

# Wetenschappelijk Jaaroverzicht 2012

Onder redactie van:

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Oplage: 400

Een uitgave van het Catharina Ziekenhuis  
Eindhoven, 2013

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## Woord Vooraf

Het Catharina Ziekenhuis heeft een opleidings- en onderzoekstraditie hoog te houden. Daarvan getuigt ook dit jaaroverzicht met wetenschappelijke publicaties in 2012. Onze medewerkers hebben ook dit jaar weer meer gepubliceerd dan vorig jaar. In totaal in 2012 314 publicaties ten opzichte van 277 in 2011. In 2012 zijn elf collega's gepromoveerd en momenteel zijn 60 medewerkers, vooral medici, medisch-ondersteunende professionals en verpleegkundigen, bezig met hun promotietraject. Daarnaast begeleiden medewerkers van het Catharina Ziekenhuis nog 20 promovendi die verbonden zijn aan universiteiten en zijn er vijf medisch specialisten, die tevens als hoogleraar werkzaam zijn. Deze professionals zorgen er voor dat er vele constructieve samenwerkingsverbanden zijn ontstaan tussen universiteiten, ziekenhuizen en expertisecentra.

De indrukwekkende wetenschappelijke output is reden genoeg om als succes gevierd te worden. Het zegt iets over de eigenschappen van onze professionals. Een goede onderzoeker is immers nieuwsgierig en kritisch en heeft het lef om buiten gebaande of gebruikelijke paden te treden. Dit alles om de kwaliteit en doelmatigheid van de patiëntenzorg te verbeteren.

Dat neemt niet weg dat we ook als organisatie kritisch naar onze processen moeten kijken. Om als STZ ziekenhuis ook in de toekomst geaccrediteerd te blijven, moeten we aantonen hoe wij als organisatie het wetenschappelijk onderzoek stimuleren en faciliteren. Inhoudelijk hebben we stappen gemaakt; er is een wetenschapsbureau waar je terecht kunt voor inhoudelijke ondersteuning, er worden wetenschapsavonden georganiseerd en er wordt gewerkt aan het stimuleren van onderzoek door verpleegkundigen. Maar een wetenschappelijke onderzoekscultuur bestendigen vraagt ook investeren in de ruimste zin van het woord. Het gaat om het stroomlijnen van processen, faciliteiten, transparantie in financiering maar ook de ontwikkeling van een Onderzoeksfonds. Hoe we dat gaan organiseren, daar zijn we nu volop mee bezig, samen met de Medische Staf. Dat is wat wij gaan doen in 2013.

Iedereen die direct of indirect een bijdrage heeft geleverd aan het wetenschappelijk onderzoek in het Catharina Ziekenhuis willen we hartelijk bedanken voor het mooie resultaat over 2012. We mogen met zijn allen trots zijn en we gaan deze lijn ook naar de toekomst verder uitbouwen en vast houden!

Dr. P.L. Batenburg,

Voorzitter Raad van Bestuur

Dr. F. Haak- van der Lely

Voorzitter Medische Staf



# **Algemeen Klinisch Laboratorium**

**Berkel M van**

**Moderate elevations of high-sensitivity cardiac troponin I and B-type natriuretic peptide in chronic hemodialysis patients are associated with mortality**

Geerse DA, Berkel M van\*, Vogels S, Kooman JP, Konings CJ\*, Scharnhorst V\*

Clin Chem Lab Med. 2012 Dec 10:1-8

Background: Several biomarkers are associated with mortality in hemodialysis patients. In particular, elevated cardiac troponin T and B-type natriuretic peptide (BNP) are strong predictors of mortality; however, less is known about cardiac troponin I (cTnI). Elevated troponin I is detected in many hemodialysis patients, but the association of moderate elevations with mortality is unclear.

Methods: The relation between mortality and cTnI, using a high-sensitivity cTnI assay, as well as BNP and C-reactive protein (CRP) was evaluated in 206 chronic hemodialysis patients.

Results: Median follow-up was 28 months with a total mortality of 35%. Mortality was significantly associated with elevated cTnI, BNP and CRP. Even patients with only moderate elevation of cTnI (0.01-0.10 g/L) showed 2.5-fold increased mortality. Interestingly, hazard ratios for mortality for single (random) measurements were comparable to those for mean/median measurements. Subsequently, subgroup analysis based on combined markers was performed. Patients with both cTnI <0.01 g/L and BNP in the first quartile had 100% survival. Patients with either cTnI <0.01 g/L or BNP in the lowest quartile had significantly lower mortality (12% and 13%, respectively) than patients with BNP levels in the second quartile or higher and cTnI of 0.01-0.05 g/L and patients with cTnI  $\geq$  0.05 g/L (mortality 46 and 58%, respectively).

Conclusions: A combination of moderate elevation of cTnI and BNP provided additional prognostic value. A single measurement of these biomarkers performed comparably to the mean/median of multiple measurements.

*Impactfactor: 2.150*

**Boer AK**

**The new Roche Vitamin D Total assay: fit for its purpose?**

Emmen JM, Wielders JP, Boer AK\*, Ouweland JM van den, Vader HL

Clin Chem Lab Med. 2012 Jun 8;50(6):1-4

Background: Measurement of serum 25-hydroxyvitamin D [25(OH)D] is used to assess vitamin D status. We evaluated the analytical performance of a new automated assay, Elecsys Vitamin D Total (Roche Diagnostics, Mannheim, Germany), based on competitive protein binding. Methods: The Elecsys assay was tested for imprecision, linearity and functional sensitivity at three test-sites and compared to a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method, a highperformance liquid chromatography (HPLC) method and the Liaison 25(OH) Vitamin D Total immunoassay (Diasorin).

Results: Imprecision testing with human serum specimens showed within-run CVs of  $\leq$  6% and between-run CVs of  $\leq$  8%. The assay was linear from 33 up to at least 111 nmol/L and showed equivalent 25(OH)D levels for matched serum and heparinized plasma samples. The assay correlated reasonable to well with LC-MS/MS ( $r=0.93$ ;  $y=1.07x-5.04$  nmol/L), HPLC ( $r=0.91$ ,  $y=0.90x+3.03$  nmol/L) and the Liaison assay ( $r=0.86$ ,  $y=1.19x+2.80$  nmol/L). Some of the samples showed large between-method differences.

Conclusions: The new Elecsys assay fulfilled present analytical performance requirements and showed close agreement to other well-established methods for 25(OH)D analysis, making it fit for routine assessment of vitamin D status.

*Impactfactor:--*

**Boer AK**

**Verbeterde Cushing speekseldiagnostiek m.b.v. eigen UPLC MS/MS methode die onderscheid maakt tussen cortison en cortisol**

Boer AK\*, Heuvel D van den\*, Lentjes E

Ned Tijdschr Klin Chem Labgeneesk 2012; 37: 219-221

*Impactfactor: --*

**Boonen KJ**

**Trueness in the measurement of haemoglobin: consensus or reference method?**

Boonen KJ\*, Curvers J\*, Timmerman AA, Steurs D, Kerkhof D van de\*

Clin Chem Lab Med. 2012;50(3):511-14. Epub 2011 Nov 10

Background: For the measurement of haemoglobin a reference method exists: the haemiglobincyanide method. However, a Dutch external quality assessment organization does not use this method in the evaluation of trueness of results. The aim of this work was to assess whether trueness was compromised by the use of a consensus value.

Methods: Five Cell Dyn Sapphires (Abbott) in three independent locations were used to measure haemoglobin concentration. Results were compared to the reference method (haemiglobincyanide). Patient samples with a distribution over clinically relevant concentrations (Hb 2.5-10.2 mmol/L) were used next to samples from external quality assessment rounds. Passing and Bablok regression analysis and Bland-Altman plots were used to evaluate any systematic deviation. Results: Results measured on the Cell Dyn Sapphires deviated significantly from the results obtained with the reference method. Remarkably, consensus results from external quality control samples also deviated significantly from the reference method.

Conclusions: A significant negative bias exists in the measurement of haemoglobin on Cell Dyn Sapphires. Additionally, the consensus value as reported in external quality control assessment also shows an even greater significant negative bias compared to the reference method. As a reference method is available, external quality assessment would benefit from using this method instead of a consensus value to evaluate trueness.

*Impactfactor: 2.150*

**Curvers J**

**Blood group genotyping in a multitrauma patient: a case report**

Curvers J\*, Scharnhorst V\*, Haas M de, Warnier-Wandel L, Kerkhof D van de\*

Immunohematology. 2012 Sep;28(3):85-7

*Impactfactor: --*

**Curvers J**

**Measuring direct thrombin inhibitors with routine and dedicated coagulation assays: which assay is helpful?**

Curvers J\*, Kerkhof D van de\*, Stroobants AK, Dool EJ van den, Scharnhorst V\*

Am J Clin Pathol. 2012 Oct;138(4):551-8

The use of direct thrombin inhibitors (DTIs) for prophylactic or therapeutic anticoagulation is increasing because of the predictable bioavailability and short half-life of these DTIs. However, in certain situations, indication of the concentration is warranted. We investigated the effects of 3 DTIs (lepirudin, argatroban, and bivalirudin) in 6 pooled plasma specimens on routine coagulation assays (activated partial thromboplastin time [aPTT], prothrombin time [PT], and thrombin time [TT]) and dedicated DTI assays (Hemoclot, HemosIL, the ecarin

clotting time, and a chromogenic ecarin clotting time) on 2 coagulation analyzers. We found routine tests to be nondiscriminative between concentrations of different DTIs in the aPTT. Moreover, for PT and TT, the responses for different DTIs differed. This was similar for ecarin clotting assays. The Hemoclot and HemosIL assays showed identical linear increases for all 3 DTIs. We conclude that dedicated calibrated assays based on a diluted TT (Hemoclot and HemosIL) appear to be the most suitable for monitoring purposes.

*Impactfactor: 2.598*

## **Curvers J**

### **Reference intervals of extended erythrocyte and reticulocyte parameters**

Hoffmann JJ, Broek NM van den, Curvers J\*

Clin Chem Lab Med. 2012 Mar 2;50(5):941-8

**Background:** Optical analysis of erythrocytes can provide information on the haemoglobin concentration and content of reticulocytes and mature erythrocytes. Such parameters have proven clinical utility in anemia diagnosis and therapy monitoring. For interpretation, reliable reference ranges are needed. The aim of this study was to establish reference intervals for extended erythrocyte and reticulocyte parameters as measured with the Abbott CELL-DYN Sapphire hematology analyzer. Secondary aims were to study sample stability and to investigate gender- and age dependency of the reference ranges.

