **Cnossen J**, van Haaren P, **De Jaeger K** J Contemp Brachytherapy. 2018 Feb 10(1):17-25. Epub 2018 Feb 22

Purpose:
The purpose of this study was to analyze the effect of 2D conventional brachytherapy (CBT) compared to 3D MRI-guided brachytherapy (IGBT) with and without the use of interstitial needles on local control, overall survival, and toxicity in patients treated for cervical cancer with radiation or chemoradiation.
Material and methods:
A retrospective analysis was performed of biopsy-proven FIGO IB-IVA cervical cancer patients, treated with primary radiation or chemoradiation, followed by brachytherapy (BT) between January 1997 and July 2016. Endpoints were local control, overall survival, and toxicity.
Results:
Of 126 patients included, 35 have been treated with CBT, 31 with IGBT without needles (IC), and 60 with IGBT with needles (ICIS). External beam radiotherapy (EBRT) had mostly been delivered concurrently with chemotherapy (weekly cisplatin). Overall local control was 93% after 1 year, and 88% after 3 years. Overall 3-year survival was 75%, and 5-year survival was 66%. The 3D technique (IGBT cohorts) showed a trend for an improved local control and overall survival ($p = 0.05$) compared to the 2D technique (CBT cohort). A decrease in toxicity was observed from 17% (2D cohort) to 12% (3D cohort). The use of interstitial needles was associated with a higher high-risk clinical target volume (HR-CTV) dose (11.3 Gy vs. 9.9 Gy) and a lower D2cc bladder dose (10.9 Gy vs. 14.7 Gy, both $p < 0.01$).
Conclusions:
In cervical cancer treatment, the use of a 3D brachytherapy technique (MRI-guided with or without interstitial needles) showed a trend towards an increased local control and improved overall survival with reduced toxicity, compared to the conventional 2D brachytherapy technique. The use of interstitial needles allowed dose sculpting, resulting in delivery of higher doses to the HR-CTV, while reducing radiation doses to organs at risk, such as the bladder.

Impactfactor --

Impact of Surgical Approach on Long-term Survival in Esophageal Adenocarcinoma Patients With or Without Neoadjuvant Chemoradiotherapy

Noordman BJ, van Klaveren D, van Berge Henegouwen MI, Wijnhoven BPL, Gisbertz SS, Lagarde SM, van der Gaast A, Hulshof MCCM, Biermann K, Steyerberg EW, van Lanschot JJB; also on behalf of the CROSS-study group: Nieuwenhuijzen GA, Creemers GJ, **Sangen MJ van der**

Ann Surg. 2018 May;267(5):892-897

OBJECTIVE:
To compare overall survival in patients with esophageal adenocarcinoma who underwent transhiatal esophagectomy (THE) with limited lymphadenectomy or transthoracic esophagectomy (TTE) with extended lymphadenectomy with or without neoadjuvant chemoradiotherapy (nCRT).
BACKGROUND:
The application of neoadjuvant therapy might change the association between the extent of lymphadenectomy and survival in patients with esophageal adenocarcinoma. This may influence the choice of surgical approach in patients treated with nCRT.
METHODS:
Patients with potentially curable subcarinal esophageal adenocarcinoma treated with surgery alone or nCRT followed by surgery in 7 centers were included. The effect of surgical approach on overall survival, differentiated by the addition or omission of nCRT, was analyzed using a multivariable Cox regression model that included well-known prognostic factors and factors that might have influenced the choice of surgical approach.
RESULTS:
In total, 701 patients were included, of whom 318 had TTE with extended lymphadenectomy and 383 had THE with limited lymphadenectomy. TTE had differential effects on survival (P for interaction = 0.02), with a more favorable prognostic effect in patients who were treated with surgery alone [hazard ratio (HR) = 0.77, 95% confidence interval (CI) 0.58-1.03]. This association was statistically significant in a subgroup of patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 0.62, 95% CI 0.43-0.90). The favorable prognostic effect of TTE over THE was absent in the nCRT and surgery group (HR = 1.16, 95% CI 0.80-1.66) and in the subgroup of nCRT patients with 1 to 8 positive lymph nodes in the resection specimen (HR = 1.00, 95% CI 0.61-1.68).
CONCLUSIONS:
Compared to surgery alone, the addition of nCRT may reduce the need for TTE with extended lymphadenectomy to improve long-term survival in patients with esophageal adenocarcinoma.

Impactfactor *1.536*

Improved pharmacodynamic (PD) assessment of low dose PARP inhibitor PD activity for radiotherapy and chemotherapy combination trials

de Haan R, Pluim D, van Triest B, van den Heuvel M, **Peulen H**, van Berlo D, George J, Verheij M, Schellens JHM, Vens C

Radiother Oncol. 2018 Mar;126(3):443-449. doi: Epub 2017 Nov 14

BACKGROUND:

PARP inhibitors are currently evaluated in combination with radiotherapy and/or chemotherapy. As sensitizers, PARP inhibitors are active at very low concentrations therefore requiring highly sensitive pharmacodynamic (PD) assays. Current clinical PD-assays partly fail to provide such sensitivities. The aim of our study was to enable sensitive PD evaluation of PARP inhibitors for clinical sensitizer development.
MATERIAL AND METHODS:
PBMCs of healthy individuals and of olaparib and radiotherapy treated lung cancer patients were collected for ELISA based PD-assays.
RESULTS:
PAR-signal amplification by ex vivo irradiation enabled an extended quantification range for PARP inhibitory activities after ex vivo treatment with inhibitors. This "radiation-enhanced-PAR" (REP) assay provided accurate IC50 values thereby also revealing differences among healthy individuals. Implemented in clinical radiotherapy combination Phase I trials, the REP-assay showed sensitive detection of PARP inhibition in patients treated with olaparib and establishes strong PARP inhibitory activities at low daily doses.
CONCLUSIONS:
Combination trials of radiotherapy and novel targeted agent(s) often require different and more sensitive PD assessments than in the monotherapy setting. This study shows the benefit and relevance of sensitive and adapted PD-assays for such combination purposes and provides proof of clinically relevant cellular PARP inhibitory activities at low daily olaparib doses.

Impactfactor 4.942

Inter-observer variation of hippocampus delineation in hippocampal avoidance prophylactic cranial irradiation

Bartel F, van Herk M, Vrenken H, Vandaele F, Sunaert S, **de Jaeger K**, Dollekamp NJ, Carbaat C, Lamers E, Dieleman EMT, Lievens Y, de Ruysscher D, Schagen SB, de Ruiter MB, de Munck JC, Belderbos J

Clin Transl Oncol. 2018 Jun 6. [Epub ahead of print]

BACKGROUND:
Hippocampal avoidance prophylactic cranial irradiation (HA-PCI) techniques have been developed to reduce radiation damage to the hippocampus. An inter-observer hippocampus delineation analysis was performed and the influence of the delineation variability on dose to the hippocampus was studied.
MATERIALS AND METHODS:
For five patients, seven observers delineated both hippocampi on brain MRI. The intra-class correlation (ICC) with absolute agreement and the generalized conformity index (CIgen) were computed. Median surfaces over all observers' delineations were created for each patient and regional outlining differences were analysed. HA-PCI dose plans were made from the median surfaces and we investigated whether dose constraints in the hippocampus could be met for all delineations.
RESULTS:
The ICC for the left and right hippocampus was 0.56 and 0.69, respectively, while the CIgen ranged from 0.55 to 0.70. The posterior and anterior-medial hippocampal regions had most variation with SDs ranging from approximately 1 to 2.5 mm. The mean dose (Dmean) constraint was met for all delineations, but for the dose received by 1% of the hippocampal volume (D1%) violations were observed.
CONCLUSION:
The relatively low ICC and CIgen indicate that delineation variability among observers for both left and right hippocampus was large. The posterior and anterior-medial border have the largest delineation inaccuracy. The hippocampus Dmean constraint was not violated.

Impactfactor 2.392

Intermittent versus continuous first-line treatment for HER2-negative metastatic breast cancer: the Stop & Go study of the Dutch Breast Cancer Research Group (BOOG)

Claessens AK, Bos ME, Lopez-Yurda M, Bouma JM, Rademaker-Lakhai JM, Honkoop AH, de Graaf H, van Druten E, van Warmerdam LJ, **van der Sangen MJ**, Tjan-Heijnen VC, Erdkamp FL, Dutch Breast Cancer Research Group (BOOG)Breast Cancer Res Treat. 2018 Nov;172(2):413-423

PURPOSE:
We determined if intermittent first-line treatment with paclitaxel plus bevacizumab was not inferior to continuous treatment in patients with HER2-negative, advanced breast cancer.
METHODS:
Patients were randomized to 2?×?4 cycles or continuous 8 cycles of paclitaxel plus bevacizumab, followed by bevacizumab maintenance treatment until disease progression or unacceptable toxicity. The primary endpoint was overall progression-free survival (PFS). A proportional-hazards regression model was used to estimate the HR. The upper limit of the two-sided 95% CI for the HR was compared with the non-inferiority margin of 1.34.
RESULTS:
A total of 420 patients were included with well-balanced characteristics. In the intention-to-treat analysis, median overall PFS was 7.4 months (95% CI 6.4-10.0) for intermittent and 9.7 months (95% CI 8.9-10.3) for continuous treatment, with a stratified HR of 1.17 (95% CI 0.88-1.57). Median OS was 17.5 months (95% CI 15.4-21.7) versus

20.9 months (95% CI 17.8-24.0) for intermittent versus continuous treatment, with a HR of 1.38 (95% CI 1.00-1.91). Safety results and actually delivered treatments revealed longer durations of treatment in the continuous arm, without significant unexpected findings.

CONCLUSION:

Intermittent first-line treatment cannot be recommended in patients with HER2-negative advanced breast cancer.

Impactfactor 3.605

Interobserver variability in the delineation of the primary lung cancer and lymph nodes on different four-dimensional computed tomography reconstructions

Mercieca S, Belderbos JSA, **De Jaeger K**, Schinagl DAX, van der Voort Van Zijp N, Pomp J, **Theuws J**, Khalifa J, van de Vaart P, van Herk M

Radiother Oncol. 2018 Feb;126(2):325-332. Epub 2017 Dec 5

PURPOSE:

The study compared interobserver variation in the delineation of the primary tumour (GTVp) and lymph nodes (GTVln) between three different 4DCT reconstruction types; Maximum Intensity Projection (MIP), Mid-Ventilation (Mid-V) and Mid-Position (Mid-P).

MATERIAL AND METHODS:

Seven radiation oncologists delineated the GTVp and GTVln on the MIP, Mid-V and Mid-P 4DCT image reconstructions of 10 lung cancer patients. The volumes, the mean standard deviation (SD) and distribution of SD (SD/area) over the median surface contour were compared for different tumour regions.

RESULTS:

The overall mean delineated volume on the MIP was significantly larger (p?<?0.001) than the Mid-V and Mid-P. For the GTVp the Mid-P had the lowest interobserver variation (SD?=?0.261?cm), followed by Mid-V (SD?=?0.314?cm) and MIP (SD?=?0.330?cm) For GTVln the Mid-V had the lowest interobserver variation (SD?=?0.425?cm) followed by the MIP (SD?=?0.477?cm) and Mid-P (SD?=?0.543?cm). The SD/area distribution showed a statistically significant difference between the MIP versus Mid-P and Mid-P versus Mid-V for both GTVp and GTVln (p?<?0.001), with outliers indicating interpretation differences for GTVp located close to the mediastinum and GTVln.

CONCLUSION:

The Mid-P reduced the interobserver variation for the GTVp. Delineation protocols must be improved to benefit from the improved image quality of Mid-P for the GTVln.

Impactfactor 4.942

Long-term survival improvement in oesophageal cancer in the Netherlands

van Putten M, de Vos-Geelen J, Nieuwenhuijzen GAP, Siersema PD, Lemmens VEPP, Rosman C, **van der Sangen MJC**, Verhoeven RHA

Eur J Cancer. 2018 May 94:138-147. Epub 2018 Mar 20

BACKGROUND:

Treatment for oesophageal cancer has evolved due to developments including the centralisation of surgery and introduction of neoadjuvant treatment. Therefore, this study evaluated trends in stage distribution, treatment and survival of oesophageal cancer patients in the last 26 years in the Netherlands.

PATIENTS AND METHODS:

Patients with oesophageal cancer diagnosed in the period 1989-2014 were selected from the Netherlands Cancer Registry. Patients were divided into two groups: non-metastatic (M0) and metastatic (M1). Trends in stage distribution, treatment and relative survival rates were evaluated according to histology.

RESULTS:

Among all 35,760 patients, the percentage of an unknown tumour stage decreased from 34% to 10% during the study period, whereas the percentage of patients with metastatic disease increased from 21% to 34%. Among surgically treated patients 32% underwent a resection in a high-volume hospital in 2005 which increased to 92% in 2014. Use of neoadjuvant chemoradiotherapy increased in non-metastatic oesophageal adenocarcinoma (OAC) and squamous cell carcinoma (OSCC) patients from respectively 4% and 2% in 2000-2004 to 43% and 26% in 2010-2014. Five-year relative survival increased from 8% to 22% for all patients; from 12% to 36% for non-metastatic OAC and from 9% to 27% for non-metastatic OSCC over 26 years. Median overall survival of metastatic patients improved from 18 to 22 weeks.

CONCLUSION:

In the Netherlands, survival for oesophageal cancer patients improved significantly, especially in the period 2005-2014 which might be the result of better treatment related to the centralisation of surgery and introduction of neoadjuvant chemoradiotherapy.

Impactfactor 7.191

Molecular-integrated risk profile to determine adjuvant radiotherapy in endometrial cancer: Evaluation of the pilot phase of the PORTEC-4a trial

Wortman BG, Bosse T, Nout RA, Lutgens LC, van der Steen-Banasik EM, Westerveld H, **van den Berg H**, Slot A, De Winter KA, Verhoeven-Adema KW, Smit VT, Creutzberg CL; PORTEC Study Group

Gynecol Oncol. 2018 Oct;151(1):69-75

OBJECTIVE:
The Post-Operative Radiation Therapy in Endometrial Carcinoma (PORTEC)-4a trial is a randomized trial for women with high-intermediate risk endometrial cancer (EC), comparing individualized adjuvant treatment based on a molecular-integrated risk profile to standard adjuvant treatment; vaginal brachytherapy. To evaluate patient acceptability and pathology logistics of determining the risk profile, a pilot phase was included in the study.
METHODS:
PORTEC-4a is ongoing and the first 50 patients enrolled were included in the pilot phase. Primary endpoints of the pilot phase were patient acceptance, evaluated by analyzing the screening logs of the participating centers, and logistical feasibility of determination of the risk profile within 2?weeks, evaluated by analyzing the pathology database.
RESULTS:
In the first year, 145 eligible women were informed about the trial at 13 centers, of whom 50 (35%) provided informed consent. Patient accrual ranged from 0 to 57% per center. Most common reasons for not participating were: not willing to participate in any trial (43.2%) and not willing to risk receiving no adjuvant treatment (32.6%). Analysis of the pathology database showed an average time between randomization and determination of the molecular-integrated risk profile of 10.2?days (1-23?days). In 5 of the 32 patients (15.6%), pathology review took >2?weeks.
CONCLUSIONS:
The PORTEC-4a trial design was proven feasible with a satisfactory patient acceptance rate and an optimized workflow of the determination of the molecular-integrated risk profile. PORTEC-4a is the first randomized trial to investigate use of a molecular-integrated risk profile to determine adjuvant treatment in EC.

Impactfactor 4.540

Neoadjuvant chemoradiotherapy plus surgery versus active surveillance for oesophageal cancer: a stepped-wedge cluster randomised trial

Noordman BJ, Wijnhoven BPL, Lagarde SM, Boonstra JJ, Coene PPLO, Dekker JWT, Doukas M, van der Gaast A, Heisterkamp J, Kouwenhoven EA, Nieuwenhuijzen GAP, Pierie JEN, Rosman C, van Sandick JW, **van der Sangen MJC**, Sosef MN, Spaander MCW, Valkema R, van der Zaag ES, Steyerberg EW, van Lanschot JJB SANO-study group.: Creemers GJ, Schoon EJ, Wyndaele D

BMC Cancer. 2018 Feb 6 18(1):142

BACKGROUND: Neoadjuvant chemoradiotherapy (nCRT) plus surgery is a standard treatment for locally advanced oesophageal cancer. With this treatment, 29% of patients have a pathologically complete response in the resection specimen. This provides the rationale for investigating an active surveillance approach. The aim of this study is to assess the (cost-)effectiveness of active surveillance vs. standard oesophagectomy after nCRT for oesophageal cancer.
METHODS: This is a phase-III multi-centre, stepped-wedge cluster randomised controlled trial. A total of 300 patients with clinically complete response (cCR, i.e. no local or disseminated disease proven by histology) after nCRT will be randomised to show non-inferiority of active surveillance to standard oesophagectomy (non-inferiority margin 15%, intra-correlation coefficient 0.02, power 80%, 2-sided a 0.05, 12% drop-out). Patients will undergo a first clinical response evaluation (CRE-I) 4-6 weeks after nCRT, consisting of endoscopy with bite-on-bite biopsies of the primary tumour site and other suspected lesions. Clinically complete responders will undergo a second CRE (CRE-II), 6-8 weeks after CRE-I. CRE-II will include 18F-FDG-PET-CT, followed by endoscopy with bite-on-bite biopsies and ultra-endosonography plus fine needle aspiration of suspected lymph nodes and/or PET- positive lesions. Patients with cCR at CRE-II will be assigned to oesophagectomy (first phase) or active surveillance (second phase of the study). The duration of the first phase is determined randomly over the 12 centres, i.e., stepped-wedge cluster design. Patients in the active surveillance arm will undergo diagnostic evaluations similar to CRE-II at 6/9/12/16/20/24/30/36/48 and 60 months after nCRT. In this arm, oesophagectomy will be offered only to patients in whom locoregional regrowth is highly suspected or proven, without distant dissemination. The main study parameter is overall survival; secondary endpoints include percentage of patients who do not undergo surgery, quality of life, clinical irresectability (cT4b) rate, radical resection rate, postoperative complications, progression-free survival, distant dissemination rate, and cost-effectiveness. We hypothesise that active surveillance leads to non-inferior survival, improved quality of life and a reduction in costs, compared to standard oesophagectomy.
DISCUSSION: If active surveillance and surgery as needed after nCRT leads to non-inferior survival compared to standard oesophagectomy, this organ-sparing approach can be implemented as a standard of care.

Impactfactor 3.288

Optimal image guided radiation therapy strategy for organs at risk sparing in radiotherapy of the prostate including pelvic lymph nodes

van Nunen A, **van der Toorn PPG**, **Budiharto TCG**, Schuring D

Radiother Oncol. 2018 Apr 127(1):68-73. Epub 2018 Mar 2

BACKGROUND AND PURPOSE:
Purpose of this study was to quantify the OAR dose for different position correction strategies, and to determine which strategy is most optimal for treating patients on the prostate and pelvic lymph nodes.
MATERIALS AND METHODS:
For 30 patients, four different treatment plans were made reflecting different correction strategies: online correction on bony anatomy; offline correction on bony anatomy; online correction on the prostate fiducials; using 1?cm margins around both CTVs. The dose to the PTVs and OARs was quantified and a pairwise statistical analysis was performed.
RESULTS:
No statistically significant differences were observed in the dose to the PTVs, ensuring that any OAR sparing is not caused by differences in PTV coverage. Dose to the rectum and anal canal was lowest when applying an online correction on prostate fiducials, although the total PTV volume was higher. Dose to the small bowel bag and femoral heads was slightly higher compared to online correction on bony structures, but well within clinically acceptable limits.
CONCLUSION:
Although the total PTV volume is higher when applying an online correction on the prostate, this strategy leads to the most optimal sparing of relevant OARs, at the cost of a slightly higher dose to the femoral heads and small bowel bag.

Impactfactor 4.942

Predicting breast and axillary response after neoadjuvant treatment for breast cancer: The role of histology vs receptor status

Vugts G, Van den Heuvel F, Maaskant-Braat AJ, Voogd AC, Van Warmerdam LJ, Nieuwenhuijzen GA, **Van der Sangen MJ**

Breast J. 2018 Nov;24(6):894-901

PURPOSE:
Neoadjuvant systemic treatment (NST) is increasingly administered in breast cancer patients. This study was conducted to identify predictors for tumor response in the breast and axilla.
METHODS:
All female patients with nonmetastatic, noninflammatory breast cancer receiving NST between 2003-2013 at the Catharina Cancer Institute in Eindhoven, The Netherlands, were included.
RESULTS:
The majority of 216 of the 337 patients receiving NST (65%) presented with a cT2 tumor. In 159 patients (47%), the axilla was clinically node positive. A pathologic complete response (pCR) in the breast was achieved in 83 patients (24.6%), and a pCR in the axilla in 65 node-positive patients (40.9%). The triple-negative (OR 4.29, 95% CI 2.15-8.55) and hormone receptor (HR)-negative/HER2-positive tumors (OR 3.73, 95% CI 1.59-8.75) were associated with in-breast pCR. Patients with invasive lobular carcinoma (ILC) were less likely to experience in-breast pCR (OR 0.10, 95% CI 0.01-0.73) than those with invasive ductal cancer. Axillary pCR was found in 65 clinically node-positive patients (41%). Axillary pCR was more likely to occur in HR-positive/HER2-positive (OR 6.24, 95% CI 1.86-20.90) and HR-negative/HER2-positive tumors (OR 6.41, 95% CI 1.95-21.06), compared to HER2-negative disease. In-breast pCR was strongly associated with axillary pCR (OR 10.89, 95% CI 4.20-28.22).
CONCLUSION:
Response to NST in the breast and axilla is largely determined by receptor status, with high pCR rates occurring in HER2-positive and triple-negative tumors. For axillary pCR, in-breast pCR and HER2-positive disease are the most important predictive factors.

Impactfactor 2.424

Preliminary results of a cohort study of induction chemotherapy-based treatment for locally recurrent rectal cancer

van Zoggel DMGI, Bosman SJ, Kusters M, Nieuwenhuijzen GAP, **Cnossen JS**, Creemers GJ, van Lijnschoten G, Rutten HJT.

Br J Surg. 2018 Mar;105(4):447-452.Epub 2017 Nov 23

BACKGROUND:
A significant number of patients treated for locally recurrent rectal cancer have local or systemic failure, especially after incomplete surgical resection. Neoadjuvant treatment regimens in patients who have already undergone preoperative (chemo)radiotherapy for the primary tumour are limited. The objective of the present study was to evaluate the influence of a neoadjuvant regimen incorporating induction chemotherapy (ICT) in patients with locally

recurrent rectal cancer who had preoperative (chemo)radiotherapy for the primary cancer or an earlier local recurrence.

METHODS:

Patients were treated with a sequential neoadjuvant regimen including three or four cycles of 5-fluorouracil and oxaliplatin-containing chemotherapy. When no progressive disease was found at evaluation, neoadjuvant treatment was continued with chemoradiation therapy (CRRT) using 30?Gy with concomitant capecitabine. If there was a response to ICT, the patient was advised to continue with systemic chemotherapy after CRRT as consolidation chemotherapy while waiting for resection. These patients were compared with patients who received CRRT alone in the same time interval.

RESULTS:

Of 58 patients who had ICT, 32 (55 per cent) had surgery with clear resection margins, of whom ten (17 per cent) exhibited a pathological complete response (pCR). The remaining 26 patients had 23 R1 and three R2 resections. In 71 patients who received CRRT, a similar rate of R0 (35 patients) and R1 (36) resection was found (P?=?0·506), but only three patients (4 per cent) had a pCR (P?=?0·015).

CONCLUSION:

The incorporation of ICT in neoadjuvant regimens for locally recurrent rectal cancer is a promising strategy.

Impactfactor 5.433

Prognostic implications of MRI-detected lateral nodal disease and extramural vascular invasion in rectal cancer

Schaap DP, Ogura A, Nederend J, Maas M, **Cnossen JS**, Creemers GJ, van Lijnschoten I, Nieuwenhuijzen GA, Rutten HJ, Kusters M

Br J Surg. 2018 Dec;105(13):1844-1852

BACKGROUND:

Lateral nodal disease in rectal cancer remains a subject of debate and is treated differently in the East and the West. The predictive value of lateral lymph node and MRI-detected extramural vascular invasion (mrEMVI) features on oncological outcomes was assessed in this study.

METHODS:

In this retrospective cohort study, data on patients with cT3-4 rectal cancer within 8?cm from the anal verge were considered over a 5-year period (2009-2013). Lateral lymph node size, malignant features and mrEMVI features were evaluated and related to oncological outcomes.

RESULTS:

In total, 192 patients were studied, of whom 30 (15·6 per cent) underwent short-course radiotherapy and 145 (75·5 per cent) received chemoradiotherapy. A lateral lymph node short-axis size of 10?mm or more was associated with a significantly higher 5-year lateral/presacral local recurrence rate of 37 per cent, compared with 7·7 per cent in nodes smaller than 10?mm (P?=?0·041). Enlarged nodes did not result in a higher 5-year rate of distant metastasis (23 per cent versus 27·7 per cent in nodes smaller than 10?mm; P?=?0·563). However, mrEMVI positivity was related to more metastatic disease (5-year rate 43 versus 26·3 per cent in the mrEMVI-negative group; P?=?0·014), but not with increased lateral/presacral recurrence. mrEMVI occurred in 46·6 per cent of patients with nodes smaller than 10?mm, compared with 29 per cent in patients with nodes of 10?mm or larger (P?=?0·267).

CONCLUSION:

Although lateral nodal disease is more a local problem, mrEMVI mainly predicts distant recurrence. The results of this study showed an unacceptably high local recurrence rate in patients with a short axis of 10?mm or more, despite neoadjuvant (chemo)radiotherapy

Impactfactor 5.433

Quality assurance of four-dimensional computed tomography in a multicentre trial of stereotactic body radiotherapy of centrally located lung tumours

Marie Lambrecht, Jan-Jakob Sonke, Ursula Nestle, **Heike Peulen**, Damien C. Weber, Marcel Verheij, Coen W. Hurkmans

Physics and Imaging in Radiation Oncology 2018;8:57-62

Background and Purpose:

Extensive radiation therapy quality assurance (RTQA) programs are needed when advanced radiotherapy treatments are used. As part of the RTQA four dimensional computed tomography(4DCT) imaging performance needs to be assessed. Here we present the RTQA Data related to 4DCT proceduresused within the context of stereotactic bodyradiotherapy (SBRT) of centrally located lung tumours. It providesan overview of the 4DCT acquisition methods and achievable accuracy of imaging lung tumour volumes.

Materials and Methods:

3DCT and 4DCT images were acquired from a CIRS phantom with spheres of 7.5 and 12.5mm radius using the institutional scan protocols. Regular asymmetric tumour motion was simulated with varying amplitude sandperiods.Target volumes werere constructed using auto-contouring with scanner specific thresholds. Volume and amplitudes deviations were assessed.

Results:
Although acquisition parameters were rather homogeneous over the eleven institutions analysed, volume deviations were observed. Average volume deviations for the 12.5mm sphere were 15%(-4%to69%) at end of inspiration, 2% (-2% to 9.0%) at end of expiration and 12% (0% to 36%) at mid-ventilation. For the 7.5mm sphere deviations were 13% (-99% to 65%), 16% (-34% to 66%) and 1% (-13% to 20%), respectively. The amplitude deviation was generally within 2mm although underestimations up to 6mm were observed.
Conclusions:
The expiration phase was the most accurate phase to define the tumour volume and should be preferred for GTV delineation of tumours exhibiting large motion causing motion artefacts when using mid-ventilation or tracking techniques. The large variation found among the institutions indicated that further improvements in 4DCT imaging were possible. Recommendations for 4DCT QA have been formulated.

Impactfactor --

Risk of diabetes after para-aortic radiation for testicular cancer

Groot HJ, Gietema JA, Aleman BM, Incrocci L, de Wit R, Witjes JA, Groenewegen G, de Brouwer P, Meijer OW, Hulshof MC, **van den Berg HA**, Smilde TJ, Vanneste BG, Aarts MJ, van den Bergh AC, Kerst JM, van den Belt-Dusebout AW, Lubberts S, Józwiak K, Horenblas S, van Leeuwen FE, Schaapveld M

Br J Cancer. 2018 Oct;119(7):901-907

BACKGROUND: While the risk of diabetes is increased following radiation exposure to the pancreas among childhood cancer survivors, its association among testicular cancer (TC) survivors has not been investigated.
METHODS: Diabetes risk was studied in 2998 1-year TC survivors treated before 50 years of age with orchidectomy with/without radiotherapy between 1976 and 2007. Diabetes incidence was compared with general population rates. Treatment-specific risk of diabetes was assessed using a case-cohort design.
RESULS: With a median follow-up of 13.4 years, 161 TC survivors were diagnosed with diabetes. Diabetes risk was not increased compared to general population rates (standardised incidence ratios (SIR): 0.9; 95% confidence interval (95% CI): 0.7-1.1). Adjusted for age, para-aortic radiotherapy was associated with a 1.66-fold (95% CI: 1.05-2.62) increased diabetes risk compared to no radiotherapy. The excess hazard increased with 0.31 with every 10?Gy increase in the prescribed radiation dose (95% CI: 0.11-0.51, P?=?0.003, adjusted for age and BMI); restricted to irradiated patients the excess hazard increased with 0.33 (95% CI: -0.14 to 0.81, P?=?0.169) with every 10?Gy increase in radiation dose.
CONCLUSION: Compared to surgery only, para-aortic irradiation is associated with increased diabetes risk among TC survivors.

Impactfactor *5.922*

Risk of Solid Cancer After Treatment of Testicular Germ Cell Cancer in the Platinum Era

Groot HJ, Lubberts S, de Wit R, Witjes JA, Kerst JM, de Jong IJ, Groenewegen G, van den Eertwegh AJ, Poortmans PM, Klümpen HJ, **van den Berg HA**, Smilde TJ, Vanneste BG, Aarts MJ, Incrocci L, van den Bergh AC, Józwiak K, van den Belt-Dusebout AW, Horenblas S, Gietema JA, van Leeuwen FE, Schaapveld M

J Clin Oncol. 2018 Aug 20;36(24):2504-2513

Purpose Testicular cancer (TC) treatment increases risk of subsequent malignant neoplasms (SMNs). It is unknown whether changes in TC treatment over time have affected SMN risk. Methods Solid SMN risk was evaluated in a multicenter cohort comprising 5,848 1-year survivors treated for TC before age 50 years between 1976 and 2007. SMN incidence was compared with cancer incidence in the general population. Treatment-specific risks were assessed using multivariable regression in a case-cohort design. Results After a median follow-up of 14.1 years, 350 solid SMNs were observed, translating into a 1.8-fold (95% CI, 1.6-2.0) increased risk compared with general population rates. Solid SMN risk was increased in patients with seminoma and those with nonseminoma (standardized incidence ratio, 1.52 and 2.21, respectively). Patients with nonseminoma experienced increased risk of SMNs of the thyroid, lung, stomach, pancreas, colon, and bladder and of melanoma and soft tissue sarcoma, whereas those with seminoma experienced increased risk of SMNs of the small intestine, pancreas, and urinary bladder. The 25-year cumulative incidence of solid SMNs was 10.3% (95% CI, 9.0% to 11.6%). In multivariable analysis, platinum-based chemotherapy was associated with increased risk of a solid SMN (hazard ratio [HR], 2.40; 95% CI, 1.58 to 3.62), colorectal SMN (HR, 3.85; 95% CI, 1.67 to 8.92), and noncolorectal GI SMN (HR, 5.00; 95% CI, 2.28 to 10.95). Receipt of platinum 400 to 499 and = 500 mg/m2 increased solid SMN risk compared with surgery only (HR, 2.43; 95% CI, 1.40 to 4.23 and HR, 2.42; 95% CI, 1.50 to 3.90, respectively), whereas risk was not significantly increased with lower doses (HR, 1.75; 95% CI, 0.90 to 3.43). The HR of a GI SMN increased by 53% (95% CI, 26% to 80%) per 100 mg/m2 of platinum-containing chemotherapy. The HR of an infradiaphragmatic SMN increased by 8% per Gray of radiation dose administered (95% CI, 6% to 9%; P < .001). Conclusion Radiotherapy and platinum-containing chemotherapy are associated with increased solid SMN risk, specifically with GI SMNs.

Impactfactor *26.303*

Salvage endoscopic resection in patients with esophageal adenocarcinoma after chemoradiotherapy

Noordzij IC, Curvers WL, Huysentruyt CJ, Nieuwenhuijzen GA, Creemers GJ, **van der Sangen MJ**, Schoon EJ

Endosc Int Open. 2018 Sep;6(9):E1126-E1129.