**Methods:** Extended RBC parameters were measured in routine samples of a primary health care laboratory. The study cohort included 8161 samples of unique individuals, which were analyzed using Bhattacharya statistics. As a comparison, reference intervals were calculated in a subset of individuals without iron depletion.

**Results:** The majority of erythrocyte and reticulocyte parameters were normally distributed, allowing calculation of reference intervals. Only for hypo- and hyperchromic erythrocytes non-parametric statistics had to be used. The reference range for mean cellular hemoglobin content of reticulocytes (MCHR) was 28.5-34.5 pg (1.77-2.14 fmol) in the entire study group and 26.0-35.1 pg (1.60-2.17 fmol) in the non iron-depleted subgroup. No differences between sexes were found. Most parameters showed significant age effects in children and adolescents. **Conclusions:** Reference intervals have been established for extended RBC and reticulocyte parameters for the CELL-DYN Sapphire. Gender effects could not be demonstrated and age effects were of limited size, except for individuals younger than 18 years. Extended RBC parameters are stable for at least 6 h after blood collection.

*Impactfactor: 2.150*

## **Curvers J**

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*Voor abstract zie: Algemeen Klinisch Laboratorium - Boonen KJ*

*Impactfactor: 2.150*

## **Heuvel D van den**

### **Verbeterde Cushing speekseldiagnostiek m.b.v. eigen UPLC MS/MS methode die onderscheid maakt tussen cortisol en cortison**

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*Impactfactor:--*

### **Kerkhof D van de**

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Curvers J\*, Scharnhorst V\*, Haas M de, Warnier-Wandel L, Kerkhof D van de\*  
Immunohematology. 2012 Sep;28(3):85-7

*Impactfactor: --*

### **Kerkhof D van de**

#### **Early double stent thrombosis associated with clopidogrel hyporesponsiveness**

Rademakers LM\*, Dewilde W\*, Kerkhof D van de \*

Neth Heart J. 2012 Jan;20(1):38-41. Epub 2011 May 21

*Voor abstract zie: Cardiologie - Rademakers LM*

*Impactfactor: 1.438*

### **Kerkhof D van de**

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Curvers J\*, Kerkhof D van de\*, Stroobants AK, Dool EJ van den, Scharnhorst V\*  
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*Impactfactor: 2.598*

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*Impactfactor: 2.150*

### **Scharnhorst V**

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### **Scharnhorst V**

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Geerse DA, Berkel M van\*, Vogels S, Kooman JP, Konings CJ\*, Scharnhorst V\*

Clin Chem Lab Med. 2012 Dec 10:1-8

*Voor abstract zie: AKL - BerkeL M van*

*Impactfactor: 2.150*

### **Scharnhorst V**

#### **Molecular detection of Plasmodium knowlesi in a Dutch traveler by real-time PCR**

Link L\*, Bart A, Verhaar N, Gool T van, Pronk M, Scharnhorst V\*

J Clin Microbiol. 2012 Jul;50(7):2523-4. Epub 2012 May 9

*Voor abstract zie: Inwendige geneeskunde - Link L*

*Impactfactor: 4.153*

### **Scharnhorst V**

#### **Prophylactic treatment with alkaline phosphatase in cardiac surgery induces endogenous alkaline phosphatase release**

Kats S, Brands R, Soliman Hamad MA\*, Seinen W, Scharnhorst V\*, Wulkan RW, Schönberger JP\*, Oeveren W van

Int J Artif Organs. 2012 Feb;35(2):144-51

*Voor abstract zie: Cardiothoracale Chirurgie- Soliman Hamad MA*

*Impactfactor: 1.861*

### **Scharnhorst V**

#### **Variation of cardiac troponin I and T measured with sensitive assays in emergency department patients with noncardiac chest pain**

Scharnhorst V\*, Krasznai K\*, Veer M van 't\*, Michels RH\*

Clin Chem. 2012 Aug;58(8):1208-14

**BACKGROUND:** New-generation high-sensitivity assays for cardiac troponin have lower detection limits these new assays are also lower, leading to higher frequencies of positive test results. When cardiac troponin concentrations are minimally increased, serial testing allows discrimination of myocardial infarction from other causes of increased cardiac troponin. We assessed various measures of short-term variation, including absolute concentration changes, reference change values (RCVs), and indices of individuality (II) for 2 cardiac troponin assays in emergency department (ED) patients.

**METHODS:** We collected blood from patients presenting with cardiac chest pain upon arrival in the ED and 2, 6, and 12 h later. Cardiac troponin was measured with the high-sensitivity cardiac troponin T (hs-cTnT) assay (Roche Diagnostics) and a sensitive cTnI assay (Siemens Diagnostics). Cardiac troponin results from 67 patients without acute coronary syndrome or stable angina were used in calculating absolute changes in cardiac troponin, RCVs, and II.

**RESULTS:** The 95th percentiles for absolute change in cardiac troponin were 8.3 ng/L for hs-cTnT and 28 ng/L for cTnI. Within-individual and total CVs were 11% and 14% for hs-cTnT and 18% and 21% for cTnI, respectively. RCVs were 38% (hs-cTnT) and 57% (cTnI). The corresponding log-normal RCVs were +46%/-32% for hs-cTnT and +76%/-43% for cTnI. II values were 0.31 (cTnI) and 0.12 (hs-cTnT).

**CONCLUSIONS:** The short-term variations and IIs of cardiac troponin were low in ED patients free of ischemic myocardial necrosis. The detection of cardiac troponin variation exceeding

reference thresholds can help to identify ED patients with acute myocardial necrosis whereas variation within these limits renders acute coronary syndrome unlikely.  
*Impactfactor: 7.905*

*\* = Werkzaam in het Catharina Ziekenhuis*



# Anesthesiologie

## **Beckers A**

### **Inadvertent epidural injection of drugs for intravenous use. A review**

Beckers A\*, Verelst P\*, Zundert A van\*

Acta Anaesthesiol Belg. 2012;63(2):75-9

**INTRODUCTION:** The frequency of inadvertent injection of drugs in the epidural space is probably underestimated and underreported, but it can cause serious morbidity and possibly mortality.

**OBJECTIVE:** The aim of this review is to collate reported incidents of this type, to describe the potential mechanisms of occurrence and to identify possible therapeutic solutions.

**METHODS:** We searched into medical databases and reviewed reference lists of papers retrieved.

**RESULTS:** A list is reported of more than 50 drugs that were inadvertently injected into the epidural space. This list includes drugs which produce no, little or short-lasting neurological deficits, but also includes drugs that may be more etching and can result in temporary or even permanent neurological deficit.

**DISCUSSION:** Most drugs do not lead to sequelae other than pain during injection or transient neurological complaints. Other drugs may have more deleterious consequences, such as paraplegia. Both the dose of the inadvertent injected drug and the time frame play an important role in the patient's outcome. "Syringe swap", "ampoule error", and epidural/intravenous line confusion due to inaccurate or absent colour coding of epidural catheters were the main sources of error. Preventive strategies, including non Luer-lock epidural injection ports, might increase safety.

*Impactfactor: --*

## **Buise MP**

### **Bariatric surgery with operating room teams that stayed fixed during the day: a multicenter study analyzing the effects on patient outcomes, teamwork and safety climate, and procedure duration**

Stepaniak PS\*, Heij C, Buise MP\*, Mannaerts GH, Smulders F, Nienhuijs SW\*

Anesth Analg. 2012 Dec;115(6):1384-92. Epub 2012 Nov 9

*Voor abstract zie: Anesthesiologie - Stepaniak PS*

*Impactfactor: 3.286*

## **Gaag A van der**

### **Intervention techniques for chronic postherniorrhaphy pain**

Thomassen I\*, Suijlekom HA van\*, Gaag A van der\*, Nienhuijs SW\*

European Surgery 2012;44(3):132-7

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: 0.283*

## **Haanschoten MC**

### **Fast-track practice in cardiac surgery: results and predictors of outcome.**

Haanschoten MC\*, Straten AH van\*, Woorst JF ter\*, Stepaniak PS\*, Meer AD van der\*, Zundert AA van\*, Soliman Hamad MA\*

Interact Cardiovasc Thorac Surg. 2012 Dec;15(6):989-94. Epub 2012 Sep 5

**OBJECTIVES:** Various studies have shown different parameters as independent risk factors in predicting the success of fast-track postoperative management in cardiac surgery. In the

present study, we evaluated our 7-year experience with the fast-track protocol and investigated the preoperative predictors of successful outcome.

**METHODS:** Between 2004 and 2010, 5367 consecutive patients undergoing cardiac surgery were preoperatively selected for postoperative admission in the postanesthesia care unit (PACU) and were included in this study. These patients were then transferred to the ordinary ward on the same day of the operation. The primary end-point of the study was the success of the PACU protocol, defined as discharge to the ward on the same day, no further admission to the intensive care unit and no operative mortality. Logistic regression analysis was performed to detect the independent risk factors for failure of the PACU pathway.

**RESULTS:** Of 11 895 patients undergoing cardiac surgery, 5367 (45.2%) were postoperatively admitted to the PACU. The protocol was successful in 4510 patients (84.0%). Using the multivariate logistic regression analysis, older age and left ventricular dysfunction were found to be independent risk factors for failure of the PACU protocol [odds ratio of 0.98/year (0.97-0.98) and 0.31 (0.14-0.70), respectively].

**CONCLUSIONS:** Our fast-track management, called the PACU protocol, is efficient and safe for the postoperative management of selected patients undergoing cardiac surgery. Age and left ventricular dysfunction are significant preoperative predictors of failure of this protocol.