Background and study aims For early esophageal adenocarcinoma, endoscopic resection is an accepted curative treatment with an excellent long-term prognosis. Case series from Japan have reported endoscopic resection of residual esophageal squamous cell carcinoma after chemoradiotherapy. This is the first report describing endoscopic resection of residual esophageal adenocarcinoma after chemoradiotherapy. Two patients with advanced esophageal adenocarcinoma had been treated with chemoradiotherapy because comorbidity precluded esophageal resection. When residual tumor was observed endoscopically, complete remission was achieved by salvage endoscopic therapy alone or in combination with argon plasma coagulation (APC). Both patients achieved long-term sustained remission and died of non-tumor-related causes.

Impactfactor --

Survival after whole brain radiotherapy for brain metastases from lung cancer and breast cancer is poor in 6325 Dutch patients treated between 2000 and 2014

Jeene PM, de Vries KC, van Nes JGH, Kwakman JJM, Wester G, Rozema T, Braam PM, Zindler JD, Koper P, Nuyttens JJ, Vos-Westerman HA, **Schmeets I**, Niël CGHJ, Hutschemaekers S, van der Linden YM, Verhoeff JJC, Stalpers LJA

Acta Oncol. 2018 May 57(5):637-643. Epub 2017 Dec 23

BACKGROUND:

Whole brain radiotherapy (WBRT) is considered standard of care for patients with multiple brain metastases or unfit for radical treatment modalities. Recent studies raised discussion about the expected survival after WBRT. Therefore, we analysed survival after WBRT for brain metastases 'in daily practice' in a large nationwide multicentre retrospective cohort.

METHODS:

Between 2000 and 2014, 6325 patients had WBRT (20?Gy in 4?Gy fractions) for brain metastases from non-small cell lung cancer (NSCLC; 4363 patients) or breast cancer (BC; 1962 patients); patients were treated in 15 out of 21 Dutch radiotherapy centres. Survival was calculated by the Kaplan-Meier method from the first day of WBRT until death as recorded in local hospital data registration or the Dutch Municipal Personal Records Database.

FINDINGS:

The median survival was 2.7 months for NSCLC and 3.7 months for BC patients (p?<?.001). For NSCLC patients aged <50, 50-60, 60-70 and >70 years, survival was 4.0, 3.0, 2.8 and 2.1 months, respectively (p?<?.001). For BC patients, survival was 4.5, 3.8, 3.2 and 2.9 months, respectively (p?=?.047). In multivariable analyses, higher age was related to poorer survival with hazard ratios (HR) for patients aged 50-60, 60-70 and >70 years being 1.05, 1.19 and 1.34, respectively. Primary BC (HR: 0.83) and female sex (HR: 0.85) were related to better survival (p?<?.001).

INTERPRETATION:

The survival of patients after WBRT for brain metastases from NSCLC treated in Dutch 'common radiotherapy practice' is poor, in breast cancer and younger patients it is disappointingly little better. These results are in line with the results presented in the QUARTZ trial and we advocate a much more restrictive use of WBRT. In patients with a more favourable prognosis the optimal treatment strategy remains to be determined. Prospective randomized trials and individualized prognostic models are needed to identify these patients and to tailor treatment.

Impactfactor *3.473*

The rationale for and long-term outcome of incomplete axillary staging in elderly women with primary breast cancer

Poodt IG, Schipper RJ, Vugts G, Woensdregt K, **van der Sangen M**, Voogd AC, Nieuwenhuijzen GA

Eur J Surg Oncol. 2018 Nov;44(11):1714-1719

BACKGROUND:

The proportion of elderly women diagnosed with breast cancer is rising. Standard treatment, including axillary staging, is often not given to these patients. This study aimed to investigate reasons to omit any surgical axillary staging or to refrain from completion axillary lymph node dissection (cALND) after positive-sentinel lymph node biopsy (SLNB); so-called "incomplete staging". Furthermore, the impact of incomplete staging on regional control and survival in patients aged 75 or older was evaluated.

METHODS:

A retrospective cohort study was conducted including all primary breast cancer patients aged 75 or older, diagnosed between 2001 and 2008, and documented by the Netherlands Cancer Registry (NCR). Patients with incomplete staging were compared to patients with complete axillary staging. Survival analyses were used to determine the risk of local, regional and distant recurrence and overall survival.

RESULTS:

In total, 1467 of 2116 (69%) patients were considered eligible, of whom 258 (17.2%) had incomplete axillary staging. For 93 patients, diagnosed in 6 of the 10 hospitals in the NCR-area, examination of clinical records revealed that age, comorbidities and patient preferences were the main reason for omitting complete axillary staging. The 10-

year axillary recurrence rate in these 93 patients was 5.2% (95% CI, 0.03-10.1). Of the 77 patients who had died, 64 (83%) died of non-breast-cancer-related causes. No significant difference in overall survival was observed between patients with or without complete axillary staging.

CONCLUSION:

This study demonstrates that the omission of complete axillary staging is common in selected elderly breast cancer patients with =2 comorbidities, with no apparent impact on regional control and 10-year overall survival.

Impactfactor 3.688

Spoed Eisende Hulp

Does X-ray imaging by GPC at emergency care access points in the Netherlands change patient flow and reduce ED crowding? A cohort study

van den Bersselaar DLCM, Maas M, Thijssen WAMH

Health Sci Rep. 2018 Feb 8;1(2):e26. eCollection 2018 Feb

Objective:

Organizing out-of-hours emergency care is a challenge in many countries. In the Netherlands, general practitioner cooperatives (GPCs) and emergency departments (EDs) are increasingly working together, creating one emergency care access point (ECAP). This has redirected the majority of patients with musculoskeletal problems from the ED to the GPC in out-of-hours care, due to the treatment of self-referrals by the general practitioner (GP). Only a minority of the GPs at ECAPs have the possibility to request X-rays, and expanding these facilities could reduce patient presentations to the ED even more. The aim of our study was to explore patient flow and possible reductions in ED referrals at an ECAP with X-ray facilities for GPs.

Methods:

This retrospective cohort study examines all patients that visited an ECAP at a general city hospital in the Netherlands and had an X-ray imaging requested by the GPC between January 1, 2014 and December 31, 2014. General practitioner cooperatives could request X-rays between 5 pm and 10 pm on weekdays and between 8 am and 10 pm during weekends. Recorded data included sex, age, number and type of X-ray, X-ray abnormalities, referral to the ED, and treatment. The annual number of patients presenting to the GPC and ED in 2014 were gathered. Patient outcome was stated negative when the X-ray revealed no abnormality.

Results:

A total of 2243 patients received 2663 X-ray examinations. The mean age was 31 years and 48% was male. A total of 1517 (68%) patients were treated at the GPC without an ED referral, a reduction of 4.5% of the annual ED patients.

Conclusions:

With a majority (68%) of the patients examined and treated at the GPC, X-ray facilities at ECAPs will substantially reduce ED population, change patient flow, and have a positive effect on ED crowding. Implementing 24/7 X-ray facilities at all ECAPs will further enhance these effects.

Impactfactor --

Urologie

Development and validation of the TOCO-TURBT tool: a summative assessment tool that measures surgical competency in transurethral resection of bladder tumour

de Vries AH, Muijtjens AMM, van Genugten HGJ, **Hendrikx AJM, Koldewijn EL**, Schout BMA, van der Vleuten CPM, Wagner C, Tjiam IM, van Merrienboer JJG

Surg Endosc. 2018 Jun 5. [Epub ahead of print]

BACKGROUND:

The current shift towards competency-based residency training has increased the need for objective assessment of skills. In this study, we developed and validated an assessment tool that measures technical and non-technical competency in transurethral resection of bladder tumour (TURBT).

METHODS:

The 'Test Objective Competency' (TOCO)-TURBT tool was designed by means of cognitive task analysis (CTA), which included expert consensus. The tool consists of 51 items, divided into 3 phases: preparatory (n?=?15), procedural (n?=?21), and completion (n?=?15). For validation of the TOCO-TURBT tool, 2 TURBT procedures were performed and videotaped by 25 urologists and 51 residents in a simulated setting. The participants' degree of competence was assessed by a panel of eight independent expert urologists using the TOCO-TURBT tool. Each procedure was assessed by two raters. Feasibility, acceptability and content validity were evaluated by means of a quantitative cross-sectional survey. Regression analyses were performed to assess the strength of the relation between experience and test scores (construct validity). Reliability was analysed by generalizability theory.

RESULTS:

The majority of assessors and urologists indicated the TOCO-TURBT tool to be a valid assessment of competency and would support the implementation of the TOCO-TURBT assessment as a certification method for residents. Construct validity was clearly established for all outcome measures of the procedural phase (all r?>?0.5, p?<?0.01). Generalizability-theory analysis showed high reliability (coefficient Phi?=?0.8) when using the format of two assessors and two cases.

CONCLUSIONS:

This study provides first evidence that the TOCO-TURBT tool is a feasible, valid and reliable assessment tool for measuring competency in TURBT. The tool has the potential to be used for future certification of competencies for residents and urologists. The methodology of CTA might be valuable in the development of assessment tools in other areas of clinical practice.

Impactfactor *3.117*

High-precision Bladder Cancer Irradiation in the Elderly: Clinical Results for a Plan-of-the-day Integrated Boost Technique with Image Guidance Using Lipiodol Markers

Alexander J.W. Beulens, Peter-Paul van der Toorn, **Michel J. de Wildt** , **Wout A. Scheepens**

European Urology Oncology Available online 7 September 2018

Background

For most elderly patients with muscle-invasive bladder cancer (MIBC), surgery is not an option because of patient frailty. Conventional radiotherapy, with its high-dose irradiation of surrounding healthy tissues, remains the only curative treatment for this patient population.

Objective

To determine whether targeted radiotherapy with Lipiodol demarcation and plan-of-the-day integrated boost technique (LPOD) is a viable curative treatment for elderly patients with MIBC.

Design, setting, and participants

Between September 2008 and September 2016 all MIBC patients in our hospital were screened for eligibility. We included patients with localised, unifocal T2–T4N0M0 grade 2–3 MIBC. Patients with a tumour volume >50% of the bladder wall surface, previous pelvic radiotherapy, and unilateral or bilateral hip prostheses were excluded. Intervention: Targeted radiotherapy using LPOD.

Outcome measurements and statistical analysis

Overall survival, urothelial cell cancer–specific survival (UCCSS), disease recurrence, and Radiation Therapy Oncology Group (RTOG) toxicity were measured. Statistical analyses included independent-sample t tests, ?2 tests, and Mann-Whitney U tests.

Results and limitations

A total of 44 patients (median age 80 yr) were included. Over median follow-up of 38 mo, one patient ceased treatment and 23 patients died. LPOD resulted in a 11.4% chance of local recurrence, high 3-yr UCCSS of 77%, RTOG grade >3 toxicity of 2.3–12.9%, and 3-yr overall survival of 49%.

Conclusions

LPOD is a feasible first-line treatment option for older patients with limited-volume T2–T4N0M0 grade 2–3 MIBC.

Impactfactor --

Injectable Bulking Agent to Treat Postprostatectomy Urinary Incontinence: A Safety and Effectiveness Pilot Study.

van Uhm JIM, Vermeer M, Elzevier HW, Noordzij JW, **Koldewijn EL**, Cornel EB

Biomed Res Int. 2018 Dec 6;2018:2796967. doi: eCollection 2018

Objectives:

To evaluate the safety and effectiveness of the injectable bulking agent Opsys® (Promedon, Cordoba, Argentina) for treating minimal postprostatectomy stress urinary incontinence (SUI).

Patients and Methods:

Single-centre, pilot study on ten male patients with SUI, < 30 g urine loss/ 24 h, more than 1 year after radical prostatectomy. Patients were treated by endoscopic transurethral injections of bulking agent in the presphincteric zone of the urethral submucosa. The results were evaluated using a pad weight test to quantify the differences in urine loss at 1, 3, and 6 months after intervention. Subsequently, the results of treatment were also evaluated by International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF), Incontinence Impact Questionnaire (IIQ-7), Urogenital Distress Inventory Short Form (UDI-6-SF), and the Patient Global Impression of Improvement (PGI-I) at 1, 3, and 6 months after intervention.

Results:

The primary outcome was the absolute result of the 24-hour pad weight test after treatment. Treatment success was defined as <3 g urine loss/24 h, improvement as =50% decrease in urine loss/ 24h, failure as <50% decrease in urine loss/24 h, or worsening of urine loss. Success was demonstrated in one, improvement in one, and failure in eight patients one month after treatment. One patient improved and 9 failed 3 and 6 months after treatment. The median 24-hour pad weight test was higher at all three moments of follow-up (1, 3, and 6 months after treatment). The median 24-hour pad weight test was before treatment 17.3g (6.4-20.9) and 1, 3, and 6 months after treatment, respectively, 40.3g (5.9-130.6) p= 0.038, 38.3g (18.3-202.1) p= 0.014, 55.0g (16.5-314.6) p= 0.028. The ICIQ-SF was significantly higher at 3 and 6 months, respectively 15.0 (12.0-18.5) p= 0.007 and 16.0 (12.5-17.5) p=0.012 versus 10.0 (9.0-12.0) before injection. No significant differences were found between IIQ-7, UDI-6-SF, and PGI-I before and after injection. Complications occurred in four patients: two patients reported spontaneously resolved haematuria and two patients reported urinary frequency. All complications were classified as Clavien-Dindo 1.

Conclusion:

Injection therapy with Opsys® bulking agent is not an effective treatment option for male SUI after radical prostatectomy. It is not a safe treatment option, due to worsening urine loss after treatment.

Impactfactor 2.583

Penile intraepithelial neoplasia: Nomenclature, incidence and progression to malignancy in the Netherlands

Hoekstra RJ*, Trip EJ, Ten Kate FJ, Horenblas S, Lock MT

Int J Urol. 2018 Dec 3. [Epub ahead of print]

OBJECTIVE:

To determine the incidence of penile intraepithelial neoplasia in the Netherlands using a nationwide histopathology registry and to discuss the nomenclature of premalignant penile lesions.

METHODS:

Data from patients in the Netherlands diagnosed with a premalignant penile lesion between January 1998 and December 2007 were collected from the nationwide histopathology registry (PALGA); this database covers all pathology reports of inhabitants in the Netherlands. The premalignant lesions included were erythroplasia of Queyrat; Bowen's disease; bowenoid papulosis; mild, moderate and severe dysplasia; and carcinoma in situ of the penis. The terminology used in the pathological reports was translated to penile intraepithelial neoplasia. The grading was made analogous to that of vulvar premalignant lesions.

RESULTS:

The PALGA database enrolled 380 patients with premalignant penile lesions. Severe premalignant lesions, penile intraepithelial neoplasia III, were found in 254 patients (67%), penile intraepithelial neoplasia II in 84 (22%) and penile intraepithelial neoplasia I in 42 patients (11%). Most lesions were located on the prepuce (45%), followed by glans (38%) and shaft (3%). The median age of patients with penile intraepithelial neoplasia was 58 years. Progression to malignant disease occurred (2% for penile intraepithelial neoplasia I vs 7% for penile intraepithelial neoplasia III) In 26 patients.

CONCLUSIONS:

Penile intraepithelial neoplasia is a rarely diagnosed condition. Because of the wide variation of terms used for premalignant intraepithelial neoplasia of the penis, we recommend restricting this nomenclature to penile intraepithelial neoplasi

Impactfactor 1.941

**Ten tijde van publicatie verbonden aan: Department of Urology, University Medical Center Utrecht, Utrecht*

Residents' readiness for out-of-hours service: a Dutch national survey

Baten A, Bleeker-Rovers CP, **van den Heijkant F**, de Graaf J, Fluit CR

Neth J Med. 2018 Mar;76(2):78-83

BACKGROUND:
Residents play a crucial role in out-of-hours service. Their perceived readiness for out-of-hours service, however, remains underexposed. This national exploratory study assesses whether or not Dutch residents feel sufficiently prepared to provide out-of-hours service at the time of their first shift, and aims to identify factors influencing perceived readiness.
METHODS:
An online questionnaire focussing on residents' working conditions was accessible from 21 September to 10 November 2015. Questions targeting perceived readiness for out-of-hours service were presented to all responding medical residents actively involved in out-of-hours service. Residents who felt sufficiently prepared were compared with residents who did not, exploring both individual characteristics and environmental factors.
RESULTS:
A total of 960 residents (mean age 32.5 years ±; 3.5, 72.4% female) from over 30 different medical specialties were included. Thirty-six percent of responding residents felt insufficiently prepared to provide out-of-hours service at the time of their first shift. Current junior status ($p = 0.020$), prolonged clinical experience prior to the first shift ($p < 0.001$), targeted training ($p < 0.001$), assessment of relevant skills and competencies ($p < 0.001$), and formal consequences following negative assessment ($p = 0.001$) were positively associated with perceived readiness.
CONCLUSION:
One-third of responding residents felt insufficiently prepared for their first out-of-hours shift. Our results emphasise the need for sufficient time to gain clinical experience as a new graduate, and underline the positive contribution of targeted training and assessment of skills and competencies relevant to out-of-hours service.