*Impactfactor: --*

#### **Korsten HH**

##### **An electronic system to document reasons for medication discontinuation and to flag unwanted recriptions in geriatric patients**

Linden CM van der\*, Jansen PA\*, Marum RJ van, Grouls RJ\*, Egberts TC, Korsten EH\*  
Drugs Aging. 2012 Dec;29(12):957-62.. Epub 2012 Nov 10

*Voor abstract zie: Geriatrie - Linden CM van der*

*Impactfactor: 2.671*

#### **Korsten HH**

##### **Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter \*, Korsten EH\*, Borne BE van den\*,  
Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72. Epub 2012 May 25

*Voor abstract zie: Cardiothoracale chirurgie - Ponten JE*

*Impactfactor: --*

#### **Korsten HH**

##### **Inability to ventilate after tube exchange postoperative to pneumonectomy**

Verstraeten SE\*, Straten AH van\*, Korsten HH\*, Weber EW\*, Wiolders PL\*,  
Berreklouw E\*

Case Rep Anesthesiol. 2012;2012:801093. Epub 2012 Apr 5

*Voor abstract zie: Cardiothoracale chirurgie - Verstraeten SE*

*Impactfactor: --*

**Maassen RL**

**Forces applied to the maxillary incisors by video laryngoscopes and the Macintosh laryngoscope**

Lee RA, Zundert AA van\*, Maassen RL\*, Wieringa PA

Acta Anaesthesiol Scand. 2012 Feb;56(2):224-9. Epub 2011 Oct 14

*Voor abstract zie: Anesthesiologie - Zundert AA van*

*Impactfactor: 2.188*

**Meer AD van der**

**Fast-track practice in cardiac surgery: results and predictors of outcome**

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*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*Impactfactor: --*

**Pieters B**

**Avoiding palatopharyngeal trauma during videolaryngoscopy: do not forget the 'blind spots'**

Zundert AA van\*, Pieters B\*, Zundert T van, Gatt S

Acta Anaesthesiol Scand. 2012 Apr;56(4):532-4. Epub 2012 Jan 31

*Impactfactor: 2.188*

**Pieters B**

**Combined technique using videolaryngoscopy and Bonfils for a difficult airway intubation**

Zundert AA van\*, Pieters BM\*

Br J Anaesth. 2012 Feb;108(2):327-8

*Impactfactor: 4.243*

**Pieters B**

**Videolaryngoscopy allows a better view of the pharynx and larynx than classic laryngoscopy**

Zundert A van\*, Pieters B\*, Doerges V, Gatt S

Br J Anaesth. 2012 Dec;109(6):1014-5

*Impactfactor: 4.243*

**Pieters B**

**Videolaryngoscopy offers advantages over classic laryngoscopy in a patient with seriously limited lip opening**

Zundert AA van\*, Pieters B\*, Hoogbergen M\*

J Anesth. 2012 Jun;26(3):468-9. Epub 2012 Jan 12

*Impactfactor: 0.831*

**Suijlekom JA van**

**Effect of spinal cord stimulation in refractory angina pectoris**

Suijlekom HA van\*, Strijbosch-Wilderbeek L, Tielen-van Laarhoven T, Lammers J, Botman CJ

Asean Heart Journal 2012;2:47-8

*Impactfactor: --*

**Suijlekom JA van**

**Intervention techniques for chronic postherniorrhaphy pain**

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European Surgery 2012;44(3):132-7

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**Verelst P**

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*Voor abstract zie: Anesthesiologie - Beckers A*

*Impactfactor: --*

**Weber EW**

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*Voor abstract zie: Cardiothoracale chirurgie - Verstraeten SE*

*Impactfactor: --*

**Zundert AA van**

**Applied pharmacology in anaesthesiology and critical care / Analee Milner, Ernest Welch**

Zundert A van\*

Acta Anaesthesiol Belg 2012: 63

*Impactfactor: --*

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Acta Anaesthesiol Scand. 2012 Apr;56(4):532-4. Epub 2012 Jan 31

*Impactfactor: 2.188*

### **Zundert AA van**

#### **Carl Koller gold medal award to prof Joseph M. Neal**

Zundert AA van

Reg Anesth Pain Med. 2012 Nov;37(6):645-6

*Impactfactor: --*

### **Zundert AA van**

#### **Carl Koller, cocaine, and local anesthesia: some less known and forgotten facts**

Goerig M, Bacon D, Zundert AA van\*

Reg Anesth Pain Med. 2012 May-Jun;37(3):318-24

Modern-day local anesthesia began in 1884 with a discovery by a young unknown ophthalmologist from Vienna named Carl Koller, who placed a cocaine solution on the cornea, thus producing insensibility. The news of his discovery spread throughout the world in less than a month. "Not surprisingly," a controversial priority discussion emerged. There is little information about this "dark side" of Koller's discovery and only sparse data about the personalities involved in this controversy. In addition, Carl Koller's decision to leave Vienna is also surrounded in secrecy. The story surrounding the revelation of the local anesthetic effect of cocaine and the personalities involved is fascinating and relatively unknown.

*Impactfactor: 4.079*

### **Zundert AA van**

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*Impactfactor: 4.243*

### **Zundert AA van**

#### **Comparison of forces applied to the maxillary incisors by direct and indirect laryngoscopes**

Lee RA, Zundert AA van\*

Acta Anaesthesiol Scand 2012; 56:664-665

*Impactfactor: 2.188*

### **Zundert AA van**

#### **Ensuring direct laryngoscopy will not become an extinct skill**

#### **Comment on GlideScope videolaryngoscope vs. Macintosh direct laryngoscope for intubation of morbidly obese patients: a randomized trial. [Acta Anaesthesiol Scand. 2011]**

Lee RA, Zundert AA van\*

Acta Anaesthesiol Scand. 2012 Jul;56(6):803. Epub 2012 May 10

*Impactfactor: 2.188*

## **Zundert AA van**

### **Evaluation of the Mediseus epidural simulator**

Lee RA, Zundert TC van, Koesveld JJ van, Zundert AA van\*, Stolker RJ, Wieringa PA, Gatt SP

*Anaesth Intensive Care.* 2012 Mar;40(2):311-8

The demand for increased patient safety has led to greater use of simulation training of health professionals performing medical procedures. The study aim was to evaluate the usefulness of the Mediseus® Epidural Simulator in teaching basic epidural needle-handling skills. Three groups of 15 anaesthetists (Novice=zero to two year anaesthesia trainees; Intermediate=three- to five-year anaesthesia trainees; Expert=consultants and regional-specialist anaesthetists) from three different medical centres participated. Each participant performed 20 simulated epidural needle insertions and was scored on several parameters (e.g. time, success of the insertion, bone collisions). Following familiarisation with the simulator and the needle insertions, participants answered seven questions on the applicability of the simulator to the teaching of basic epidural needle-handling skills. There was a clear learning effect with regard to the simulation procedure time, this decreasing throughout the experiment ( $P=0.037$ ). There was no significant influence of either group or experience with the simulator in the study on the number or type of errors made. The quality of the simulation was scored 2.3 out of 5.0 (for bone simulation) and 4.7 (for loss-of-resistance simulation). All groups considered that the simulator was best suited for training prospective anaesthetists. Each group rated the usefulness of the simulator for training novices at greater than 3.0 out of 5.0. The Mediseus® Epidural Simulator seems to be an appropriate training device for an introduction to epidural needle insertion. For medical professionals with procedural knowledge, the simulation is not realistic enough and the simulator did not distinguish between the groups based on the errors made.

*Impactfactor: 1.279*

## **Zundert AA van**

### **Fast-track practice in cardiac surgery: results and predictors of outcome**

Haanschoten MC\*, Straten AH van\*, Woorst JF ter\*, Stepaniak PS, Meer AD van der\*, Zundert AA van\*, Soliman Hamad MA\*

*Interact Cardiovasc Thorac Surg.* 2012 Dec;15(6):989-94. Epub 2012 Sep 5

*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*Impactfactor: --*

## **Zundert AA van**

### **Forces applied to the maxillary incisors by video laryngoscopes and the Macintosh laryngoscope**

Lee RA, Zundert AA van\*, Maassen RL\*, Wieringa PA

*Acta Anaesthesiol Scand.* 2012 Feb;56(2):224-9. Epub 2011 Oct 14

**BACKGROUND:** Modern video laryngoscopes (VLSs) provide a superior view of the glottis, facilitating easier intubations. This study evaluates the forces applied to the maxillary incisors when using various VLSs and a Macintosh blade.

**METHODS:** Fifty consecutive surgery patients were randomly assigned to receive laryngoscopy from a pair of four blades investigated in the study - the VLS GlideScope® (Verathon Inc., Bothell, WA, USA), V-Mac" Storz® (Karl Storz, Tuttlingen, Germany), and McGrath" (Aircraft Medical, Edinburgh, United Kingdom); and the classic Macintosh blade also from Storz® (Karl Storz). An endotracheal tube (ETT) was brought into position anterior

to the vocal cords, with actual intubation carried out only with the second of the laryngoscopes. Sensors measured the forces directly applied to the patient's maxillary incisors while inserting the ETT. Other common metrics of intubation difficulty (e.g. Mallampati grade, Cormack-Lehane grade, and time) were also recorded.

RESULTS: Only one patient was not intubated within the standard study parameters and was converted to the hospital protocols for difficult intubations. The forces applied to the maxillary incisors were significantly greater with the Macintosh blade compared with all VLSs. There were no differences between the VLSs with regard to the forces. Patient characteristics, including Mallampati grade, were not predictive of the forces applied.

CONCLUSIONS: All VLSs considered were safer for the patient than was the Macintosh blade in terms of the forces applied to the maxillary teeth, time, number of insertion attempts, and view achieved of the glottic arch. There is a small, but significant, difference in the time and number of insertion attempts required during laryngoscopy with the different VLSs. There was no difference in the forces applied. The geometry of the respective blades may be an important component in the ease of laryngoscopy.

*Impactfactor: 2.188*

### **Zundert AA van**

#### **Inadvertent epidural injection of drugs for intravenous use. A review**

Beckers A\*, Verelst P\*, Zundert A van\*

Acta Anaesthesiol Belg. 2012;63(2):75-9

*Voor abstract zie: Anesthesiologie - Beckers A*

*Impactfactor:--*

### **Zundert AA van**

#### **Measurement of forces during direct laryngoscopy and videolaryngoscopy**

Pieters B, Zundert A van\*, Lee R

Anaesthesia. 2012 Oct;67(10):1182-3; author reply 1183

*Impactfactor: 2.958*

### **Zundert AA van**

#### **Reply - Towards reducing palatoglossal, laryngeal and oropharyngeal injury occurring with some videolaryngoscopy intubation devices**

Zundert AA van\*, Pieters B\*, Zundert T van, Gatt S

Acta Anaesthesiol Scand 2012;56:1070-1

*Impactfactor: 2.188*

### **Zundert AA van**

#### **Videolaryngoscopy allows a better view of the pharynx and larynx than classic laryngoscopy**

Zundert A van\*, Pieters B\*, Doerges V, Gatt S

Br J Anaesth. 2012 Dec;109(6):1014-5

*Impactfactor: 4.243*

**Zundert AA van**

**Videolaryngoscopy offers advantages over classic laryngoscopy in a patient with seriously limited lip opening**

Zundert AA van\*, Pieters B\*; Hoogbergen M\*

J Anesth. 2012 Jun;26(3):468-9. Epub 2012 Jan 12

*Impactfactor: 0.831*

\* = *Werkzaam in het Catharina Ziekenhuis*



**Apotheek**

## Grouls RJ

### **An electronic system to document reasons for medication discontinuation and to flag unwanted represcriptions in geriatric patients**

Linden CM van der\*, Jansen PA, Marum RJ van, Grouls RJ\*, Egberts TC, Korsten EH\*