Impactfactor *1.156*

The learning environment and resident burnout: a national study

van Vendeloo SN, Prins DJ, Verheyen CC, Prins JT, **van den Heijkant F**, van der Heijden FM, Brand PL

Perspectives on Medical Education 2018;7(2):120–5

Geen impactfactor beschikbaar

Impactfactor --

The relationship between burnout personality traits and medical specialty. A national study among Dutch residents

Prins DJ, van Vendeloo SN, Brand PLP, Van der Velpen I, de Jong K, **van den Heijkant F**, Van der Heijden FMMA, Prins JT

Med Teach. 2018 Nov 3:1-7. [Epub ahead of print]

PURPOSE:
To examine the associations between residents' personality traits, type of specialty, and symptoms of burnout.
METHOD:
A cross-sectional online survey among Dutch residents was conducted (see Supplementary Material). The 20-item Dutch translation of the Maslach Burnout Inventory was used to ascertain burnout. Personality traits were assessed with the 44-item Dutch Big Five Inventory. Logistic regression analyses, including all five personality traits, were used to assess associations with burnout. Analyses were stratified by specialties.
RESULTS:
One thousand two hundred thirty one residents participated, 185 (15.0%) of whom met the criteria for burnout. Neuroticism was significantly associated with resident burnout in all specialties, more strongly in supportive (odds ratio (OR) 6.19, 95% CI 2.12-18.12) and surgical (OR 4.37, 95% CI 1.76-10.86) than in medical residents (OR 1.99, 95% CI 1.22-3.24). Extraversion was significantly associated with less burnout in surgical residents (OR 0.26, 95% CI 0.13-0.58). These findings remained highly significant after controlling for gender, overtime, autonomy at work, satisfaction between work and private life, and the perceived quality of the learning environment.
CONCLUSIONS:
Burnout risk was associated with personality traits in residents. Consistently, residents scoring high on neuroticism reported more burnout. Extraverted surgical residents were less susceptible to burnout. Residents scoring high on neuroticism may require more intense monitoring during their training years.

Impactfactor *2.450*

The value of a 1-day multidisciplinary robot surgery training for novice robot surgeons.

Beulens AJW, Brinkman WM, Porte PJ, Meijer RP, van Merrienboer JJG, Van der Poel HG, Wagner C.

J Robot Surg. 2018 Nov 22. [Epub ahead of print]

INTRODUCTION:

To fulfil the need for a basic level of competence in robotic surgery (Brinkman et al., Surg Endosc Other Interv Tech 31(1):281-287, 2017; Dutch Health inspectorate (Inspectie voor de gezondheidszorg), Insufficient carefulness at the introduction of surgical robots (in Dutch: Onvoldoende zorgvuldigheid bij introductie van operatierobots), Igz, Utrecht, 2010), the NIVEL (Netherlands Institute for Healthcare Research) developed the 'Basic proficiency requirements for the safe use of robotic surgery' (BPR). Based on the BPR a 1-day robotic surgery training was organised to answer the following research questions: (1) Are novice robot surgeons able to accurately self-assess their knowledge and dexterity skills? (2) Is it possible to include the teaching of all BPRs in a 1-day training?

MATERIALS AND METHODS:

Based on the BPR, a robot surgery course was developed for residents and specialists (surgery, gynaecology and urology). In preparation, the participants completed an online e-module. The 1-day training consisted of a practical part on robot set-up, a theoretical section, and hands-on exercises on virtual reality robot simulators. Multiple online questionnaire was filled out by the participants at the end of the training to evaluate the perceived educational value of the course and to self-assess the degree to which BPRs were reached.

RESULTS:

20 participants completed the training during the conference of the Dutch Association for Endoscopic Surgery (NVEC) in 2017. Participants indicated nearly all competency requirements were mastered at the end of the training. The competency requirements not mastered were, however, critical requirements for the safe use of the surgical robot. Skill simulation results show a majority of participants are unable to reach a proficient simulation score in basic skill simulation exercises.

CONCLUSION:

Results show novice robot surgeons are too positive in the self-assessment of their own dexterity skills after a 1-day training. Self-assessment revealed uncertainty of the obtained knowledge level on requirements for the safe use of the surgical robot. Basic courses on robotic training should inform trainees about their results to enhance learning and inform them of their competence levels.

Impactfactor --

Boeken

Anesthesiologie

Monitoring
Bouwman RA, Keizer C
In: Leerboek anesthesiologie - 4e herziene druk
Redactie: Auteurs: dr. P.J. Hennis, dr. H.P.A van Dongen en prof. dr. W.A van Klei (redactie)
Houten : Bohn Stafleu van Loghum, 2018
ISBN: 9789036821124

Cardiologie

Chapter 18 – Fractional Flow Reserve – p 313-328
Zimmermann FM, Pijls NH, Tonino WA
In: Textbook of Catheter-based Cardiovascular Interventions : a knowledge-based approach
Authors: Peter Lanzer
[sl] : Springer, 2018
ISBN: 978-3-319-55994-0

Chirurgie

Chapter 3 - What are the issues in the treatment of elderly patients - pp 21-29
RG Orsini, HJT Rutten
Chapter 5 - What is the history of rectal cancer treatment? - pp 37-45
MM Lange, **HJT Rutten**
Chapter 49: Will the extralevator approach for low rectal cancer become the new standard? - pp 389-403
AC Kraima, P Quirke, MC de Ruiter, CJH van de Velde, **HJT Rutten**
Chapter 52: Which are the key tools for the management of locally recurrent rectal cancer? – pp 439-449
SJ Bosman, **HJT Rutten**
In: Multidisciplinary management of rectal cancer 2nd edition
Eds: Valentini, Schmoll, van de Velde
Berlin Heidelberg : Springer Verlag, 2018
ISBN: 978-3-319-43215-1

Intensive Care

Cardiac Function (Cardiac Output and Its Determinants) – p 51-76
Meijs LP, **Bindels AJ**, Bakker J, Pinsky MR
In: Monitoring Tissue Perfusion in Shock : from Physiology to the Bedside
Ed: Pinto Lima AA, Silva E
Cham : Springer Verlag, 2018
ISBN: 97833194313075

Klinische Fysica

NCS Report 30: Code of Practice for Quality Assurance of Brachytherapy with Ir-192 Afterloaders
Steenhuijsen J Harbers M Hoffmann A De Leeuw A Rijnders A Unipan M
Delft : NCS, 2018

Orthopedie

Letsels van het steun- en bewegingsapparaat

P.R.G. Brink, **A.T. Besselaar**, J.B.A. van Mourik, F.C. Öner, K.J. Ponsen, R.K.J. Simmermacher
Bohn Stafleu van Loghum 2018
9789036818711

Promoties

Promovendi

Algemeen Klinisch Laboratorium

Schmitz E
Development and evaluation of protein quantitation assays for use in health care
Eindhoven: Technische Universiteit Eindhoven, 2018
ISBN: 978-90-386-4466-0
Promotiedatum: 4-4-2018

Cardiologie

Otterspoor LC
Intracoronary hypothermia
Eindhoven: Technische Universiteit Eindhoven, 2018
ISBN: 978-90-386-4408-0
Promotiedatum: 11-1-2018

Chirurgie

Rijn S van
Implications of surgical and endoscopic interventions in the upper GI tract (with focus on management of GERD and Weight Control)
Maastricht, Universiteit Maastricht, 2018
ISBN: 9789462338876
Promotiedatum: 21 Mar 2018

Castelijns PSS
Outcome after laparoscopic antireflux surgery and hiatal hermia repair
Maastricht : Universiteit Maastricht, 2018
ISBN: 978-94-9301495-4
Promotiedatum: 19-12-2018

Stokmans RA
Simplifying management strategies in contemporary practice of endovascular abdominal aortic aneurysm repair
Maastricht: University of Maastricht, 2018
ISBN: 9789402812480
Promotiedatum: 14-12-2018

Gynaecologie

Hamerlynck T
New insights in hysteroscopic morcellation
Ghent : Ghent University, faculty of Medicine and Health Sciences, 2018
Promotiedatum: 5-3-2018

Inwendige Geneeskunde

Sörensen B
Determinants of microvascular function in individuals with and without type 2 diabetes: a population-based approach
Maastricht : Maastricht university 2018
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Dermatologie

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Gynaecologie

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- Hamerlynck T - New insights in hysteroscopic morcellation
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Co-promotor bij:

- Nicole Kraaijvanger - Self-reffered patients in Emergency Departments in the Netherlands
  Promotiedatum: 27-06-2018

Wetenschapsavond

Presentaties

Cardiologie

Fractional Flow Reserve-Guided Percutaneous Coronary Intervention Versus Medical Therapy for patients with stable coronary lesions: meta-analysis of individual patient data

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Aims

To assess the effect of fractional flow reserve (FFR)-guided percutaneous coronary intervention with contemporary drug-eluting stents on the composite of cardiac death or myocardial infarction versus medical therapy in patients with stable coronary lesions.

Methods and results

We performed a systematic review and meta-analysis of individual patient data (IPD) from the 3 available randomized trials of contemporary FFR-guided PCI versus medical therapy for patients with stable coronary lesions: FAME 2 (NCT01132495), DANAMI-3-PRIMULTI (NCT01960933), and Compare-Acute (NCT01399736). FAME 2 enrolled patients with stable coronary artery disease, while the other two focused on non-culprit lesions in stabilized patients after ACS. A total of 2400 subjects were recruited from 54 sites world-wide with 1056 randomly assigned to FFR-guided PCI and 1344 to medical therapy. The pre-specified primary outcome was a composite of cardiac death or myocardial infarction. We included data from extended follow-ups for FAME 2 (up to 5.5 years follow-up) and DANAMI-3-PRIMULTI (up to 4.7 years follow-up). After a median follow-up of 35 months (interquartile range 12 to 60 months), a reduction in the composite of cardiac death or MI was observed with FFR-guided PCI as compared with medical therapy (hazard ratio 0.72, 95% confidence interval 0.54 to 0.96, p=0.02). The difference between groups was driven by myocardial infarction.

Conclusion

In this individual patient data meta-analysis of the 3 available randomized controlled trials to date, FFR-guided PCI resulted in a reduction of the composite of cardiac death or myocardial infarction compared with medical therapy, which was driven by a decreased risk of myocardial infarction.

Chirurgie

Direct oral feeding following minimally invasive esophagectomy (NUTRIENT II trial): an international, multicenter, open-label randomized controlled trial

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* Both authors contributed equally.

Background

Elements of enhanced recovery after surgery (ERAS) protocols have been successfully introduced in patients undergoing an esophagectomy. However, start of oral intake, which is an essential part of the ERAS protocols, remains a matter of debate.

Objective

Patients undergoing an esophagectomy are often kept nil-by-mouth postoperatively out of fear for increasing anastomotic leakage and pulmonary complications. This study investigates the effect of direct start of oral feeding following minimally invasive esophagectomy (MIE) compared to standard of care.

Methods

Patients in this multicenter, international randomized controlled trial were randomized to directly start oral feeding (intervention) after a MIE with intrathoracic anastomosis or to receive nil-by-mouth and tube feeding for five days postoperative (control group). Primary outcome was time to functional recovery. Secondary outcome parameters were anastomotic leakage, pneumonia rate and other surgical complications scored by predefined definitions.

Results

Baseline characteristics were similar in the intervention (n=65) and control (n=67) group. Functional recovery was seven days for patients receiving direct oral feeding compared to eight days in the control group (p-value 0.436). Anastomotic leakage rate did not differ in the intervention (18.5%) and control group (16.4%, p-value 0.757). Pneumonia rates were comparable between the intervention (24.6%) and control group (34.3%, p-value 0.221).

Other morbidity rates were similar, except for chyle leakage which was more prevalent in the standard of care group (p-value 0.032).
Conclusions
Direct oral feeding after an esophagectomy does not affect functional recovery and did not increase incidence or severity of postoperative complications.
Innovative elements
A nil-by-mouth period for 5 days and tube feeding is the current standard following MIE. However, this regime is associated with complications and patient discomfort. This is the first trial showing that direct oral intake following MIE has similar functional recovery and postoperative morbidity rates compared with standard of care.

Gynaecologie

Signal transduction pathway activation analysis in normal epithelium of the Fallopian tube

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Introduction
Recently, Fallopian tube epithelium (FTE) has been identified as the cell type of origin of high grade serous ovarian carcinoma (HGSC). Signal transduction pathways (STP's) are responsible for normal cell proliferation and differentiation. In malignancies, these STP's are often aberrantly activated. We aim to identify important STP's in normal FTE during the follicular and luteal phase of the menstrual cycle, allowing us eventually to identify abnormal signal transduction pathway activation (STA) leading to HGSC.
Methods
First, STA was measured in FTE using public Affymetrix microarray datasets. Then, we determined STA in lasermicrodissected fimbrial and tubal epithelial cells from women who had hysterectomy with salpingectomy for benign reasons. The use of a novel computational approach allowed quantitative assessment based on measurement of target gene mRNA levels. Activity scores were statistically analyzed with SPSS using the Kruskall-Wallis and Mann-Whitney U Test.
Results
Preliminary data showed similarities in the AR, HH, NFkB, NOTCH, TGFβ and Wnt pathway activity between the follicular and luteal phase. ER pathway activity is associated with the estradiol-driven proliferative phase and is decreased due to lower estradiol concentrations during the luteal phase (p=0.001). FOXO transcription factor was more actived during the luteal phase, indicating lower activity of the PI3K growth factor pathway (p=0.000).
Conclusion
We described, for the first time, activity of eight STP's in normal FTE cells during the menstrual cycle. The PI3K pathway is the most frequently mutated STP and is frequently active in HGSC. As can be seen from these results, during the menstrual cycle the PI3K pathway is activated in a controlled manner. Disturbance of this control is expected to result in abnormal cell division and, potentially, cancer.
Significance and innovation
The use of targeted therapy based on signaling pathways needs accurate diagnostic tools to predict therapy response in individuals. Currently available tests often demonstrate key proteins of signaling pathways without providing conclusive information on the functional activity status. Our approach enables quantitative measurements based on inferring target gene mRNA levels.

Intensive Care / Interne geneeskunde / e/MTIC

Effects of a Fully Automated vs Conventional Postoperative Ventilation Strategy on Time Spent in Critical, Acceptable and Optimal Zones of Ventilation in Patients after Cardiac Surgery – a randomized clinical trial

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Abstract
Background: It remains uncertain whether postoperative ventilation after cardiac surgery should use a fully automated ventilation strategy.
Aim: A single–center randomized clinical trial to determine whether a fully automated ventilation strategy compared to conventional ventilation can reduce time spent in the unacceptable critical zone of ventilation during the first three postoperative hours.
METHODS: The co–primary outcomes were the proportions of time spent in critical, acceptable and optimal ventilation zones during the first three postoperative hours and for all registered breaths. Secondary outcomes were the time to spontaneous breathing activity, and the duration of weaning and ventilation.
RESULTS: In total, 220 patients (73% male) with a median age of 70 years (interquartile range [IQR] 62–76) were enrolled. Patients were randomly assigned to fully automated ventilation ('automated', N = 109) or conventional ventilation ('conventional', N = 111). The percentage of time spent in critical, acceptable and optimal zones was 0.5 ± 2.9% vs 3.0 ± 8.3%, 16.7 ± 16.7% vs. 50.0 ± 34.0%, and 55.2 ± 28.0% vs. 25.5 ± 29.3% in the automated vs the

conventional group (mean difference in critical zones: –2.5 [95%–CI, –4.1 to –0.8]%; P = 0.003). Time to spontaneous breathing was shorter in the automated group, while the duration of ventilation and weaning did not differ.
CONCLUSIONS AND RELEVANCE: In patients after cardiac surgery, fully automated ventilation favourably changed time spent in predefined ventilation zones. The study was underpowered for clinical outcomes, and additional research may be needed to evaluate this further.
INNOVATIVE ASPECTS: Patients after cardiac surgery receive more time of “lung protective ventilation” and less time of “lung injury inducing ventilation” with a new innovative fully automated ventilation strategy compared to a convention ventilation strategy directed by ICU

Interne Geneeskunde

The limited impact of systemic therapy in patients with synchronous metastases of small bowel adenocarcinoma: a reflection of daily practice

Laura M. Legué , Nienke Bernards , Valery E.P.P. Lemmens , Ignace H.J.T. de Hingh , Geert-Jan Creemers , Felice N. van Erning

Background: Although small bowel adenocarcinoma (SBA) is rare, metastatic disease is frequently encountered. Due to the rarity of the disease, no standard systemic regimen has been defined.
Aim: The aim of this population-based study was to obtain insights into the use and effects of systemic therapy in patients with synchronous metastases of SBA in the Netherlands.
Methods: Data were retrieved from the Netherlands Cancer Registry, after additional data collection on used chemotherapy and targeted therapy, supported by the Catharina Research Fund. Patients with synchronous metastatic SBA between 2007 and 2016 were included (n = 522). Differences in systemic treatment and the subsequent effects on survival were evaluated. To eliminate potential endogeneity bias when comparing patients with and without targeted therapy, a propensity score matched sample was generated.
Results: 38% of the patients received palliative systemic therapy (n = 199). In first-line treatment, combination chemotherapy with mainly CAPOX/FOLOX was administered to 80% of the patients and 13% of the patients received additional targeted therapy, exclusively bevacizumab. Single agent chemotherapy mostly consisted of capecitabine. Second-line treatment was prescribed to 27% of the patients, mostly irinotecan-based (57%). Median overall survival (OS) with palliative chemotherapy was 9.3 months, compared to 3.0 months with best supportive care. In sub analyses, the patients who only received first-line palliative chemotherapy, had a median OS of 5.5-6.9 months, compared to 8.5 months for patients receiving additionally bevacizumab (p = 0.54). One-year overall survival rates for patients treated with and without bevacizumab in first-line treatment respectively were both 25% in the propensity-matched sample.
Conclusion: Palliative chemotherapy was administered to a minority of patients, with mostly oxaliplatin-based combination chemotherapy in first-line treatment. Palliative chemotherapy amounted in a median OS of 9 months. The equal one-year survival rates in patients treated with and without bevacizumab in addition to first-line palliative chemotherapy indicates there might be no future role for the targeted agent bevacizumab in metastatic SBA.

Posters

Algemeen Klinisch Laboratorium

Evaluatie en optimalisatie van 1) landelijke bariatrische diagnostiek en de 2) succesfactor MHI (Metabolic Health Index)

Carmen Gensen*, Arjen-Kars Boer, Natal van Riel, Simon Nienhuijs, Volkher Scharnhorst, Saskia van Loon

Wetenschap en praktijk werken samen voor de optimale bariatrische zorg

Achtergrond: een continue stijging van het aantal uitgevoerde bariatrische operaties verhoogt het belang van optimalisatie van de perioperatieve zorg rondom deze ingrepen. Bariatrische chirurgie leidt tot gewichtsafname als gevolg van een verminderde voedselinname, hormonale veranderingen in de darm en/of reductie van vertering en absorptie van voedingsstoffen. Laboratoriumdiagnostiek wordt gebruikt om deze veranderingen te monitoren en daarmee complicaties, zoals ongewenste vitamine- en/of mineralentekorten, te voorkomen. Landelijk zijn afspraken gemaakt over bariatrische laboratoriumpakketten. Echter, huidige laboratoriumpakketten verschillen enorm per ziekenhuis en dus is een evaluatie van alle pakketten en optimalisatie hard nodig. Daarnaast volgen uit deze evaluatie potentiële laboratoriumpakketten die gebruikt kunnen worden voor een multicenter validatie van de door het CZE ontwikkelde MHI. MHI is gebaseerd op een combinatie laboratoriumbepalingen, welke de obesitas-gecorreleerde comorbiditeiten objectief in één getal kwantificeert en daarmee metabole effecten van bariatrische chirurgie meetbaar maakt. Een machtige tool, die voor landelijk gebruik in een multicenter onderzoek gevalideerd moet worden. Doelstelling: evaluatie van bariatrische laboratoriumpakketten van alle 18 bariatrische centra en een multicenter validatie van de MHI. Methode: Pakketten worden op basis van inhoud, moment van afname en kosten met elkaar en met richtlijnen vergeleken. Voor de MHI-validatie wordt het ontwikkelde algoritme toegepast op externe retrospectieve datasets van vier obesitascentra, waarna regressiecoëfficiënten met het huidige model en elkaar worden vergeleken. Resultaten*: Ondanks gestelde richtlijnen meet 59% postoperatief geen leverfunctie en voldoet in totaal 83% van de centra niet aan de richtlijnen. Overige resultaten worden getoond tijdens presentatie. Conclusie: Optimalisatie van laboratoriumpakketten en/of richtlijnen is hard nodig. Daarnaast zijn 4 laboratoriumpakketten geschikt voor externe validatie.

*Het validatie-onderzoek loopt op dit moment nog. Tijdens de wetenschapsavond zullen de resultaten/conclusie hiervan worden gepresenteerd. Overige uitgebreide resultaten zullen middels figuren worden getoond tijdens (poster)presentatie

Vernieuwde elementen van de studie:

- MHI-algoritme toepassen op datasets van externe centra voor externe validatie.
- Bij positieve validatie: subanalyses (o.b.v. MHI) per centrum en tussen centra
- Bariatrische pakketten van alle bariatrische centra in Nederland met elkaar en met richtlijnen vergelijken (inhoud, moment van bepaling en kosten).

Optimized (pre) analytic conditions and workflow for ddPCR analysis of cfDNA from patients suspected of lung carcinoma

Remco de Kock*, Birgit Deiman, Raisa Kraaijvanger, Volkher Scharnhorst

BACKGROUND: For patients suspected of lung carcinoma, the analysis of circulating tumor DNA (ctDNA), obtained by liquid biopsy, has the potential to support cancer diagnosis and guide targeted therapy. To ensure sensitive and reproducible detection of ctDNA in daily routine practice, a standardized (pre) analytical workflow is required.
METHODS: Plasma was obtained from patients and healthy volunteers. Six different procedures for the isolation of cell-free DNA (cfDNA) were compared by using the Qiagen Circulating Nucleic Acid Kit. Analysis of cfDNA was performed by droplet digital PCR (ddPCR) for KRAS G12/13 mutations using the KRAS screening kit (Bio-Rad) and for EGFR Ex19Del, L858R and L861Q mutations using an in-house EGFR multiplex.
RESULTS: A new isolation procedure was selected that yielded extracts with significant higher cfDNA concentrations than described previously ($P<0.001$). EGFR and KRAS assay sensitivity of at least 0.2% fractional abundance is guaranteed for approximately 76% of the patient samples in one run, and 100% in two runs, with only 10 µL cfDNA extract used per run. A flowchart was designed that includes validity criteria for a standardized analytic workflow of ddPCR analysis.
CONCLUSIONS: An improved protocol for cfDNA isolation enables a higher cfDNA input for ddPCR than reported previously. The use of sensitive KRAS and EGFR multiplex assays and accompanying validity criteria, allows for controlled and efficient testing of patient samples at lower costs. Using the suggested workflow, a guaranteed, reliable and sensitive analysis of cfDNA can be performed using ddPCR in daily routine practice.
An improved cell-free DNA isolation method is presented together with a novel in-house developed EGFR multiplex. Validity criteria were established and represented in a flowchart, which can be used as a blueprint by clinical chemists and pathologists for the analysis of cell-free DNA using droplet digital PCR.

Anesthesiologie

The modified A-DIVA scale as a predictive scale for prospective identification of adult patients at risk of a difficult intravenous access, a multicenter validation study.

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Background: Peripheral intravenous cannulation is the most common invasive hospital procedure performed worldwide, but is associated with an unacceptable high overall failure rate. The A-DIVA scale was created to predict the likelihood of a difficult intravenous access in adults. This study aimed to improve the current A-DIVA scale by external validation, to predict the likelihood of a difficult intravenous access in adults thourghout the total inpatient population.

Methods: Participants aged over 18, regardless their ASA physical status, demographics, and medical history, were included in this multicentre study. An univariate and multivariate logistic analysis were performed to create the modified A-DIVA scale. The performance of the scale was determined in terms of discrimination and calibration.

Findings: A total of 3587 participants were included in this study. The first attempt success rate was 81%. Finally, five variables were included in the prediction model: a history of difficult intravenous cannulation, a difficult intravenous access as expected by the practitioner, the inability to detect a dilated vein by palpating and/ or visualizing the extremity, and a diameter of the selected vein less than 3 millimeters. Based on a participants individual score on the A-DIVA scale, were they classified into either a low, moderate or high risk group. A higher score on the A-DIVA scale indicates a higher risk for a difficult intravenous access.

Interpretation: The five-variable additive A-DIVA scale is a reliable and generalizable predictive scale to identify patients at risk for a difficult intravenous access.

ADDED VALUE OF THIS STUDY

The consequences of an unsuccessful first attempt of peripheral intravenous cannulation may seem innocent in nature, but can be very decisive for both patient, caregiver and the healthcare institution. To the best of our knowledge, this is the first study reporting a predictive scale for prospective identification of adult patients at risk of a difficult intravenous access that passed both internal and external validation processes. The validated and generalizable A-DIVA scale will lead to optimal care to patients with an indication peripheral intravenous cannulation, resulting in distressing patients, caregivers and the healthcare system, because of a decreased number of painful and stressful punctures, reduced nursing and medical workload, and less catheter-related infections and phlebitis.

Cardiologie

Intracoronary hypothermia in patients with ST-elevation myocardial infarction. Rationale and design of the EURO-ICE Trial.

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BACKGROUND: In patients with ST-elevation myocardial infarction (STEMI), infarct size (IS) can be considerable despite early revascularization by primary percutaneous coronary intervention (PPCI). Part of the final IS arises from reperfusion injury. Hypothermia may reduce reperfusion injury and thereby IS. Previous clinical studies applying systemic hypothermia in STEMI patients demonstrated negative results to reduce IS, likely due to an inability to deliver timely and sufficient hypothermia to the infarcted myocardium. Recently, a new method of selective intracoronary hypothermia has been developed that facilitates rapid and local cooling of the infarct area. This randomized controlled trial will evaluate the impact of this new technique on final IS in patients with anterior wall STEMI.

HYPOTHESIS: We hypothesize that selective intracoronary hypothermia in STEMI patients immediately prior to reperfusion reduces infarct size.

DESIGN: In a prospective, multicenter, randomized controlled trial, 200 patients with anterior wall STEMI will be randomized in 1:1 fashion to intracoronary hypothermia just before PPCI versus standard PPCI. The primary endpoint of the study is IS at 3 months, determined by magnetic resonance imaging. Key secondary endpoints are a composite of all-cause mortality and clinical admission for heart failure at 3 months and at 1 year.

SUMMARY: EURO-ICE (EUROpean Intracoronary Cooling Evaluation in patients with ST-elevation myocardial infarction, clinicaltrials.gov NCT03447834) is a multicenter, randomized controlled, proof-of-principle study evaluating the efficacy of selective intracoronary hypothermia during PPCI in patients with anterior wall STEMI.

Recovery of Absolute Flow and Resistance in Chronic Totally Occluded Coronary Arteries after Percutaneous Coronary Intervention.

Daniëlle C.J. Keulards MD, Nico H.J. Pijls MD, PhD, Jo M. Zelis MD, Marcel van 't Veer MD, Mohamed el Farissi MD, PhD, Koen Teeuwen MD, PhD.

Aims: This study aimed to investigate the physiology of absolute blood flow and microvascular resistance after percutaneous coronary intervention (PCI) of chronic total occlusion (CTO).
Methods and results: In this pilot study 8 patients scheduled for elective PCI of a right coronary artery CTO were selected. Before performing PCI of the CTO, absolute flow and resistance were measured in the donor vessel, using the novel thermodilution method with a multifunctional monorail infusion catheter, whereafter PCI of the CTO vessel was performed. After successful PCI, absolute flow and microvascular resistance was measured in the just opened CTO vessel and again in the donor vessel. All measurements were repeated after 6 weeks to re-evaluate absolute blood flow and resistance in the CTO territory and the donor artery. Complete measurements were obtained in all patients.
These comprehensive measurements showed a significant increase in blood flow in the CTO vessel over the course of time in all patients, (figure 1). Flow in the CTO artery increased from 161 ± 36 ml/min immediately after opening to 248 ± 73 ml/min at six week follow-up (p=0.012). In corollary absolute resistance in the myocardial territory perfused by the CTO artery, decreased from 448 ± 114 WU to 359 ± 130 WU.
Conclusions: This study demonstrates that absolute blood flow and microvascular resistance can be measured invasively ad-hoc after PCI of a CTO and recovers to normal within several weeks.

Validation of the ELAN-HF Score and self-care behaviour in patients with acute decompensated heart failure. A prospective single centre cohort study in the Netherlands

TAM Vinck, R Deneer, CCAG Verstappen,WE Kok, K Salah,V Scharnhorst, LC Otterspoor

Introduction
The European collaboration on acute decompensated heart failure (ELAN-HF) score is a validated prognostic model used at discharge for patients admitted for heart failure and was derived from 7 European registries. It predicts readmission and mortality at 6 months can therefore be used for risk stratification on a nurse-based heart failure out-patient clinic. Previous studies demonstrated that improving self-care within this patient group may lead to fewer readmissions for HF.
Purpose
To (externally) validate the predictive value of the ELAN-HF score on readmission and/or mortality, and to assess the effect of self-care behaviour on readmission and mortality in patients after a hospital admission with heart failure.
Methods
In a prospective, single centre cohort study, 88 patients (all-comers) hospitalized for ADHF were included. N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels were measured directly at admission as well as at discharge, and were used along with other clinical and laboratory parameters to calculate the ELAN-HF Score. Patients were then divided in four groups (low, intermediate, high, very high) according tot their risk score. To measure self-care behaviour, the European Heart Failure Self-care Behaviour Scale (EHFScBS-9) was used and the scaling response was analysed (a score of > 0.5 is regarded as optimal). Cox regression analysis was used to demonstrate the association between both scores and re-admission for heart failure and all-cause mortality within 90 days, in order to validate and assess their respective prognostic predictive values within the study population. Kaplan-Meier survival analysis was used to assess survival among the risk groups.
Results
The median age of the study population was 75 years (IQR 69-83), 43% woman. NYHA III/IV functional class was present at discharge in 68 patients (85%). A left ventricular ejection fraction below 40% was present in 27 patients (34%). Complete data and follow up was available in 80 patients, and the endpoint of mortality and rehospitalisation was reached in 46 % of patients. The median NT-pro BNP level at discharge was 3505 pg./ml. (IQR 1912 - 7861). There was a significant association between the ELAN-HF score and re-admission and/or mortality <90 days (HR = 1.25, 95% CI 1.08 - 1.45, P = 0.003). The median EHFScBS-9 score was 68.1 (IQR 58.3 - 77.8) with 19% patients having a low value of < 50. There was a non-significant association between the EHFScBS-9 score and re-admission and/or mortality <90 days (HR = 1.02, 95% CI 1.00 - 1.04, P = 0.111).
Conclusions
This study reinforces the potential of the ELAN-HF score to triage patients with acute decompensated heart failure after discharge, possibly adding in optimizing the nurse-based follow-up treatment in order to prevent readmission or death. Self-care behaviour was non-significantly associated with readmission and/or mortality in our study population.

Cardiothoracale Chirurgie

ENDOSCOPIC VEIN HARVESTING IN CORONARY ARTERY BYPASS GRAFTING: RATE OF RE-INTERVENTION AND QUALITY OF LIFE

V.J. KROEZE*, K.Y. LAM*, A.H.M. van STRATEN*, M.A. SOLIMAN HAMAD*

Purpose
Earlier reports concerning endoscopic vein harvesting have shown some controversy regarding the patency of the vein graft after coronary artery bypass grafting (CABG). Also, data on the quality of life are lacking. In this study, we

investigated our experience with endoscopic vein harvesting in regard to these endpoints.
Methods
All patients who underwent isolated CABG from January 2012 till December 2016 were included in the analysis. Patients were divided in two groups stratified by the technique of saphenous vein harvesting: open versus endoscopic. Primary outcome was the rate of coronary re-intervention, while secondary outcomes were the physical and mental scores of the SF-36 questionnaire. Regression analysis was performed to adjust the endpoint re-intervention for relevant covariates.
Results
In total 2123 patients were included in the open group, while 883 patients were included in the endoscopic group. The demographics of both groups showed no significant differences. Significantly more re-interventions were seen in the open group (p = 0.001). Overall mortality was significantly higher in the open group (p=<0.001). Regression analysis identified age, gender and number of anastomoses as significant covariates. Endoscopic vein harvesting showed a trend of decreased hazard of re-intervention, but was not statistically significant (p=0.056). Postoperative quality of life showed no significant differences between the two groups.
Conclusion
Endoscopic vein harvesting was comparable to open vein harvesting in terms of re-intervention rate and quality of life. In addition to the benefits on wound complications, we recommend the routine use of endoscopic vein harvesting in coronary surgery.