Drugs Aging. 2012 Dec;29(12):957-62.. Epub 2012 Nov 10

*Voor abstract zie: Geriatrie - Linden CM van der*

*Impactfactor: 2.671*

## Grouls RJ

### **Dose accuracy of new versus used Novopen 4 insulin pens**

Yucel H\*, Taks M\*, Menheere P, Grouls R\*, Bravenboer B\*

Diabetes Technol Ther. 2012 Sep;14(9):810-2. Epub 2012 Aug 6

*Voor abstract zie: Inwendige geneeskunde - Yucel H*

*Impactfactor: 1.931*

## Harmsze AM

### **Anafylaxie na ijzerdextraan bij een zwangere vrouw. [Anaphylaxis after iron dextran administration in a pregnant woman]**

Kortenhorst MS\*, Harmsze AM\*, Hasaart TH\*

Ned Tijdschr Geneesk. 2012;156(48):A5264

*Voor abstract zie: Gynaecologie - Kortenhorst MS*

*Impactfactor: --*

## Harmsze AM

### **The influence of CYP2C19\*2 and \*17 on on-treatment platelet reactivity and bleeding events in patients undergoing elective coronary stenting**

Harmsze AM\*, Werkum JW, Hackeng CM van, Ruven HJ, Kelder JC, Bouman HJ,

Breet NJ, Berg JM ten, Klungel OH, Boer A de, Deneer VH

Pharmacogenet Genomics. 2012 Mar;22(3):169-75

**OBJECTIVES:** To investigate the impact of genotypes on the basis of the loss-of-function variant CYP2C19\*2 and the gain-of-function variant CYP2C19\*17 on on-treatment platelet reactivity and on the occurrence of Thrombolysis in Myocardial Infarction (TIMI) major bleedings in 820 clopidogrel-treated patients who underwent elective coronary stenting.

**METHODS:** On-treatment platelet reactivity was quantified using ADP-induced light transmittance aggregometry (LTA) and the VerifyNow P2Y12 assay. Postdischarge TIMI major bleedings within 1 year after enrollment were recorded.

**RESULTS:** In total, 25 major bleedings (3.0% of the study population) were observed. Patients with the CYP2C19\*1/\*17 and \*17/\*17 diplotypes exhibited a lower magnitude of platelet reactivity as compared with patients with the CYP2C19\*1/\*1 diplotypes (for the light transmittance aggregometry-adjusted mean difference: -5.8%, 95% confidence interval: -9.6 to -2.1, P=0.002). Patients with the \*1/\*17 and \*17/\*17 genotype had a 2.7-fold increased risk in the occurrence of major bleedings [adjusted hazard ratio: 2.7, 95% confidence interval: 1.1-7.0, P=0.039]. The diplotypes \*2/\*17, \*1/\*2, and \*2/\*2 exhibited higher on-treatment platelet reactivity as compared with the wild type (P<0.0001). However, this was not translated into an altered risk on major bleedings as compared with the wild type [hazard ratio: 1.3 (0.45-4.0), P=0.60]. Results have not been adjusted for multiple testing.

CONCLUSION: Patients with the CYP2C19\*1/\*17 and \*17/\*17 diplotype have a lower magnitude of on-treatment platelet reactivity and are at a 2.7-fold increased risk of postdischarge TIMI major bleeding events after coronary stenting than patients with the \*1/\*1 genotype. The diplotypes \*2/\*17, \*1/\*2, and \*2/\*2 are associated with increased on-treatment platelet reactivity; however, this is not translated into a lower risk of bleeding events.

*Impactfactor: 3.485*

## **Taks M**

### **Dose accuracy of new versus used Novopen 4 insulin pens**

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*Voor abstract zie: Inwendige geneeskunde - Yucel H*

*Impactfactor: 1.931*

\* = *Werkzaam in het Catharina Ziekenhuis*



**Cardiologie**

## **Algin A**

### **Tropheryma whipplei aortic valve endocarditis, cured without surgical treatment**

Algin A\*, Wegdam-Blans M\*, Verduin K, Janssen H, Dantzig JM van\*

BMC Res Notes. 2012 Oct 30;5(1):600

**BACKGROUND:** Culture-negative endocarditis due to *Tropheryma whipplei* is a rare disease. Mostly the diagnosis is made by histologic examination of resected heart valve tissue.

**CASE PRESENTATION:** In this case report, we described a patient with a classical Whipple's disease. Transesophageal echocardiography (TEE) showed a vegetation on noncoronary cusp of the aortic valve. Whipple's disease was confirmed by positive *Tropheryma whipplei* polymerase chain reaction (PCR) in EDTA blood and a duodenal biopsy with positive periodic acid-Schiff stain (PAS) macrophages.

**CONCLUSION:** Due to timely diagnosis, our patient was treated with antibiotics without valve replacement..

*Impactfactor: --*

## **Bracke FA**

### **Decrease of the right ventricular electrogram amplitude in a Sprint Fidelis shock lead: a sign of lead malfunction?**

Gelder BM van\*, Nathoe R\*, Bracke FA\*

Europace. 2012 Dec;14(12):1758. Epub 2012 Jun 20

*Impactfactor: 1.980*

## **Bracke FA**

### **Familial evaluation in catecholaminergic polymorphic ventricular tachycardia: disease penetrance and expression in cardiac ryanodine receptor mutation-carrying relatives**

Werf C van der, Nederend I, Hofman N, Geloven N van, Ebink C, Frohn-Mulder IM, Alings AM, Bosker HA, Bracke FA\*, Heuvel F van den, Waalewijn RA, Bikker H, Tintelen JP van, Bhuiyan ZA, Berg MP van den, Wilde AA

Circ Arrhythm Electrophysiol. 2012 Aug 1;5(4):748-56

**BACKGROUND:** Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmia syndrome associated with mutations in the cardiac ryanodine receptor gene (*Ryr2*) in the majority of patients. Previous studies of CPVT patients mainly involved probands, so current insight into disease penetrance, expression, genotype-phenotype correlations, and arrhythmic event rates in relatives carrying the *Ryr2* mutation is limited.

**METHODS AND RESULTS:** One-hundred sixteen relatives carrying the *Ryr2* mutation from 15 families who were identified by cascade screening of the *Ryr2* mutation causing CPVT in the proband were clinically characterized, including 61 relatives from 1 family. Fifty-four of 108 antiarrhythmic drug-free relatives (50%) had a CPVT phenotype at the first cardiological examination, including 27 (25%) with nonsustained ventricular tachycardia. Relatives carrying a *Ryr2* mutation in the C-terminal channel-forming domain showed an increased odds of nonsustained ventricular tachycardia (odds ratio, 4.1; 95% CI, 1.5-11.5;  $P=0.007$ , compared with N-terminal domain) compared with N-terminal domain. Sinus bradycardia was observed in 19% of relatives, whereas other supraventricular dysrhythmias were present in 16%. Ninety-eight (most actively treated) relatives (84%) were followed up for a median of 4.7 years (range, 0.3-19.0 years). During follow-up, 2 asymptomatic relatives experienced exercise-induced syncope. One relative was not being treated, whereas the

other was noncompliant. None of the 116 relatives died of CPVT during a 6.7-year follow-up (range, 1.4-20.9 years).

**CONCLUSIONS:** Relatives carrying an Ryr2 mutation show a marked phenotypic diversity. The vast majority do not have signs of supraventricular disease manifestations. Mutation location may be associated with severity of the phenotype. The arrhythmic event rate during follow-up was low.

*Impactfactor: --*

### **Bracke FA**

#### **Is acute hemodynamic response a predictor of long-term outcome in cardiac resynchronization therapy?**

Prinzen FW, Houthuizen P\*, Bogaard MD, Gelder B van\*, Bracke F\*, Cramer MJ, Leenders GE, Meine M

J Am Coll Cardiol. 2012 Mar 27;59(13):1198; author reply 1198-9

*Impactfactor: 14.156*

### **Bracke FA**

#### **Left ventricular endocardial pacing in cardiac resynchronisation therapy: Moving from bench to bedside**

Bracke FA\*, Gelder BM van\*, Dekker LR\*, Houthuizen P\*, Woorst JF ter\*, Tejjink JA\*  
Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

In cardiac resynchronisation therapy, failure to implant a left ventricular lead in a coronary sinus branch has been reported in up to 10% of cases. Although surgical insertion of epicardial leads is considered the standard alternative, this is not without morbidity and technical limitations. Endocardial left ventricular pacing can be an alternative as it has been associated with a favourable acute haemodynamic response compared with epicardial pacing in both animal and human studies. In this paper, we discuss left ventricular endocardial pacing and compare it with epicardial surgical implantation. Ease of application and procedural complications and morbidity compare favourably with epicardial surgical techniques. However, with limited experience, the most important concern is the still unknown long-term risk of thromboembolic complications. Therefore, for now endovascular implants should remain reserved for severely symptomatic heart failure patients and patients at high surgical risk of failed coronary sinus implantation.

*Impactfactor: 1.438*

### **Bracke FA**

#### **Letter by van Gelder and Bracke Regarding Article, "Left Ventricular Versus Simultaneous Biventricular Pacing in Patients With Heart Failure and a QRS Complex >120 Milliseconds"**

Gelder BM van\*, Bracke FA\*

Circulation. 2012 Oct 9;126(15):e238

*Impactfactor: 14.739*

## **Bracke FA**

### **Pathways for training and accreditation for transvenous lead extraction: a European Heart Rhythm Association position paper**

Deharo JC, Bongiorni MG, Rozkovec A, Bracke F\*, Defaye P, Fernandez-Lozano I, Golzio PG, Hansky B, Kennergren C, Manolis AS, Mitkowski P, Platou ES; European Heart Rhythm Association

Europace. 2012 Jan;14(1):124-34

*Impactfactor: 1.980*

## **Broek KC van den**

### **Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den \*, Woorst JF ter\*, Elenbaas TW\*, Dantzig JM van \*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

*Voor abstract zie: Cardiothoracale chirurgie - Straten AH van*

*Impactfactor: 3.741*

## **Brueren BR**

### **Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

## **Brueren BR**

### **Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death**

Houthuizen P\*, Garsse LA van, Poels TT, Jaegere P de, Boon RM van der, Swinkels BM, Berg JM ten, Kley F van der, Schalijs MJ, Baan J Jr, Cocchieri R, Brueren GR\*, Straten AH van\*, Heijer P den, Bentala M, Ommen V van, Kluin J, Stella PR, Prins MH, Maessen JG, Prinzen FW

Circulation. 2012 Aug 7;126(6):720-8. Epub 2012 Jul 12

*Voor abstract zie: Cardiologie - Houthuizen P*

*Impactfactor: 14.739*

## **Dantzig JM van**

### **A rare case of diffuse mitral valve fibroelastoma**

Jonge M de\*, Straten A van\*, Dantzig JM van\*, Merrienboer F van\*, Elenbaas T\*

Ann Thorac Surg. 2012 Aug;94(2):e53

*Impactfactor: 3.741*

### **Dantzig JM van**

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BMC Res Notes. 2012 Oct 30;5(1):600

*Voor abstract zie: Cardiologie - Algin A*

*Impactfactor: --*

### **Dekker LR**

#### **Left ventricular endocardial pacing in cardiac resynchronisation therapy: Moving from bench to bedside**

Bracke FA\*, Gelder BM van\*, Dekker LR\*, Houthuizen P\*, Woorst JF ter\*, Teijink JA\*

Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

*Voor abstract zie: Cardiologie - Bracke FA*

*Impactfactor: 1.438*

### **Dekker LR**

#### **Mild to moderate kidney dysfunction and the risk of sudden cardiac death in the setting of acute myocardial infarction**

Dalal D, Jong J de, Tjong FV, Wang Y, Bruinsma N, Dekker L\*, Wilde AA

Heart Rhythm. 2012 Apr;9(4):540-5. Epub 2011 Nov 10

**BACKGROUND:** Although end stage renal disease is known to elevate risk of sudden cardiac death (SCD), the role of less severe renal impairment in SCD is unclear.