Surgical Treatment and long-term outcomes of advanced Aortic Valve Endocarditis complicated by Annular Abscess

Angkarina Angkasuwan, Sophie Croon, Albert H. van Straten, MD, PhD, Arash Khamooshian, MD, Ted W. Elenbaas, MD, and Mohamed A. Soliman-Hamad, MD, PhD

Objectives: This study was conducted to investigate the long-term outcomes (post-complications and mortality) of patients having advanced aortic valve endocarditis complicated by annular abscess formation, which was surgically managed with annular reconstruction, aortic valve replacement, and gentamicin filling of abscess cavities.
Methods: Between 1998 and 2018, 69 patients were identified with IE complicated by a periannular abscess, in which the abscess cavities were treated with gentamicin sponges. Surgery consisted of infected tissue debridement, gentamicin filling of the abscess cavities, annulus reconstruction with bovine pericardium and valve replacement. The Kaplan-Meier method was used to calculate estimates of survival and freedom from events.
Results: Mean age was 58±15 years, and the infected valve was native in 51% of all patients. Five and 10 year survival was 69.4 ± 12.0% and 55.7 ± 14.3%, respectively. Freedom from recurrent endocarditis at 10 years was 83.5 ± 13.3%. A significantly negative effect on survival time was found for prosthetic endocarditis ($?^2(1)=5.472$, p=0.019), having a tricuspid aortic valve ($?^2(1)=5.083$, p=0.024), receiving a biological valve ($?^2(1)=7.049$, p=0.008), and suffering from diabetes mellitus ($?^2(1)=4.878$, p=0.027), peripheral vascular disease ($?^2(1)=5.276$, p=0.022), or transient ischemic attack ($?^2(1)=10.714$, p=0.001).
Conclusion: Endocarditis with annular abscess remains associated with high morbidity and mortality (36%) and early treatment of the infected tissue and abscess cavities is crucial.

Chirurgie

Elderly patients should not be withheld curative colorectal cancer treatment: significant improvement in postoperative and 1-year mortality in the recent years

Ketelaers S.H.J., Orsini R.G., Burger J.W.A., Nieuwenhuijzen G.A.P., Rutten H.J.T.

Background
There is a tendency to withheld curative treatment in elderly colorectal cancer (CRC) patients. This is due to earlier studies showing an association between elderly and higher morbidity and mortality, especially in the first postoperative year.
Aim
To investigate if there is an improvement in postoperative morbidity and mortality in elderly CRC patients over time.
Methods
All patients who received elective curative CRC surgery between 2006 and 2017 in the Catharina Hospital (Eindhoven, the Netherlands) were selected retrospectively. Differences in mortality and relative survival between different age groups (<80 and ?80 years), period of surgery (2006-2012 and 2013-2017) and type of tumor (colon and rectum) were investigated.
Results
In total 2190 patients, of whom 57,6% is male, were selected (n=1088 colon and n=1102 rectum). Median age is 68,4 years old. For all patients regardless of age no major differences were seen for grade I-IV complications between both time periods. For patients aged >80 years old grade V (death) improved from 10,5% to 1,5% (p=0,005) in favour of the latest time period. 1-year mortality rate for all patients dropped from 21,8% to 12,9% (p=0,055). Relative one-year survival rates of all CRC patients were no longer significantly different between young and elderly patients in the latest time period (5,5% vs. 8.3%, p=0.11).

Conclusion

Our results show significant improvement in postoperative morbidity and mortality over time and relative one-year survival rates are no longer different. Therefore elderly CRC patients should not be withheld curative treatment based on age.

Innovative elements of the study

Elderly CRC patients are withheld curative treatment based on earlier reports of increased mortality rates in contrast to younger patients. To our knowledge, this is the first study showing significant improvement in these rates and hopefully change the current vision of clinicians leading to improved cancer care in the elderly.

Induction chemotherapy in addition to the current neoadjuvant treatment increases the pathologic complete response for locally recurrent rectal cancer

E.L.K.Voogt, D.M.G.I van Zoggel, J.S.Cnossen, G.J.Creemers, M.Roef, J. Nederend, G. van Lijnschoten, M.Kusters, J.W.A Burger, H.J.T Rutten.

Background and objective

Despite improvements in the multimodality treatment for patients with locally recurrent rectal cancer (LRRC), overall survival remains poor.

This study evaluated the effect of induction chemotherapy (ICT) administrated prior to neoadjuvant (chemo)radiotherapy. We aimed to increase survival by local downstaging and thereby increasing the percentage of radical resections. Additionally, introducing systemic chemotherapy in a population with a high risk for systemic disease may result in increased survival.

Methods

Between January 2010 and August 2018, 119 patients were treated with neoadjuvant ICT followed by chemoradiotherapy or (chemo)reirradiation. ICT consisted of three cycles of CAPOX or

CAPOX/bevacizumab or four cycles of FOLFOX. Radiotherapy comprised 30Gy or 45-50Gy, depending on previously received radiotherapy. Concomitant chemotherapy agent was capecitabine.

Endpoints were pathologic response, radicality and 3-year overall, local recurrence and metastasis free survival (OS, LRFS and MFS).

Results

A pathologic complete response (pCR) was seen in 20/119 patients (16.8%) and a radical resection in 74 patients (62%). The OS for patients with a pCR was 92% versus 61% for patients with Mandard =2 (p=0.03). The LRFS for pCR was 54% versus 49% for Mandard =2 (p=0.142). The MFS was 58% for pCR versus 30%

for Mandard =2 (p=0.05).

Conclusion

The addition of ICT is a promising treatment strategy with a 17% pCR rate and an excellent and unprecedented survival in these patients. These results have led to the design of a national consortium, the implementation of a national database and the idea of a randomized controlled trial evaluating the role of ICT in the treatment of LRRC.

Innovating elements:

Induction chemotherapy as an addition to the neoadjuvant treatment of locally recurrent rectal cancer is a promising treatment strategy, aiming to improve survival in a group of patients where survival rates are still rather disappointing despite former adjustment to the treatment regimen.

The effect of postoperative complications after a minimally invasive esophagectomy on long-term survival; an international, multi-center cohort study

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Background An esophagectomy is a technically challenging procedure, associated with significant morbidity. Introduction of minimally invasive esophagectomy (MIE) has improved recovery and reduced postoperative morbidity on the short-term.

Objective To investigate the effect of short-term complications following MIE on long-term survival. Methods Data were collected from the EsoBenchmark database composed by 13 high-volume, internationally renowned expert centers routinely performing MIE. Patients were included from June 1, 2011 until May 31, 2016. The Clavien-Dindo classification was used to stratify surgical complications. All data were corrected for 90-day mortality, thereby correcting for the short-term effect of postoperative complications on mortality. Overall survival was assessed univariable using Kaplan Meier and Log Rank test, and multivariable using Cox-regression analysis. Results A total of 915 patients were analyzed with a mean follow-up time of 30.8 months (SD 17.9). Complications occurred in 542 patients (59.2%) of which 39.3% had a Clavien-Dindo grade =3 complication (i.e. (re)intervention, ICU stay or death). The incidence of anastomotic leakage (AL) was 14.8% of which 9.2% were classified as a Clavien-Dindo grade =3. Multivariable analysis showed a significantly shorter long-term survival in all patients with AL (HR

1.73, p <0.001), especially in patients with Clavien-Dindo grade =3 AL (HR 1.91, p <0.001). For all other complications, no significant influence on long-term survival was found.
Conclusion The occurrence and severity of anastomotic leakage after MIE negatively affects long-term survival of esophageal cancer patients.
Innovative elements
Minimally invasive esophagectomy (MIE) is becoming standard of care throughout the Netherlands since it improves short-term patient outcomes. However, this technically challenging procedure is subject to learning-associated morbidity. This is the first international study showing an inverse relation between anastomotic leakage and long-term survival in high-volume, expert centers performing MIE.

Gynaecologie

Estrogen receptor pathway in high grade serous ovarian cancer: targeted treatment options.

Ottenheijm MPM*, van der Ploeg P, Piek JMJ

Background: High grade serous ovarian cancer (HGSC) is the most lethal gynecological malignancy. The fast and mainly asymptomatic tumor progression, high recurrence rates and therapy resistance makes it hard to find an optimal curative treatment. The estrogen receptor (ER) is expressed at high levels in many HGSCs and represents a potential target for endocrine therapy. We present a systematic review of the current treatment options targeting the estrogen receptor pathway in HGSC and compare and discuss their effect on clinical benefit.
Methods: Clinical research on estrogen receptor targeted therapies, published in the last five years, were identified through a PubMed, Cochrane Library and Clinicaltrials.gov search.
Results: Tamoxifen (a selective estrogen receptor modulator), Anastrozole and Letrozole (aromatase inhibitors) are the most investigated ER-inhibitors in HGSC. The use of various ER expression methods and different outcome measures makes it difficult to compare study results. In general, a subset of patients shows clinical benefit without demonstrating evident superiority between therapeutics. Interestingly, no distinct correlation between ER positivity and prognosis was found as studies reported contradictory results. However, due to the limited adverse effects and low costs, estrogen receptor targeted therapy is proposed as a rational treatment option.
Conclusion: Anastrozole, Letrozole and Tamoxifen give promising results as anti-estrogen receptor targeted therapy in patients with HGSC. Estrogen receptor presence and activity is no exclusive biomarker for treatment response. Therefore, the need for a sensitive biomarker to predict therapy response remains.
Innovative elements:
This study shows results of a systematic review on estrogen receptor targeted therapies including selective estrogen receptor modulators and aromatase inhibitors used in recent clinical practice. In contrast to other recent reviews regarding this topic, our study aims on responses in HGSC specifically, observes ER status and excludes outdated trials.

Intensive Care

A Guardian on the surgical ward

Eveline Mestrom, Ashley De Bie, Melissa van de Steeg, Merel Driessen,Louis Atallah, Rick Bezemer ,R.Arthur Bouwman, Erik Korsten

Introduction:
Early warning scores (EWS) are being increasingly embedded in hospitals over the world due to their promise to reduce adverse events and improve the outcomes of clinical patients.
The aim of this study was to evaluate the clinical use of an automated modified EWS (MEWS) for patients after surgery.
Methods:
This study conducted retrospective before-and-after comparative analysis of non-automated and automated MEWS (Philips Intellivue Guardian Solution®) for patients admitted to the surgical high-dependency unit in a tertiary hospital. Operational outcomes included number of recorded assessments of the individual MEWS elements, number of complete MEWS assessments, as well as adherence rate to related protocols. Clinical outcomes included hospital length of stay, in-hospital and 28-day mortality, and ICU readmission rate.
Results:
During the control period, 199 (2.5%) complete MEWS were recorded versus 3991 (45.5%) during intervention period. With the automated MEWS systems, the percentage of missing assessments and the time until the next assessment for patients with a MEWS of =2 decreased significantly. The protocol adherence improved from 1.1% during the control period to 25.4% when the automated MEWS system was involved. There were no significant differences in clinical outcomes.
Conclusion:
Implementation of an automated EWS system on a surgical high dependency unit improves the number of complete

MEWS assessments, registered vital signs, and adherence to the EWS hospital protocol. However, this positive effect did not translate into a significant decrease in mortality, hospital length of stay, or ICU readmissions.
Innovative aspects:
Previous studies have shown a reduction in mortality and hospital stay after implementation of automated MEWS systems in general wards. The automation of MEWS systems may be even more effective for subgroups such as high-risk surgical patients, since postoperative complications are frequently encountered and can lead to major adverse events.

A watch to watch over perioperative patients.

Mestrom, E.H.J., Deneer R., van Aartrijk, M., Gelissen J., Haakma R., Bouwman, R.A., Korsten, E.H.H.M., Scharnhorst, V.

Background
Timely recognition of deterioration in hospitalized patients is important for early intervention. Prior to an adverse event, deterioration in vital signs such as heart rate (HR) can often be detected long before the event itself. Currently, vital signs on the general ward are assessed on average every 8 hours. Measurement of HR through an unobtrusive, wrist-worn optical HR monitor (OHRM) in the form of a watch could enable earlier recognition of patient deterioration and early intervention. However, OHRMs have not been validated for clinical use.
Goal
To assess the agreement between HR extracted from an OHRM and the golden standard patient monitor, in the pre- per- and postoperative period.
Methods
100 patients undergoing surgery and requiring anesthesia in the Catharina Hospital in Eindhoven were included in this study. During the perioperative period, an OHRM developed by Philips research was put round the patients' wrist. The agreement between the golden standard electrocardiogram (ECG) from the patient monitor and the HR extracted from the photopletysmography (PPG) sensor by the OHRM was evaluated by interbeat intervals and beats per minute.
Results
A total of … hours were recorded simultaneously with the OHRM and patient monitor. Agreement analysis show the limits of agreement of the difference between the OHRM and the chest strap HR were within the range of … bpm. The OHRM showed a concordance correlation coefficient of …. Overall, the mean absolute error was not larger than … bpm.
Conclusion
An OHRM can (not) be considered clinically acceptable for perioperative monitoring.
Innovative elements
To the authors' knowledge, this is the largest comparison between wrist-worn PPG-based HR and patient monitor ECG-based HR during the perioperative period. Previous studies were based on small sample sizes or did not analyze agreement on beat-to-beat level. This study shows the potential for wearable devices to continuously monitor patients.

Prevalence of Post Intensive Care Syndrome (PICS) in a Dutch Intensive Care Unit (ICU) population.

Inoek C.M. Koopmans, Femke A.M. Janssen, Marianne Hendriks, Ilona Kox, Marc P. Buise, Ashley J.R. de Bie Dekker, Pablo J.E.J. van de Berg

Background –
Survivors of intensive care unit (ICU) are at risk of developing long-term decrease in mental, cognitive and physical performance. This so-called post-intensive care syndrome (PICS) impacts the quality of life for years post-discharge. The prevalence of PICS is uncertain but ranges from 15 to 75% in literature.
Aim –
A prospective cohort study to establish the prevalence of PICS over a year after ICU discharge in a tertiary hospital specialized in cardiothoracic surgery.
Methods –
The inclusion criteria for this study were adult patients treated in the ICU for >48 hours. All patients, or relatives if patients were unable to answer, were interviewed on admission to evaluate the level of functioning prior to admission. This was done using validated questionnaires. During follow up patients and relatives were interviewed by phone at 2 and 4 weeks, 6 and 12 months after ICU discharge to assess level of functioning in the physical, cognitive and mental domain and quality of life. PICS was defined as a reduction in one of the aforementioned domains.
(Provisional)
Results –
We included 121 patients of which 88 were used for further analysis. The prevalence of PICS reduced from 36.3% at 2 weeks, to 18.8% at 4 weeks, 14.7% at 6 months and xx% at 12 months.

Conclusion –
The prevalence of PICS in ICU patients of a tertiary hospital in the Netherlands is lower than most current literature reports. Furthermore, our data shows a decrease of PICS over time.
New elements
For the first time, longitudinal analysis for development and prevalence of PICS the first year post-discharge was performed. In ongoing research, telephone interviews could be used to evaluate the effect of interventions in preventing or treating PICS.

The association between Acute Kidney Injury (AKI) and Intensive Care Unit (ICU) acquired hypernatremia

ME te Pas*, EHJ Mestrom*, AJGH Bindels, JA van der Stam, V Scharnhorst

Background
Intensive care unit (ICU) acquired hypernatremia is a highly prevalent condition in critically ill patients and is associated with increased mortality and length of stay. The kidneys play an important role in the volume and osmolality regulation, and are therefore a possible key player in sodium derangements. Approximately 30% of ICU admissions is complicated by acute kidney injury (AKI). Therefore, this study focuses on AKI in the development of hypernatremia.
Aims
This study aimed to provide insight in the effect of AKI on the development of ICU acquired hypernatremia and to possibly identify opportunities for prevention of ICU acquired hypernatremia.
Methods
A retrospective comparative analysis was performed using prospectively collected data of ICU patients in a tertiary referral hospital. All adult patients requiring ICU admission more than 48hours were identified and included between April and December 2018. Urine samples were collected and analyzed for electrolytes and osmolality. Additional serum osmolality analyses were performed. Further data collection consisted of detailed fluid balances and medication use.
Results
A total of 199 patients were included, of whom … (%) developed hypernatremia. According to the RIFLE classification, … (%) patients were at risk for acute kidney injury, … (%) patients showed to have kidney injury already and … (%) patients had acute kidney failure in the hypernatremic group. This was (not) a significant difference compared to patients without hypernatremia in the Intensive Care Unit (P…).
Conclusion
Acute kidney injury in ICU patients seems (not) to contribute to the development of hypernatremia.
Innovative Elements
Literature is lacking evidence about the role of AKI in the development of hypernatremia. Early dysnatremia correction after ICU admission is associated with an improvement of mortality in comparison to patients with persistent dysnatremia. Since almost all patients require about two days to develop hypernatremia, it should be possible to recognize a trend towards the development of hypernatremia.

Onderwijs en Onderzoek

Digital self-management support interventions in the care plan of cancer patients: a review and meta-analysis

Daniëlle Adriaans , MSc, Angelique Dierick-van Daele, Marc van Bakel, Grard Nieuwenhuijzen, Joep Teijink, Fanny Heesakkers, Hanneke van Laarhoven

Abstract
Background: Cancer patients are increasingly challenged to self-manage their condition. Self-management support is defined as the systematic provision of education and supportive interventions by health-care professionals to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support(1). Nowadays, this support may be provided via digital support tools (DSMST).
Objective: The aims of this study are to (1) review the evidence regarding existing interventions with DSMST for cancer patients; and (2) explore the effectiveness of these interventions in the treatment of cancer patients
Methods: Pubmed, PsycInfo, Cochrane, CINAHL and Embase databases were searched from January 2013 up to January 2018. Studies had to be prospective phase II or III randomized controlled trials comparing digital self-management support to no intervention/usual care/alternative interventions/or a combination, written in English or Dutch, and had to include patients > 18 years of age with pathologically proven cancer in the active treatment or survivorship phases. To rate methodological quality, the CONSORT methodology was used. When possible, a meta-analysis was conducted.
Results: 19 publications were selected. Three types of digital self-management support tools were described, namely apps, websites and an automated home monitoring system. The average rating for methodological quality was good, with 13 of 19 studies scoring high. Most studies observed significant positive effects on quality of life(2-4), anxiety and depression(5, 6), symptom distress (7-11), physical activity(2, 12, 13), dietary behavior(2) and fatigue(2, 3). Significant negative effects were observed on anxiety (14). Other studies reported no significant effects on quality of life(5, 15-17), anxiety and depression(2, 4, 10, 12, 15, 16), symptom distress(4, 17), physical activity(18, 19), dietary behavior(12, 13, 18) and fatigue(5, 12, 15). Meta-analyses showed statistically significant

improvement on quality of life subdomains emotional functioning(2, 3, 15, 17), social functioning(2, 3, 15, 17), physical functioning(2, 3, 17), global health status(2, 3, 17) and depression(2, 14, 15). No statistical significant difference was found for the quality of life subdomain role functioning(2, 3, 17). Although the content, duration, and frequency of interventions varied considerably across studies, commonly observed program elements were 1. an assessment component 2. tailored symptom self-management support 3. information section 4. communication section 5. Diary

Conclusions: This review shows an added value of digital self-management support tools to improve quality of life and depression for cancer patients. For effects on other patient outcomes the evidence is inconsistent, limited, or suggests no effect. Future research should focus on specific tumor types, study different types of interventions separately and assess the effect of specific interventions in different stages of disease progression and tailored to individual patients' needs.

Keywords: Web-based intervention; Digital self-management support tool; Chronic patient groups; Review; Cancer patients

Plastische Chirurgie

Abstract: De vertaling van de WOUND-Q, een nieuwe PROM voor chronische wonden

Tert van Alphen, Emiel van Haren, Lotte Poulsen, Amalie Lind Jacobsen, Jens Ahm Sørensen, René van der Hulst, Maarten Hoogbergen, Andrea Pusic, Anne Klassen

Achtergrond:

Chronische wonden, bijvoorbeeld veroorzaakt door diabetische ulcera of decubitus hebben een enorme invloed op de kwaliteit van leven van de patiënt. De WOUND-Q is een nieuwe Patient Reported Outcome Measure (PROM) die, naast de traditionele uitkomstmaten, de ervaren resultaten van de behandeling, de kwaliteit van leven en zorg bij patiënten met chronische wonden evalueert.

Doelstelling

Het doel van deze studie is het vertalen en cultureel aanpassen van de WOUND-Q van het Engels naar het Nederlands en Deens.

Methode:

Voor de vertaling en culturele aanpassing van de Nederlandse en Deense versies van de WOUND-Q hebben we een combinatie van de van de International Society for Pharmacoeconomics and Outcomes Research (ISPOR) en World Health Organization (WHO) richtlijnen gevolgd. De focus ligt op het ontwikkelen van conceptueel vergelijkbare vertaling in plaats van een letterlijke vertalingen die begrijpelijk is voor alle patiënten.

Resultaten:

Resultaten uit de voorwaartse en achterwaartse vertaling van de Nederlandse en de Deense versie toonde 24 en respectievelijk 23 items waarvan de betekenis zodanig was veranderd dat deze items opnieuw vertaald moest worden. Een totaal van 38 cognitieve debriefinginterviews resulteerden in kleine aanpassingen en toonden aan dat de vragenlijst voor de patiënten gemakkelijk leesbaar en begrijpelijk was.

Conclusie:

Het vertaal- en culturele aanpassingsproces is een essentiële stap om PROM's aan te passen voor gebruik in een andere taal of cultuur. De door ons beschreven vertaalmethode zorgt ervoor dat de WOUND-Q gebruikt kan worden ter evaluatie van de behandeling van patiënten met een chronische wond in Nederland en Denemarken.

Vernieuwde elementen:

- De WOUND-Q is een nieuwe PROM voor patiënten met chronische wonden die gebruikt kan worden in Engels, Nederlands en Deens.
- De vertaalmethode is een combinatie van de vooraanstaande ISPOR- en WHO-richtlijnen voor een zo nauwkeurig mogelijk vertaling
- Het vertaal- en culturele aanpassingsproces kan worden toegepast voor het vertalen van andere PROM's.

BODY CONTOURING SURGERY: IMPROVEMENT IN PHYSICAL SYMPTOMS AFTER ABDOMINOPLASTY

H. Kazato, L. Van Den Berg, L. Poulsen, J.A. Sorensen, M. Rose , A.F. Klassen, A.L. Pusic, M.M. Hoogbergen.

Background/Introduction

Post-bariatric patients can suffer from excess skin caused by massive weight loss, which then limits physical mobility and cause physical symptoms such as skin infections and back and joint pain. The main treatment of this excess skin is body contouring surgery, (BCS) such as abdominoplasty.

Objectives

Our aim was to determine if abdominoplasty improves physical movement and symptoms using the BODY-Q, a patient reported outcome measures for weight loss and body contouring treatments.

Methods

Physical movement and symptoms were measured pre- and post abdominoplasty at 3 and 12 months using the BODY-Q, in centres in Denmark and the Netherlands in 85 patients.

The total score for physical movement had a value between 0-100 (higher score indicates better physical movement). Physical symptoms were scored between 1-4 (higher score indicates fewer physical symptoms).
Results
Eighty-five patients (29 Danish, 56 Dutch) at least 3 months postoperative abdominoplasty were included. Physical movement significantly improved overall after 3 months postoperative (68.0 to 81.8 ($p<0.001$)). Walking improved (3.2 to 3.7 ($p<0.001$)) as well as climbing stairs (3.1 to 3.6 ($p=0.001$)). Skin infections significantly improved (3.0 to 3.7 ($p<0.001$)), as well as joint pain (3.0 to 3.3 ($p=0.012$)) and back pain (2.8 to 3.1 ($p=0.016$)). This trend of improvement sustained in patients 1 year postoperative.
Conclusion
Abdominoplasty significantly improves physical movement and symptoms caused by excess skin. This indicates that BCS is important in restoring normal physical functioning in postbariatric patients and is an essential part in their treatment of morbid obesity.
Innovative features of current study:
Our study features use of patient-reported outcome measures to determine treatment success. In addition, we evaluated the impact of body contouring surgery on physical functioning and symptoms, while traditionally there is a lot of emphasis on the psychological benefits of such surgical procedures in patients recovering from massive weight loss.

BODY-Q: SIGNIFICANT BETTER HEALTH RELATED QUALITY OF LIFE 1YR AFTER ABDOMINOPLASTY

L. van den Berg*, D. Geerards, C. de Vries, A. Klassen, A. Pusic, M.M. Hoogbergen

Background
The increasing amount of bariatric surgery in the past years leads to a higher demand for body contouring surgery during the treatment of morbid obesity. Our aim is to measure the change in Quality of Life (QoL) and satisfaction with appearance after an abdominoplasty or lower body lift (LBL).
Aim
To deliver better care for massive weight loss patients and better health for the (post)bariatric population.
Methods
Prospective study including all patients after massive weight loss (bariatric surgery or lifestyle changes) who undergo an abdominoplasty or LBL. All included patients fill out the BODY-Q preoperatively, 3-months postoperatively and 1-year postoperatively to measure HRQoL and satisfaction with appearance.
Results
178 patients were included, the loss to follow-up was 53 patients. Mean BMI before bariatric surgery was 49, with a drop to 29 before body contouring surgery. Patient reported outcomes measured the following scores preoperatively (on a scale from 0-100): Body image (1 out of 5 QoL scales) was preoperatively 20 and 53 postoperatively. Satisfaction with abdomen was 12 and 80 postoperatively. The difference in outcomes preoperatively and 3-months and 1 year postoperatively was significant ($p < 0.001$).
Conclusion
An abdominoplasty or LBL leads to a significant better HRQoL and a significant higher satisfaction with appearance 3 months and 1 year postoperatively. This study shows the undeniable effect and role of body contouring surgery in the treatment of morbid obesity.

FACE-Q: a first analysis of patient satisfaction following oncological resection on the nose.

P Brouwer,MJ Ottenhof, C Gibbons, A Pusic, MM Hoogbergen, E Lee

Achtergrond:
Excisie van huidkanker in het gelaat is mutilerend. 60% van de basaalcel carcinomen (BCC) bevindt zich in hoofd-hals gebied. Er is onderzoek gedaan naar effectiviteit van excisies maar niet naar patiënttevredenheid. De FACE-Q is een recent ontwikkelde 'patient reported outcome measure' (PROM) die ons in staat stelt lichamelijke klachten, tevredenheid met uiterlijk, gezondheid gerelateerde levenskwaliteit en psychologisch welzijn te meten en te kwantificeren. Dit met als doel te komen tot een "patient-centered" model, waarbij shared decision-making leidt tot keuze voor juiste behandeling. Dit is de eerste evaluatie van de Nederlandse versie FACE-Q, in een populatie die excisie en reconstructie van de neus ondergaat, in samenwerking met Harvard Medical School
Doelstelling:
Tentoonstellen van de eerste resultaten met betrekking tot reconstructie na excisie van basaalcelcarcinomen op de neus. Een vergelijking tussen Nederland en de Verenigde staten.
Methode:
De Nederlandse vertaling van de psychometrisch gevalideerde FACE-Q is geaccepteerd door Mapi Research Trust. De FACE-Q evalueert; uiterlijk, kwaliteit van leven en patiëntervaring. Deze vragenlijst bestaat uit veertig subcategorieën, elk met vier tot elf vragen op een vierpuntenschaal. Voor elke subcategorie wordt gescoord tussen 0-100, waarbij een hoge score positief is. In het lopende onderzoek staat de patiënt met een behandeling van een BCC op de neus centraal. De vragenlijst wordt door deze groep preoperatief, één week postoperatief en drie en twaalf maanden postoperatief ingevuld. De resultaten worden geanalyseerd in R.
Resultaten:
Het betreft een lopend prospectief cohortonderzoek. Tijdens de wetenschapsavond zijn alle resultaten van deze

specifieke groep, patiënten na een reconstructie bij BCC resectie op neus, klaar om gepresenteerd te worden. Dan zal ook onderscheid in type reconstructie worden gemaakt en de resultaten van de VS gepresenteerd.
Conclusie:
De FACE-Q is de eerste PROM specifiek voor aangezichtsreconstructies na resectie van BCC in het gelaat. De eerste resultaten zullen een veelbelovende reflectie van het medisch handelen na reconstructie laten zien. Het uiteindelijke doel is specifiekere informatie per deel in het gelaat te achterhalen. De FACE-Q zal in de toekomst per esthetic unit ingericht kunnen worden.

Streamlining the Assessment of Patient-Reported Outcomes in Weight Loss and Body Contouring Patients: Applying Computerized Adaptive Testing to the BODY-Q"

Daan Geerards, MD, Anne F. Klassen, DPhil; Maarten M. Hoogbergen, MD, PhD, René R.W.J. van der Hulst, MD, PhD, Lisa van den Berg, MD; Andrea L. Pusic, MD, MHS, Chris J. Gibbons, PhD

Achtergrond
The BODY-Q is a widely-used Patient Reported Outcome Measure (PROM) of surgical outcomes in weight loss and body contouring patients. Reducing the length of the BODY-Q assessment could overcome implementation barriers in busy clinics. A shorter BODY-Q could be achieved by using Computerized Adaptive Testing (CAT), a method to shorten and tailor assessments while maintaining reliability and accuracy.
Doelstelling
In this study, we apply CAT to the BODY-Q and assess CAT performance in terms of item reduction and accuracy. The goal is to make BODY-Q assessment as efficient as possible.
Methode
Parameters describing the psychometric properties of 138 BODY-Q items (i.e., questions) were derived from the original validation sample (n=734). The 138 items are arranged into 18 scales reflecting appearance, health-related quality of life, and experience of care domains. We simulated 1000 administrations of the CAT until a stopping rule, reflecting assessment accuracy of SE<.55, was met. We described the reduction of assessment length in terms of the mean and range of items administered. We assessed accuracy by determining correlation between full test and CAT scores.
Resultaten
We ran 54 simulations. Mean item reduction was 36.9% (51 items, range 48-138). Highest item reduction was achieved for the experience of care domain (56.2%, 22.5 items). Correlation between full test scores and the BODY-Q CAT scores averaged 0.99.
Conclusie
Substantial item reduction is possible by using the BODY-Q CAT. Reduced assessment length using the BODY-Q CAT could reduce patient burden whilst preserving the accuracy of clinical patient-reported outcomes for patients undergoing weight loss and body countering surgeries.
Vernieuwende elementen
Tegenwoordig zijn niet alleen mortaliteit en complicaties relevante uitkomsten, maar is de invloed van zorg op kwaliteit van leven van patiënten minstens zo belangrijk. Deze patient-geraporteerde uitkomsten zijn de laatste tijd erg in opkomst. Ten behoeve van implementatie en patiëntlast is het zeer wenselijk deze vragenlijsten zo efficiënt en betrouwbaar af te nemen, iets dat mogelijk is met Computerized Adaptive Testing.

Radiotherapie

Samen werken aan integrale oncologische zorg

Nicole Mols- van Knegsel

Doelstelling:
De doelstelling van dit onderzoek is inzicht geven in hoe de samenwerking tussen Catharina Kanker Instituut (CKI) en de huisartsen in de regio verbeterd kan worden om de integrale zorg voor de oncologische patiënt te verbeteren.
Methode:
Onderzoek is verricht volgens een inductieve en kwalitatieve onderzoeksmethode. Literatuuronderzoek naar de kenmerken van de oncologische zorg en de succesfactoren van interorganisationele samenwerking heeft geleid tot het gevalideerde ontwikkelingsmodel ketenzorg (OMK) van Minkman (2012) als conceptueel model. Middels het OMK is de samenwerking in en organisatie van de integrale oncologische zorg voor de patiënten van het CKI onderzocht. Huisartsen, medisch specialisten, casemanagers en patiënten zijn geïnterviewd.
Resultaten en conclusie:
Dit onderzoek laat zien dat de centrale onderzoeksvraag niet eenduidig te beantwoorden is. Zowel in het literatuuronderzoek als in het praktijkonderzoek worden dezelfde factoren genoemd die de basis vormen voor een succesvolle samenwerking tussen het CKI en de huisartsen. Echter zijn de geïnterviewden niet eenduidig over de vormgeving en organisatie van de integrale oncologische zorg. Resultaten laten zien dat zowel de patiënten als de professionals niet ontevreden zijn over de huidige zorg en de onderlinge samenwerking, waarin de casemanager door zowel de patiënten als de professionals als zeer waardevol wordt ervaren. Verbeterpunten zijn onderlinge

communicatie, onduidelijkheid over de regierol in de follow-upfase en het tekort aan specifieke oncologische kennis bij de huisarts.
Sleutelwoorden:
Integrale zorg, interorganisationele samenwerking, oncologische zorg.
Vernieuwende elementen:
Het aantal oncologische patiënten groeit en is een veelzijdig en belangrijk volksgezondheidsprobleem (Korevaar, 2013). Behandeling van kanker is zaak van meerdere professionals waarin patiënt centraal staat. Dit onderzoek richt zich op de samenwerking tussen het CKI en de verwijzende huisartsen om de integrale zorg aan de oncologische patiënt in de regio te verbeteren. Mogelijk kunnen verworven inzichten een bijdrage leveren aan vergelijkbare integrale vraagstukken. Wetenschappelijk kan dit onderzoek een bijdrage leveren om inzicht te krijgen in de factoren die van invloed zijn op integrale oncologische zorg en de samenwerking tussen eerste en tweede lijn.