**OBJECTIVE:** To examine the association between mild-moderate renal impairment and first ischemic ventricular fibrillation.

**METHODS:** Renal function in patients included in the Arrhythmia Genetics in the NETHERlands Study (AGNES) were compared. Cases (n=337, age: 56±1 yr, 80% men) were defined as patients who had survived VF at the time of their first acute ST elevation myocardial infarction (STEMI), and controls (n=339, age: 58±1 yr, 80% men) as those without VF during

their first acute STEMI. Estimated glomerular filtration rate (eGFR) at the time of the acute STEMI was computed using the 4-variable Modification of Diet in Renal Disease equation.

RESULTS: eGFR less than 105 ml/min, decrease in eGFR was associated with elevated odds of developing VF during STEMI. The association was essentially flat at eGFR levels greater than 105ml/min. The lowest eGFR quintile was associated with over a 6-fold increase in odds of developing VF compared to the fourth quintile. This association between eGFR and VF at the time of STEMI remained significant after adjusting for potential confounders including electrolyte levels.

CONCLUSIONS: Mild to moderate kidney dysfunction is associated with a significantly elevated risk of VF in the setting of acute STEMI. Further studies should investigate the precise mechanisms by which mild kidney function results in VF.

*Impactfactor: 4.102*

### **Dekker LR**

#### **Three-dimensional computed tomography overlay for pulmonary vein antrum isolation: Follow-up and clinical outcomes**

Voort PH van der\*, Stevenhagen J, Dekker LR\*, Bullens R\*, Meijer A\*

Neth Heart J. 2012 Aug;20(7-8):302-6. Epub 2012 Jun 1

*Voor abstract zie: Cardiologie - Voort PH van der*

*Impactfactor: 1.438*

### **Dewilde W**

#### **Early double stent thrombosis associated with clopidogrel hyporesponsiveness**

Rademakers LM\*, Dewilde W\*, Kerkhof D van de \*

Neth Heart J. 2012 Jan;20(1):38-4. Epub 2011 May 21

*Voor abstract zie: Cardiologie - Rademakers LM*

*Impactfactor: 1.438*

### **Gelder BM van**

#### **Decrease of the right ventricular electrogram amplitude in a Sprint Fidelis shock lead: a sign of lead malfunction?**

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#### **Is acute hemodynamic response a predictor of long-term outcome in cardiac resynchronization therapy?**

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J Am Coll Cardiol. 2012 Mar 27;59(13):1198; author reply 1198-9

*Impactfactor: 14.156*

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Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

*Voor abstract zie: Cardiologie - Bracke FA*

*Impactfactor: 1.438*

### **Gelder BM van**

#### **Letter by van Gelder and Bracke regarding article, "left ventricular versus simultaneous biventricular pacing in patients with heart failure and a QRS complex >120 Milliseconds"**

Gelder BM van\*, Bracke FA\*

Circulation. 2012 Oct 9;126(15):e238

*Impactfactor: 14.739*

### **Habibovic M**

#### **Posttraumatic stress 18 months following cardioverter defibrillator implantation: Shocks, anxiety, and personality**

Habibovic M\*, Broek KC van den\*, Alings M, Voort PH van der \*, Denollet J  
Health Psychol. 2012 Mar;31(2):186-93. Epub 2011 Aug 1

Objective: Posttraumatic stress disorder (PTSD) has been observed in cardiac patients, but little is known about PTSD in implantable cardioverter defibrillator (ICD) patients. We examined the prevalence and predictors (clinical variables, personality, and anxiety) of PTSD in ICD patients.

Method: Three hundred ninety-five ICD patients (20.1% female; mean age = 62.8 ± 10.3 years) from two Dutch referral hospitals completed the 14-item Type D scale (DS14) and the State-Trait Anxiety Inventory to assess Type D (distressed) personality (high negative affect with social inhibition) and anxiety (on the State Anxiety Inventory) at the time of implantation. Logistic regression analysis was performed to identify independent predictors of PTSD at 18 months postimplantation.

Results: At 18 months postimplantation, 30 patients (7.6%) qualified for a PTSD diagnosis. Of these patients, 55% (n = 16) had a Type D personality, 83% (n = 25) experienced anxiety at baseline, and 24% (n = 7) had experienced shocks during follow-up. Both Type D personality (odds ratio [OR] = 3.5) and baseline anxiety (OR = 4.3) were significant predictors of posttraumatic stress at 18 months postimplantation, independent of shocks and other clinical and demographic covariates. Shocks were not significantly associated with PTSD.

Conclusion: A significant group of ICD patients is at risk of posttraumatic stress 18 months postimplantation, especially Type D patients and patients with increased levels of baseline anxiety. Identification of patients with Type D personality and anxiety at the time of implantation may be warranted to prevent PTSD in ICD patients.

*Impactfactor: 3.873*

## Hauer HA

### **European survey on efficacy and safety of duty-cycled radiofrequency ablation for atrial fibrillation**

Scharf C, Ng GA, Wieczorek M, Deneke T, Furniss SS, Murray S, Debruyne P, Hobson N, Berntsen RF, Schneider MA, Hauer HA\*, Halimi F, Boveda S, Asbach S, Boesche L, Zimmermann M, Brigadeau F, Taieb J, Merkel M, Pfyffer M, Brunner-La Rocca HP, Boersma LV

Europace. 2012 Dec;14(12):1700-7

**AIMS:** Duty-cycled radiofrequency ablation (RFA) has been used for atrial fibrillation (AF) for around 5 years, but large-scale data are scarce. The purpose of this survey was to report the outcome of the technique.

**METHODS AND RESULTS:** A survey was conducted among 20 centres from seven European countries including 2748 patients (2128 with paroxysmal and 620 with persistent AF). In paroxysmal AF an overall success rate of 82% [median 80%, interquartile range (IQR) 74-90%], a first procedure success rate of 72% [median 74% (IQR 59-83%)], and a success of antiarrhythmic medication of 59% [median 60% (IQR 39-72%)] was reported. In persistent AF, success rates were significantly lower with 70% [median 74% (IQR 60-92%)] ( $P = 0.05$ ) as well as the first procedure success rate of 58% [median 55% (IQR 47-81%)] ( $P = 0.001$ ). The overall success rate was similar among higher and lower volume centres and were not dependent on the duration of experience with duty-cycled RFA ( $r = -0.08$ ,  $P = 0.72$ ). Complications were observed in 108 (3.9%) patients, including 31 (1.1%) with symptomatic transient ischaemic attack or stroke, which had the same incidence in paroxysmal and persistent AF (1.1 vs. 1.1%) and was unrelated to the case load ( $r = 0.24$ ,  $P = 0.15$ ), bridging anticoagulation to low molecular heparin, routine administration of heparin over the long sheath, whether a transoesophageal echocardiogram was performed in every patient or not and average procedure times.

**CONCLUSION:** Duty-cycled RFA has a self-reported success and complication rate similar to conventional RFA. After technical modifications a prospective registry with controlled data monitoring should be conducted to assess outcome.

*Impactfactor: 1.980*

## Helmes, HJ

### **Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

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*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

## Houthuizen P

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*Impactfactor: 14.156*

## Houthuizen P

### **Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death**

Houthuizen P\*, Garsse LA van, Poels TT, Jaegere P de, Boon RM van der, Swinkels BM, Berg JM ten, Kley F van der, Schalijs MJ, Baan J Jr, Cocchieri R, Brueren GR\*, Straten AH van\*, Heijer P den, Bentala M, Ommen V van, Kluijn J, Stella PR, Prins MH, Maessen JG, Prinzen FW

Circulation. 2012 Aug 7;126(6):720-8. Epub 2012 Jul 12

**BACKGROUND:** Transcatheter aortic valve implantation (TAVI) is a novel therapy for treatment of severe aortic stenosis. Although 30% to 50% of patients develop new left bundle-branch block (LBBB), its effect on clinical outcome is unclear.

**METHODS AND RESULTS:** Data were collected in a multicenter registry encompassing TAVI patients from 2005 until 2010. The all-cause mortality rate at follow-up was compared between patients who did and did not develop new LBBB. Of 679 patients analyzed, 387 (57.0%) underwent TAVI with the Medtronic CoreValve System and 292 (43.0%) with the Edwards SAPIEN valve. A total of 233 patients (34.3%) developed new LBBB. Median follow-up was 449.5 (interquartile range, 174-834) days in patients with and 450 (interquartile range, 253-725) days in patients without LBBB (P=0.90). All-cause mortality was 37.8% (n=88) in patients with LBBB and 24.0% (n=107) in patients without LBBB (P=0.002). By multivariate regression analysis, independent predictors of all-cause mortality were TAVI-induced LBBB (hazard ratio [HR], 1.54; confidence interval [CI], 1.12-2.10), chronic obstructive lung disease (HR, 1.56; CI, 1.15-2.10), female sex (HR, 1.39; CI, 1.04-1.85), left ventricular ejection fraction < 50% (HR, 1.38; CI, 1.02-1.86), and baseline creatinine (HR, 1.32; CI, 1.19-1.43). LBBB was more frequent after implantation of the Medtronic CoreValve System than after Edwards SAPIEN implantation (51.1% and 12.0%, respectively; P<0.001), but device type did not influence the mortality risk of TAVI-induced LBBB.

**CONCLUSIONS:** All-cause mortality after TAVI is higher in patients who develop LBBB than in patients who do not. TAVI-induced LBBB is an independent predictor of mortality.