Fontys

A comparison of foot kinematics using the Oxford Foot Model in children with clubfoot, relapse clubfoot and healthy controls

L. Grin, A.T. Besselaar, L. van Oorschot, M.C. van der Steen, B. Vanwanseele

Background
A clubfoot is characterized by a three-dimensional deformity with an equinus, varus, cavus and adduction component. The re-occurrence of clubfoot components in treated clubfoot, a relapse, is a known problem in clubfoot patients. 3D gait analysis can be used in assessment of foot function and residual deviations in gait. In order to capture the full multi-planar and multi-joint nature of a clubfoot, it is highly important to implement multi-segment foot models in gait analysis.
Objective
The aim of this study is to identify kinematic differences between children with Ponseti treated clubfoot, relapse clubfoot and age-matched healthy controls during gait, using the Oxford Foot Model (OFM).
Methods
Six clubfoot patients, age 4-8 years old, treated following Ponseti, five relapse patients and eight healthy controls participated. Gait analysis was performed using a wireless active 3D-system in which the OFM was used to identify different foot segments. Sagittal and transversal plane kinematics were analysed.
Results
Compared to healthy controls increased adduction during the gait cycle was found in clubfoot (ankle angle and tibia versus hindfoot) and relapse patients (ankle angle, tibia versus hindfoot, hindfoot versus forefoot). Less plantar flexion was found in clubfoot patients, whereas more plantar flexion was found in relapse patients (ankle angle and tibia versus hindfoot).
Conclusions
The preliminary results show impaired ankle and foot kinematics in clubfoot and relapse patients compared to healthy controls. Due to the limited sample size and large variations between subjects, more participants are necessary. Subsequently, the relation with clinical relevant functional outcomes focused on treatment of individual relapse clubfoot will be investigated.
Innovations in this study
Gait analysis is a frequently applied tool to analyse differences in gait between clubfoot and healthy controls. However, the usage of multi-segment foot models is- although of importance considering the characteristics of the clubfoot- rare. Furthermore, this is the first study to investigate gait kinematics in patients with a relapse clubfoot treated with Ponseti.

Fontys

A systematic review on kinematic gait analyses in children with Ponseti treated clubfoot patients compared to healthy controls

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Background: A clear systematic overview of kinematic differences in gait between Ponseti treated clubfoot children and healthy control children is not available yet. Being aware of possible gait impairment might be useful for optimizing the Ponseti method, developing additional (physio)therapy or surgery.
Objective: The objective of this review is to investigate differences in kinematic outcomes between Ponseti treated clubfoot children and healthy control children.
Methods: A systematic search was conducted in multiple literature databases (e.g. Embase and Scopus). Studies comparing kinematic gait parameters of Ponseti treated clubfoot children to healthy controls were included. Risk of bias was performed for each study. Meta-analysis and qualitative analysis were conducted.
Results: A total of 39 kinematic outcome measures were presented in the seven included studies. Eight outcome measure could be included in the meta-analysis. The meta-analysis showed that 1) maximum dorsiflexion in the

ankle was significantly lower in clubfoot children during swing 2) range of motion in the ankle was significantly lower in clubfoot children 3) the foot progression angle was more inward oriented in clubfoot children 4) more external rotation in the hip during stance was seen in the clubfoot group.
Conclusion: Several kinematic outcome measures differ during gait in clubfoot patients compared to healthy controls. To fully grasp the complexity of the clubfoot deformity, implementation of enhanced foot models should be implemented in future studies. Furthermore, more homogeneity in outcome measures will improve comparability between different studies. The question remains, to what functional problems gait impairments lead and if these issues could be addressed with additional treatment.
Innovations in this study: Despite the large body available on good initial outcomes of the Ponseti method, less is known about the functional long-term outcome. 3D gait analysis is a frequently applied tool to evaluate functional outcome. The current systematic review serves as a basis of the gait analyses we perform in our clubfoot patients.

TUE_Biomedische Technologie

Towards patient-specific pulse pressure variation

Tilaï Rosalina, Arthur Bouwman, Marc van Sambeek, Kevin Lau, Frans van de Vosse, Peter Bovendeerd

Abstract
Globally there are many hemodynamic variables used to predict fluid responsiveness (Cecconi et al., 2015). Many of these variables however, have been shown not to be predictive of fluid responsiveness. One of the
more promising dynamic measurements is pulse pressure variation. Here,positive pressure ventilation of intubated patients causes a cycled change in airway pressure which influences stroke volume and thereby arterial pulse pressure (Michard et al., 2000; Cannesson et al., 2011). Here, a high pulse pressure variation (276 13 %) is associated with the recommendation of fluidadministration.
The applicability and reliability of pulse pressure variation is coupled to specific clinical constraints, such as a tidal volume 276 8 mL/kg and no arrythmia, leading to 80 % of the ICU patients being excluded from reliable pulse pressure variation analysis (Michard et al., 2000). However, there has been little research on the underlying physiology of these constraints.
Physiology-based mathematical models could help to understand and eventually make better use of pulse pressure variation by providing information that is difficult, or impossible to measure.
In this project we created such a mathematical model to identify the
dependability of pulse pressure variation on implicit patient characteristics
such as pericardial stiffness, cardiac contractility and vascular stiffening.
Results
Of the model are compared to experimental measurements to assess the accuracy of the model.
By simulating and identifying the important factors contributing to an accurate pulse pressure variation value we finally aim to develop an index thatcan be used in a wider clinical setting. Eventually this could lead to a patient specific calculated pulse pressure variation to predict fluid responsiveness.

Tabellen

Tabel 1: Overzicht aantal publicaties

Specialisme	Tijdschrift artikelen	Promoties	(Co)Promotor	Boek hoofdstuk	Totaal
Algemeen Klinisch Laboratorium	11	1	1		12
Anesthesiologie	12		1	1	14
Apotheek	5				5
Cardiologie	50	1	2	1	54
Cardiothoracale chirurgie	8				8
Chirurgie	129	3	6	4	142
Dermatologie	10		3		13
Dietetiek	5				5
ECC en Bloedmanagement	1				1
Geriatrie	2				2
Gynaecologie	35	1	1		37
Intensive Care	2			1	3
Inwendige geneeskunde	19	1			20
Kindergeneeskunde	1				1
Klinische Fysica	13			1	14
Kwaliteit		1			1
Longgeneeskunde	11				11
Maag, darm, leverziekten	19				19
Mond en Kaakchirurgie	1				1
Neurologie	7				7
Nucleaire geneeskunde	4				4
Onderwijs en Onderzoek	5				5
Orthopedie	6			1	7
Pamm	4				4
Plastische chirurgie	5				5
Psychologie	1				1
Radiologie	11				11
Radiotherapie	11				11
Spoedeisende hulp	1		1		2
Urologie	8				8
e/MTIC		1			1
Totaal	397	9	15	9	430

Tabel 2 Wetenschapsavond 2018

Specialisme	Presentaties	Posters	Totaal
Algemeen Klinisch Laboratorium		2	2
Anesthesiologie		1	1
CTC		2	2
Cardiologie	1	3	4
Chirurgie	1	4	4
Gynaecologie	1	1	2
Intensive Care	1	4	5
Inwendige geneeskunde	1		1
Orthopedie		2	2
Plastische Chirurgie		5	5
Radiotherapie		1	1
Fontys		2	2
TUE- Biomedische Technologie		1	1
Totaal	5	26	31

Tabel 3: Overzicht aantal artikelen en gemiddelde impactfactor per specialisme

Specialisme	Wi-1*	WI-2**	WN***	Totaal aantal artikelen	Gemiddelde impactfactor	Standaard deviatie
Algemeen Klinisch Laboratorium	10		1	11	2.906	1.826
Anesthesiologie	9	3		12	2.608	2.274
Apotheek	3	2		5	2.787	3.069
Cardiologie	44	6		50	9.214	14.775
Cardiothoracale chirurgie	6	2		8	3.688	5.600
Chirurgie	122	5	2	129	4.651	6.871
Dermatologie	9	1		10	1.405	2.408
Dietetiek	3	2		5	2.338	2.134
ECC en Bloedmanagement	1			1	1.147	-
Geriatrie	1	1		2	0.578	0.817
Gynaecologie	33	2		35	5.456	12.981
Intensive Care	1	1		2	2.932	4.146
Inwendige geneeskunde	17	2		19	6.480	10.727
Kindergeneeskunde	1			1	3.258	-
Klinische Fysica	10	3		13	4.203	1.960
Longgeneeskunde	7	2	2	11	1.999	1.990
Maag, darm, leverziekten	15	4		19	7.389	12.053
Mond en Kaakchirurgie	1			1	4.305	
Neurologie	7			7	15.210	18.891
Nucleaire geneeskunde	2	1	1	4	0.845	0.989
Onderwijs en Onderzoek	4	1		5	11.250	20.395
Orthopedie	6			6	2.398	0.928
Pamm	3		1	4	3.416	3.060
Plastische chirurgie	4		1	5	2.428	1.628
Psychologie	1			1	1.388	-
Radiologie	10	1		11	4.891	6.253
Radiotherapie	10	1		11	6.397	6.881
SEH		1		1	-	-
Urologie	5	3		8	1.406	1.292
Totaal	345	44	8	397	3.258	7.056

WI-1* = Wetenschappelijk artikel in peer reviewed internationaal tijdschrift met Impact Factor
WI-2**= Wetenschappelijk artikel in peer reviewed internationaal tijdschrift zonder Impact Factor
WN***= Wetenschappelijk artikel in peer reviewed nationaal tijdschrift zonder Impact Factor

Tabel 4: Impactfactor per tijdschrift

Tijdschrift	Impactfactor
Acta Chir Belgica	0.420
Acta Obstet Gynecol Scand	2.649
Acta Oncol	3.473
Acta Orthop	3.076
Aliment Pharmacol Ther	7.357
Am Heart J	4.171
Am J Cardiol	3.171
Ann Clin Biochem	1.983
Ann Oncol	13.926
Ann Surg	1.536
Ann Surg Oncol	3.857
Ann Vasc Surg	1.363
Anticancer Res	1.865
Appl Health Econ Health Policy	1.885
Arch Dis Child	3.258
Arch Phys Med Rehabil	3.077
Biomed Res Int	2.583
BJOG	4.876
BMC Cancer	3.288
BMC Musculoskelet Disord	1.998
BMC Pregnancy Childbirth	2.331
BMC Surg	1.692
BMC Womens Health	1.806
BMJ	23.259
BMJ Open	2.413
Br J Anaesth	6.499
Br J Cancer	5.922
Br J Dermatol	6.129
Br J Haematol	5.128
Br J Surg	5.433
Breast	2.951
Breast Cancer Res Treat	3.605
Breast J	2.424
Cancer	6.537
Cardiol Rev	1.951
Catheter Cardiovasc Interv	2.602
Circ Cardiovasc Interv	6.504
Circulation	18.880
Climateric	2.807
Clin Appl Thromb hemost	1.852
Clin Biochem	2.584

Clin Cancer Res	10.199
Clin Chem Lab Med	3.556
Clin Chim Acta	2.926
Clin Colorectal Canc	3.861
Clin Gastroenterol Hepatol	7.683
Clin Microbiol Infect	5.394
Clin Oral Implants Res	4.305
Clin Radiol	2.282
Clin Trans Oncol	2.392
Cochrane Database Syst Rev	6.754
Colorectal Dis	2.778
Comput Human Behav	3.536
Curr Opin Clin Nutr Metab Care	4.534
Cytopathology	1.376
Dig Surg	2.031
Dis Esophagus	2.702
Dysphagia	2.531
Endocr Connect	3.041
Endoscopy	6.629
Eur Geriatr Med	1.169
Eur Heart j	23.425
Eur Heart J - Cardiovasc Img	8.336
Eur J Anaesthesiol	3.958
Eur J Cancer	7.191
Eur J Cardiothorac Surg	3.504
Eur J Clin Pharmacol	2.679
Eur J Nucl Med Mol Imaging	7.704
Eur J Obstet Gyn R B	1.809
Eur J Pediatr	2.242
Eur J Radiol	2.843
Eur J Surg Oncol	3.688
Eur J Trauma emerg Surg	1.704
Eur J Vasc Endovasc Surg	3.877
Eurointervention	4.417
Europace	5.231
Fertil Steril	4.803
Gait Posture	2.273
Gastric cancer	5.045
Gastroenterology	20.773
Gastrointest Endosc	7.204
Gut	17.016

Gynecol Oncol	4.540
Haemophilia	2.768
Health Qual Life Outcomes	2.278
Heart	5.420
Heart Rhythm	4.743
Hemodial int	1.237
Hernia	2.417
Histopathology	3.267
HPB	3.131
IEEE J Biomed Health Inform	3.850
IEEE T Ultrason Ferr	2.704
IEEE Trans Vis Comput graph	3.078
Indian J Surg	0.509
Int J Cancer	7.360
Int J Cardiovasc Imag	2.036
Int J Clin Oncol	2.610
Int J Radiat Oncol Biol phys	5.554
Int J Sports Med	2.453
Int J Urol	1.941
Int Urogynecol J	2.078
Int Urol Nephrol	1.692
J Am Acad Dermatol	6.898
J Am Coll Cardiol	16.834
J Am Heart Assoc	4.450
J Asthma	2.014
J Behav Med	2.880
J Biomed Mater Res A	3.231
J Bone Miner Res	6.314
J Cancer Surviv	3.713
J Cardiac Surg	1.179
J Cardiothorac Vasc Anesth	1.574
J Clin Gastroenterol	2.968
J Clin Oncol	26.303
J Diabetes Complications	2.792
J Endovasc Ther	2.732
J Eur Acad Dermatol Venereol	4.287
J Foot Ankle Surg	1.138
J Gastrointest Surg	2.813
J Geriatr Oncol	3.359
J Gynecol Oncol	3.340
J Inherit Metab Dis	4.092
J Interv cardiol	1.728

J Invest Dermatol	6.448
J Laparoendosc Adv Surg Tech A	1.257
J Med Econ	2.264
J Minim Acc surg	1.137
J Minim Invasive gynecol	3.061
J Neurointerv Surg	3.524
J Nucl Cardiol	3.847
J Nucl Med	7.439
J Pediatr Orthop B	0.610
J Pediatr Surg	2.128
J Psychosom Res	2.947
J Ren Nutr	2.651
J Surg Educ	2.302
J Thromb Haemost	4.899
J Vasc Access	1.306
J Vasc Surg	2.758
JACC Cardiovasc Imaging	10.189
JACC Cardiovasc Interv	9.881
JAMA	47.661
Jama Neurol	11.460
Jama Surg	8.498
lancet	53.254
Lancet Neurol	27.138
Lancet Oncol	36.418
Laterality	1.388
Lung Cancer	4.486
Maturitas	3.315
Med Teach	2.450
Medicine	1.804
Minerva Anestesiol	1.784
Minerva Chir	0.554
Mol Genet Genom Med	2.695
N Engl J Med	79.258
Nephrol Dial Transplant	4.600
Neth Heart J	1.476
Neth J Med	1.156
Neurogastroenterol Motil	3.842
Nucl Med Commun	1.495
Nutr Cancer	2.261
Nutr Clin Pract	2.591
Obes Surg	3.895

Oncologist	5.306
Oncotarget	5.168
Orthop J Sports Med	0.935
Osteoporos int	3.856
Pacing Clin Electrophysiol	1.441
Pancreas	2.958
Parkinsonism Relat Disord	4.721
Perfusion	1.147
Phys Med Biol	2.665
Physiol Meas	2.006
Plast Reconstr Surg	3.475
PLoS One	2.766
Psychooncology	3.455
Q J Nucl Med Mol Imaging	2,368
Qual Life Res	2.392
Radiother Oncol	4.942
Reprod Sci	2.548
Resuscitation	5.863
Scand J Clin lab invest	1.498
Sex Transm Infect	1.981
support care cancer	2.676
Surg Endosc	3.117
Surg Obes Relat Dis	3.900
Surg Oncol	2.558
Thromb Res	2.779
Transfusion	3.423
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World J Gastroenterol	3.300
World J Surg	2.766

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