*Impactfactor: 14.739*

## Houthuizen P

### **Left ventricular endocardial pacing in cardiac resynchronisation therapy: Moving from bench to bedside**

Bracke FA\*, Gelder BM van\*, Dekker LR\*, Houthuizen P\*, Woorst JF ter\*, Teijink JA\*

Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

*Voor abstract zie: Cardiologie - Bracke FA*

## Houthuizen P

### **Why permanent pacemaker implantation after transcatheter aortic valve implantation does not affect long-term clinical outcome**

Houthuizen P\*, Boon RM van der, Garsse LA, van, Prinzen FW, Jaegere P de

J Am Coll Cardiol. 2012 Dec 4;60(22):2339-40

*Impactfactor: 14.156*

**Koolen JJ**

**A randomized multicenter comparison of hybrid sirolimus-eluting stents with bioresorbable polymer versus everolimus-eluting stents with durable polymer in total coronary occlusion: rationale and design of the Primary Stenting of Occluded Native Coronary Arteries IV study**

Teeuwen K, Adriaenssens T, Branden BJ, Henriques JP, Schaaf RJ, Koolen JJ\*, Vermeersch PH, Bosschaert MA, Tijssen JG, Suttorp MJ

Trials. 2012 Dec 15;13(1):22012

**ABSTRACT:** **BACKGROUND:** Percutaneous recanalization of total coronary occlusion (TCO) was historically hampered by high rates of restenosis and reocclusions. The PRISON II trial demonstrated a significant restenosis reduction in patients treated with sirolimus-eluting stents compared with bare metal stents for TCO. Similar reductions in restenosis were observed with the second-generation zotarolimus-eluting stent and everolimus-eluting stent. Despite favorable anti-restenotic efficacy, safety concerns evolved after identifying an increased rate of very late stent thrombosis (VLST) with drugeluting stents (DES) for the treatment of TCO. Late malapposition caused by hypersensitivity reactions and chronic inflammation was suggested as a probable cause of these VLST. New DES with bioresorbable polymer coatings were developed to address these safety concerns. No randomized trials have evaluated the efficacy and safety of the new-generation DES with bioresorbable polymers in patients treated for TCO. **METHODS:** The prospective, randomized, single-blinded, multicenter, noninferiority PRISON IV trial was designed to evaluate the safety, efficacy, and angiographic outcome of hybrid sirolimus-eluting stents with bioresorbable polymers (Orsiro; Biotronik, Berlin, Germany) compared with everolimus-eluting stents with durable polymers (Xience Prime/Xpedition; Abbott Vascular, Santa Clara, CA, USA) in patients with successfully recanalized TCOs. In total, 330 patients have been randomly allocated to each treatment arm. Patients are eligible with estimated duration of TCO  $\geq$ 4 weeks with evidence of ischemia in the supply area of the TCO. The primary endpoint is insegment late luminal loss at 9-month follow-up angiography. Secondary angiographic endpoints include in-stent late luminal loss, minimal luminal diameter, percentage of diameter stenosis, in-stent and insegment binary restenosis and reocclusions at 9-month follow-up. Additionally, optical coherence tomography is performed in the first 60 randomized patients at 9 months to assess neointima thickness, percentage of neointima coverage, and stent strut malapposition and coverage. Personnel blinded to the allocated treatment will review all angiographic and optical coherence assessments. Secondary clinical endpoints include major adverse cardiac events, clinically driven target vessel revascularization, target vessel failure and stent thrombosis to 5-year clinical follow-up. An independent clinical event committee blinded to the allocated treatment will review all clinical events. Trial registration: Clinical Trials.gov: NCT01516723. Patient recruitment started in February 2012.

*Impactfactor: 2.496*

**Koolen JJ**

**Angiographic maximal luminal diameter and appropriate deployment of the everolimus-eluting bioresorbable vascular scaffold as assessed by optical coherence tomography: an ABSORB cohort B trial sub-study**

Gomez-Lara J, Diletti R, Brugaletta S, Onuma Y, Farooq V, Thuesen L, McClean D, Koolen J\*, Ormiston JA, Windecker S, Whitbourn R, Dudek D, Dorange C, Veldhof S, Rapoza R, Regar E, Garcia-Garcia HM, Serruys PW

EuroIntervention. 2012 Jun 20;8(2):214-24. Epub 2011 Oct 28

**Aims:** Bioresorbable vascular scaffolds (BVS) present different mechanical properties as compared to metallic platform stents. Therefore, the standard procedural technique to achieve appropriate deployment may differ. **Methods and results:** Fifty-two lesions treated with a 3x18 mm BVS were imaged with optical coherence tomography (OCT) post-implantation and screened for parameters suggesting non-optimal deployment. These included minimal scaffold area (minSA)<5 mm<sup>2</sup>, residual area stenosis (RAS)>20%, edge dissections, incomplete scaffold/strut apposition (ISA)>5% and scaffold pattern irregularities. The angiographic proximal and distal maximal lumen diameters (DMAX) were measured by quantitative coronary angiography. Based on the DMAX values, the population was divided into three groups: DMAX <2.5 mm (n=13), DMAX between 2.5-3.3 mm (n=30) and DMAX >3.3 mm (n=9). All three groups presented with similar pre-implantation angiographic characteristics except for the vessel size and were treated with similar balloon/artery ratios. The group with a DMAX <2.5 mm presented with a higher percentage of lesions with minSA <5 mm<sup>2</sup> (30.8% vs. 10.0% vs. 0%; p=0.08) and edge dissections (61.5% vs. 33.3% vs. 11.1%; p=0.05). Lesions with >5% of ISA were significantly higher in the group with DMAX >3.3 mm (7.7% vs. 36.7% vs. 66.7%; p=0.02). RAS >20% was similar between all groups (46.2 vs. 53.3 vs. 77.8%; p=0.47) and scaffold pattern irregularities were only documented in three cases. **Conclusions:** BVS implantation guided with quantitative angiography may improve the OCT findings of optimal deployment. The clinical significance of these angiographic and OCT findings warranted long term follow-up of larger cohort of patients.

*Impactfactor: 3.285*

**Koolen JJ**

**Circumferential evaluation of the neointima by optical coherence tomography after ABSORB bioresorbable vascular scaffold implantation: can the scaffold cap the plaque?**

Brugaletta S, Radu MD, Garcia-Garcia HM, Heo JH, Farooq V, Girasis C, van Geuns RJ, Thuesen L, McClean D, Chevalier B, Windecker S, Koolen J\*, Rapoza R, Miquel-Hebert K, Ormiston J, Serruys PW

Atherosclerosis. 2012 Mar;221(1):106-12. Epub 2011 Dec 13

**OBJECTIVE:** To quantify the circumferential healing process at 6 and 12 months following scaffold implantation.

**BACKGROUND:** The healing process following stent implantation consists of tissue growing on the top of and in the space between each strut. With the ABSORB bioresorbable vascular scaffold (BVS), the outer circumference of the scaffold is detectable by optical coherence tomography (OCT), allowing a more accurate and complete evaluation of the intra-scaffold neointima.

**METHODS:** A total of 58 patients (59 lesions), who received an ABSORB BVS 1.1 implantation and a subsequent OCT investigation at 6 (n=28 patients/lesions) or 12 (n=30 patients with 31 lesions) months follow-up were included in the analysis. The thickness of the neointima was

calculated circumferentially in the area between the abluminal side of the scaffold and the lumen by means of an automated detection algorithm. The symmetry of the neointima thickness in each cross section was evaluated as the ratio between minimum and maximum thickness.

RESULTS: The neointima area was not different between 6 and 12 months follow-up ( $1.57 \pm 0.42$  mm<sup>2</sup>) vs.  $1.64 \pm 0.77$  mm<sup>2</sup>);  $p=0.691$ ). No difference was also found in the mean thickness of the neointima (median [IQR]) between the two follow-up time points (210 m [180-260]) vs. 220 m [150-260];  $p=0.904$ ). However, the symmetry of the neointima thickness was higher at 12 than at 6 months followup (0.23 [0.13-0.28] vs. 0.16 [0.08-0.21],  $p=0.019$ ).

CONCLUSIONS: A circumferential evaluation of the healing process following ABSORB implantation is feasible, showing the formation of a neointima layer, that resembles a thick fibrous cap, known for its contribution to plaque stability.

*Impactfactor: 3.794*

## Koolen JJ

### **Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

## Koolen JJ

### **Endothelial-dependent vasomotion in a coronary segment treated by ABSORB everolimus-eluting bioresorbable vascular scaffold system is related to plaque composition at the time of bioresorption of the polymer: indirect finding of vascular reparative therapy?**

Brugaletta S, Heo JH, Garcia-Garcia HM, Farooq V, Geuns RJ van, Bruyne B de, Dudek D, Smits PC, Koolen J\*, McClean D, Dorange C, Veldhof S, Rapoza R, Onuma Y, Bruining N, Ormiston JA, Serruys PW

Eur Heart J. 2012 Jun;33(11):1325-33. Epub 2012 Apr 16

AIMS: To analyse the vasoreactivity of a coronary segment, previously scaffolded by the ABSORB bioresorbable vascular scaffold (BVS) device, in relationship to its intravascular ultrasound-virtual histology (IVUS-VH) composition and reduction in greyscale echogenicity of the struts. Coronary segments, transiently scaffolded by a polymeric device, may in the long-term recover a normal vasomotor tone. Recovery of a normal endothelial-dependent vasomotion may be enabled by scaffold bioresorption, composition of the underlying tissue, or a combination of both mechanisms.

METHODS AND RESULTS: All patients from the ABSORB Cohort A and B trials, who underwent a vasomotion test and IVUS-VH investigation at 12 and 24 months, were included. Acetylcholine (Ach) and nitroglycerin were used to test either the endothelial-dependent or -independent vasomotion of the treated segment. Changes in polymeric strut echogenicity-a surrogate for bioresorption-IVUS-VH composition of the tissue underneath the scaffold and their relationship with the pharmacologically induced vasomotion were all

evaluated. Overall, 26 patients underwent the vasomotion test (18 at 12 and 8 at 24 months). Vasodilatory response to Ach was quantitatively associated with larger reductions over time in polymeric strut echogenicity ( $y = -0.159x - 6.85$ ;  $r = -0.781$ ,  $P < 0.001$ ). Scaffolded segments with vasoconstriction to Ach had larger vessel areas ( $14.37 \pm 2.50$  vs.  $11.85 \pm 2.54$  mm<sup>2</sup>),  $P = 0.030$ ), larger plaque burden ( $57.31 \pm 5.96$  vs.  $49.09 \pm 9.10\%$ ,  $P = 0.018$ ), and larger necrotic core (NC) areas [ $1.39 (+1.14, +1.74)$  vs.  $0.78$  mm<sup>2</sup>) ( $+0.20, +0.98$ ),  $P = 0.006$ ] compared with those with vasodilation.

**CONCLUSION:** Vasodilatory response to Ach, in coronary segments scaffolded by the ABSORB BVS device, is associated with a reduction in echogenicity of the scaffold over time, and a low amount of NC. In particular, the latter finding resembles the behaviour of a native coronary artery not caged by an intracoronary device.

*Impactfactor: 10.478*

## **Koolen JJ**

### **First serial assessment at 6 months and 2 years of the second generation of absorb everolimus-eluting bioresorbable vascular scaffold: a multi-imaging modality study**

Ormiston JA, Serruys PW, Onuma Y, Geuns RJ van, Bruyne B de, Dudek D, Thuesen L, Smits PC, Chevalier B, McClean D, Koolen J\*, Windecker S, Whitbourn R, Meredith I, Dorange C, Veldhof S, Hebert KM, Rapoza R, Garcia-Garcia HM

Circ Cardiovasc Interv. 2012 Oct 1;5(5):620-32

**BACKGROUND:** Nonserial observations have shown this bioresorbable scaffold to have no signs of area reduction at 6 months and recovery of vasomotion at 1 year. Serial observations at 6 months and 2 years have to confirm the absence of late restenosis or unfavorable imaging outcomes.

**METHODS AND RESULTS:** The ABSORB trial is a multicenter single-arm trial assessing the safety and performance of an everolimus-eluting bioresorbable vascular scaffold. Forty-five patients underwent serial invasive imaging, such as quantitative coronary angiography, intravascular ultrasound, and optical coherence tomography at 6 and 24 months of follow-up. From 6 to 24 months, late luminal loss increased from  $0.16 \pm 0.18$  to  $0.27 \pm 0.20$  mm on quantitative coronary angiography, with an increase in neointima of  $0.68 \pm 0.43$  mm<sup>2</sup> on optical coherence tomography and  $0.17 \pm 0.26$  mm<sup>2</sup> on intravascular ultrasound. Struts still recognizable on optical coherence tomography at 2 years showed 99% of neointimal coverage with optical and ultrasonic signs of bioresorption accompanied by increase in mean scaffold area compared with baseline ( $0.54 \pm 1.09$  mm<sup>2</sup>) on intravascular ultrasound,  $P = 0.003$  and  $0.77 \pm 1.33$  m<sup>2</sup>) on optical coherence tomography,  $P = 0.016$ ). Two-year major adverse cardiac event rate was 6.8% without any scaffold thrombosis.

**CONCLUSIONS:** This serial analysis of the second generation of the everolimus-eluting bioresorbable vascular scaffold confirmed, at medium term, the safety and efficacy of the new device. **CLINICAL TRIAL REGISTRATION:** URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00856856.

*Impactfactor: 6.058*

**Koolen JJ**

**Head to head comparison of optical coherence tomography, intravascular ultrasound echogenicity and virtual histology for the detection of changes in polymeric struts over time: insights from the ABSORB trial**

Brugaletta S, Gomez-Lara J, Bruining N, Radu MD, Geuns RJ van, Thuesen L, McClean D, Koolen J\*, Windecker S, Whitbourn R, Oberhauser J, Rapoza R, Ormiston JA, Garcia-Garcia HM, Serruys PW

EuroIntervention. 2012 Jul 20;8(3):352-8. Epub. 2011 Dec 1

**Aims:** To analyse and to compare the changes in the various optical coherence tomography (OCT), echogenicity and intravascular ultrasound virtual histology (VH) of the everolimus-eluting bioresorbable scaffold (ABSORB) degradation parameters during the first 12 months after ABSORB implantation. In the ABSORB study, changes in the appearance of the ABSORB scaffold were monitored over time using various intracoronary imaging modalities. The scaffold struts exhibited a progressive change in their black core area by OCT, in their ultrasound derived grey level intensity quantified by echogenicity, and in their backscattering ultrasound signal, identified as "pseudo dense-calcium" (DC) by VH.

**Methods and results:** From the ABSORB Cohort B trial 35 patients had paired OCT, echogenicity and VH assessment at baseline and at six- (n=18) or 12-months follow-up (n=17). Changes in OCT strut core area, hyperechogenicity and VH-derived DC were analysed and compared at the various time points. At six months, the change (median[IQR]) in OCT strut core area was -7.2% (-14.0--0.9) (p=0.053), in hyperechogenicity -12.7% (-33.7--1.4) (p=0.048) and VH-DC 22.1% (-10.8--48.8) (p=0.102). At 12 months, all the imaging modalities showed a decrease in the various parameters considered (OCT: -12.2% [-17.5--1.9], p=0.093; hyperechogenicity -24.64% [-36.6--16.5], p=0.001; VHDC: -24.66% [-32.0--7.0], p=0.071). However, the correlation between the relative changes in these parameters was statistically poor (Spearman's rho <0.4).

**Conclusions:** OCT, echogenicity and VH were able to detect changes in the ABSORB scaffold struts, although the correlation between those changes was poor. This is likely due to the fact that each imaging modality interrogates different material properties on different length scales. Further studies are needed to explore these hypotheses.

*Impactfactor: 3.285*

**Koolen JJ**

**Vascular compliance changes of the coronary vessel wall after bioresorbable vascular scaffold implantation in the treated and adjacent segments**

Brugaletta S, Gogas BD, Garcia-Garcia HM, Farooq V, Girasis C, Heo JH, van Geuns RJ, de Bruyne B, Dudek D, Koolen JJ\*, Smits P, Veldhof S, Rapoza R, Onuma Y, Ormiston J, Serruys PW

Circ J. 2012;76(7):1616-23. Epub 2012 Apr 24

**BACKGROUND:** Implantation of a metallic prosthesis creates local stiffness with a subsequent mismatch in the compliance of the vessel wall, disturbances in flow and heterogeneous distribution of wall shear stress. Polymeric bioresorbable ABSORB scaffolds have less stiffness than metallic platform stents. We sought to analyze the mismatch in vascular compliance after ABSORB implantation and its long-term resolution with bioresorption.

**METHODS AND RESULTS:** A total of 83 patients from the ABSORB trials underwent palpography investigations (30 and 53 patients from ABSORB Cohorts A and B, respectively) to measure the compliance of the scaffolded and adjacent segments at various time points

(from pre-implantation up to 24 months). The mean of the maximum strain values was calculated per segment by utilizing the Rotterdam Classification (ROC) score and expressed as ROC/mm. Scaffold implantation lead to a significant decrease in vascular compliance (median [IQR]) at the scaffolded segment (from 0.37 [0.24 -0.45] to 0.14 [0.09-0.23],  $P < 0.001$ ) with mismatch in compliance in a paired analysis between the scaffolded and adjacent segments (proximal: 0.23 [0.12-0.34], scaffold: 0.12 [0.07-0.19], distal: 0.15 [0.05-0.26],  $P = 0.042$ ). This reported compliance mismatch disappears at short- and mid-term follow-up.

**CONCLUSIONS:** The ABSORB scaffold decreases vascular compliance at the site of scaffold implantation. A compliance mismatch is evident immediately post-implantation and in contrast to metallic stents disappears in the mid-term, likely leading to a normalization of the rheological behavior of the scaffolded segment..

*Impactfactor: 3.766*

## **Koolen JJ**

### **Vascular response of the segments adjacent to the proximal and distal edges of the ABSORB everolimus-eluting bioresorbable vascular scaffold: 6-month and 1-year follow-up assessment: a virtual histology intravascular ultrasound study from the first-in-man ABSORB cohort B trial**

Gogas BD, Serruys PW, Diletti R, Farooq V, Brugaletta S, Radu MD, Heo JH, Onuma Y, Geuns RJ van, Regar E, De Bruyne B, Chevalier B, Thuesen L, Smits PC, Dudek D, Koolen JJ\*, Windecker S, Whitbourn R, Miquel-Hebert K, Dorange C, Rapoza R, Garcia-Garcia HM, McClean D, Ormiston JA

JACC Cardiovasc Interv. 2012 Jun;5(6):656-65

**OBJECTIVES:** This study sought to investigate in vivo the vascular response at the proximal and distal edges of the second-generation ABSORB everolimus-eluting bioresorbable vascular scaffold (BVS).

**BACKGROUND:** The edge vascular response after implantation of the BVS has not been previously investigated.

**METHODS:** The ABSORB Cohort B trial enrolled 101 patients and was divided into B(1) (n = 45) and B (2) (n = 56) subgroups. The adjacent (5-mm) proximal and distal vessel segments to the implanted ABSORB BVS were investigated at either 6 months (B(1)) or 1 year (B(2)) with virtual histology intravascular ultrasound (VH-IVUS) imaging.

**RESULTS:** At the 5-mm proximal edge, the only significant change was modest constrictive remodelling at 6 months ( vessel cross-sectional area: -1.80% [-3.18; 1.30],  $p < 0.05$ ), with a tendency to regress at 1 year ( vessel cross-sectional area: -1.53% [-7.74; 2.48],  $p = 0.06$ ). The relative change of the fibrotic and fibrofatty (FF) tissue areas at this segment were not statistically significant at either time point. At the 5-mm distal edge, a significant increase in the FF tissue of 43.32% [-19.90; 244.28], ( $p < 0.05$ ) 1-year post-implantation was evident. The changes in dense calcium need to be interpreted with caution since the polymeric struts are detected as "pseudo" dense calcium structures with the VH-IVUS imaging modality.

**CONCLUSIONS:** The vascular response up to 1 year after implantation of the ABSORB BVS demonstrated some degree of proximal edge constrictive remodeling and distal edge increase in FF tissue resulting in nonsignificant plaque progression with adaptive expansive remodeling. This morphological and tissue composition behavior appears to not significantly differ from the behavior of metallic drug-eluting stents at the same observational time points.

*Impactfactor: 6.800*

## **Koolen JJ**

### **Vascular tissue reaction to acute malapposition in human coronary arteries: sequential assessment with optical coherence tomography**

Gutiérrez-Chico JL, Wykrzykowska J, Nüesch E, van Geuns RJ, Koch KT, Koolen JJ\*, di Mario C, Windecker S, Es GA van, Gobbens P, Jüni P, Regar E, Serruys PW  
Circ Cardiovasc Interv. 2012 Feb 1;5(1):20-9, S1-8. Epub 2012 Feb 7

**BACKGROUND:** The vascular tissue reaction to acute incomplete stent apposition (ISA) is not well known. The aim of this study was to characterize the vascular response to acute ISA in vivo and to look for predictors of incomplete healing.

**METHODS AND RESULTS:** Optical coherence tomography studies of 66 stents of different designs, implanted in 43 patients enrolled in 3 randomized trials, were analyzed sequentially after implantation and at 6 to 13 months. Seventy-eight segments with acute ISA were identified in 36 of the patients and matched with the follow-up study by use of fiducial landmarks. The morphological pattern of healing in the ISA segments was categorized as homogeneous, layered, crenellated, bridged, partially bridged, or bare, depending on the persistence of ISA and on the coverage. After 6 months, acute ISA volume decreased significantly, and 71.5% of the ISA segments were completely integrated into the vessel wall. Segments with acute ISA had higher risk of delayed coverage than well-apposed segments (relative risk 2.37, 95% confidence interval 2.01-2.78). Acute ISA size (estimated as ISA volume or maximum ISA distance per strut) was an independent predictor of ISA persistence and of delayed healing at follow-up.

**CONCLUSIONS:** Neointimal healing tends to reduce ISA, with the malapposed stent struts often integrated completely into the vessel wall, resulting in characteristic morphological patterns. Coverage of ISA segments is delayed with respect to well-apposed segments. The larger the acute ISA, the greater the likelihood of persistent malapposition at follow-up and delayed healing.

*Impactfactor: 6.058*

## **Krasznai K**

### **Variation of cardiac troponin I and T measured with sensitive assays in emergency department patients with noncardiac chest pain**

Scharnhorst V\*, Krasznai K\*, Veer M van 't\*, Michels RH\*  
Clin Chem. 2012 Aug;58(8):1208-14

*Voor abstract zie: Algemeen Klinisch Laboratorium - Scharnhorst V*

*Impactfactor: 7.905*

## **Meijer A**

### **Three-dimensional computed tomography overlay for pulmonary vein antrum isolation: Follow-up and clinical outcomes**

Voort PH van der\*, Stevenhagen J, Dekker LR\*, Bullens R, Meijer A\*

Neth Heart J. 2012 Aug;20(7-8):302-6. Epub 2012 Jun 1

*Voor abstract zie: Cardiologie - Voort PH van der*

*Impactfactor: 1.438*

**Michels HR**

**Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

**Michels HR**

**Variation of cardiac troponin I and T measured with sensitive assays in emergency department patients with noncardiac chest pain**

Scharnhorst V\*, Krasznai K\*, Veer M van 't\*, Michels RH\*

Clin Chem. 2012 Aug;58(8):1208-14

*Voor abstract zie: Algemeen Klinisch Laboratorium - Scharnhorst V*

*Impactfactor: 7.905*

**Nathoe MD**

**Decrease of the right ventricular electrogram amplitude in a Sprint Fidelis shock lead: a sign of lead malfunction?**

Gelder BM van \*, Nathoe R\*, Bracke FA\*

Europace. 2012 Dec;14(12):1758. Epub 2012 Jun 20

*Impactfactor: 1.980*

**Peels CH**

**Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

**Peels CH**

**Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events**

Verberkmoes NJ\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*, Peels CH\*, Straten AH van\*

Neth Heart J. 2012 May;20(5):193-6. Epub 2012 Feb 11

*Voor abstract zie: Cardiothoracale chirurgie - Verberkmoes NJ*

*Impactfactor: 1.438*

**Peels CH**

**Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den\*, Woorst JF ter\*, Elenbaas TW\*, Dantzig JM van\*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

*Voor abstract zie: Cardiothoracale chirurgie - Straten AH van*

*Impactfactor: 3.741*

**Pijls NH**

**Circadian and weekly variation and the influence of environmental variables in acute myocardial infarction**

Wijnbergen I\*, Veer M van 't\*, Pijls NH\*, Tijssen J

Neth Heart J. 2012 Sep;20(9):354-9

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 1.438*

**Pijls NH**

**Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

**Pijls NH**

**Fractional flow reserve is not associated with inflammatory markers in patients with stable coronary artery disease**

Sels JW\*, Elsenberg EH, Hoefer IE, Zonneveld AJ van, Kuiper J, Jukema JW, Pijls NH\*, Pasterkamp G

PLoS One. 2012;7(10):e46356 Epub 2012 Oct 16

*Voor abstract zie: Cardiologie - Sels JW*

*Impactfactor: --*

**Pijls NH**

**Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease**

De Bruyne B, Pijls NH\*, Kalesan B, Barbato E, Tonino PA\*, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF; FAME 2 Trial Investigators

N Engl J Med. 2012 Sep 13;367(11):991-1001

BACKGROUND: The preferred initial treatment for patients with stable coronary artery disease is the best available medical therapy. We hypothesized that in patients with functionally significant stenoses, as determined by measurement of fractional flow reserve

(FFR), percutaneous coronary intervention (PCI) plus the best available medical therapy would be superior to the best available medical therapy alone.

**METHODS:** In patients with stable coronary artery disease for whom PCI was being considered, we assessed all stenoses by measuring FFR. Patients in whom at least one stenosis was functionally significant (FFR,  $d$  0.80) were randomly assigned to FFR-guided PCI plus the best available medical therapy (PCI group) or the best available medical therapy alone (medical-therapy group). Patients in whom all stenoses had an FFR of more than 0.80 were entered into a registry and received the best available medical therapy. The primary end point was a composite of death, myocardial infarction, or urgent revascularization.

**RESULTS:** Recruitment was halted prematurely after enrollment of 1220 patients (888 who underwent randomization and 332 enrolled in the registry) because of a significant between-group difference in the percentage of patients who had a primary end-point event: 4.3% in the PCI group and 12.7% in the medical-therapy group (hazard ratio with PCI, 0.32; 95% confidence interval [CI], 0.19 to 0.53;  $P < 0.001$ ). The difference was driven by a lower rate of urgent revascularization in the PCI group than in the medical-therapy group (1.6% vs. 11.1%; hazard ratio, 0.13; 95% CI, 0.06 to 0.30;  $P < 0.001$ ); in particular, in the PCI group, fewer urgent revascularizations were triggered by a myocardial infarction or evidence of ischemia on electrocardiography (hazard ratio, 0.13; 95% CI, 0.04 to 0.43;  $P < 0.001$ ). Among patients in the registry, 3.0% had a primary end-point event.

**CONCLUSIONS:** In patients with stable coronary artery disease and functionally significant stenoses, FFR-guided PCI plus the best available medical therapy, as compared with the best available medical therapy alone, decreased the need for urgent revascularization. In patients without ischemia, the outcome appeared to be favorable with the best available medical therapy alone. (Funded by St. Jude Medical; ClinicalTrials.gov number, NCT01132495.)

*Impactfactor: 53.298*

## **Pijls NH**

### **Functional measurement of coronary stenosis**

Pijls NH\*, Sels JW\*

J Am Coll Cardiol. 2012 Mar 20;59(12):1045-57

Fractional flow reserve (FFR) is considered nowadays as the gold standard for invasive assessment of physiologic stenosis significance and an indispensable tool for decision making in coronary revascularization. Use of FFR in the catheterization laboratory accurately identifies which lesions should be stented and improves the outcome in most elective clinical and angiographic conditions. Recently, FFR has been upgraded to a class IA classification in multivessel percutaneous coronary intervention in the guidelines on coronary revascularization of the European Society of Cardiology. In this state-of-the-art paper, the basic concept of FFR and its application, characteristics, and use in several subsets of patients are discussed from a practical point of view.

*Impactfactor: 14.156*

**Pijls NH**

**Instantaneous wave-free ratio or fractional flow reserve without hyperemia: novelty or nonsense?**

Pijls NH\*, Veer M van 't\*, Oldroyd KG, Berry C, Fearon WF, Kala P, Bocek O, Witt N, De Bruyne B, Pyxaras S

J Am Coll Cardiol. 2012 May 22;59(21):1916-7; author reply 1917-8

Comment on: Development and validation of a new adenosine-independent index of stenosis severity from coronary wave-intensity analysis: results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) study. [J Am Coll Cardiol. 2012]

*Impactfactor: 14.156*

**Pijls NH**

**The impact of downstream coronary stenoses on fractional flow reserve assessment of intermediate left main disease**

Daniels DV, Veer M van 't\*, Pijls NH\*, Horst A van der, Yong AS, De Bruyne B, Fearon WF

JACC Cardiovasc Interv. 2012 Oct;5(10):1021-5

*Voor abstract zie: Cardiologie - Veer M van 't*

*Impactfactor: --*

**Pijls NH**

**The Impact of Sex Differences on Fractional Flow Reserve-Guided Percutaneous Coronary Intervention: A FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) Substudy**

Kim HS, Tonino PA\*, De Bruyne B, Yong AS, Tremmel JA, Pijls NH\*, Fearon WF; FAME Study Investigators

JACC Cardiovasc Interv. 2012 Oct;5(10):1037-42

*Voor abstract zie: Cardiologie - Tonino PA*

*Impactfactor: --*

**Pijls NH**

**Validation of Functional State of Coronary Tandem Lesions Using Computational Flow Dynamics**

Park SJ, Ahn JM, Pijls NH\*, Bruyne B de, Shim EB, Kim YT, Kang SJ, Song H, Lee JY, Kim WJ, Park DW, Lee SW, Kim YH, Lee CW, Park SW

Am J Cardiol. 2012 Dec 1;110(11):1578-84. Epub 2012 Aug 23

Functional lesion assessment for coronary tandem lesions and its clinical applications have not been thoroughly studied. The aim of this study was to test the hypothesis that the fractional flow reserve (FFR) gradient across an individual stenosis ( FFR) during pressure-wire pullback is a surrogate of the relative functional severity of each stenosis in coronary tandem lesions. For in vitro validation, computational flow dynamic modeling of coronary tandem lesion with various degree of stenosis was constructed. For clinical validation, a total of 52 patients (104 lesions) with coronary tandem lesions (2 stenoses along 1 coronary artery) were consecutively enrolled, and tailored stent procedures based on FFR was performed, at first treating the lesion with large FFR and then subsequently reassessing the FFR for the remaining lesion. The coronary stenosis was considered functionally significant and stenting was performed when the FFR of a lesion was  $\leq 0.80$ . Using in vitro

computational flow dynamic modeling, the lesion with the large FFR of the coronary tandem lesion was indicated as the lesion with the greater degree of simulated diameter stenosis. In the clinical cohort, 28 patients (53.8%) had only single-lesion treatment, and stent implantation for 28 lesions (26.9%) was deferred according to the proposed strategy. During the 9-month follow-up period, only 1 repeat revascularization occurred among the deferred lesions. In conclusion, for the treatment of coronary tandem lesions, FFR may be a useful index for prioritizing the treatment sequence and optimizing the stenting procedure. In this way, unnecessary stent implantation can be avoided, with the achievement of favorable functional and clinical outcomes.

*Impactfactor: 3.368*

### **Rademakers LM**

#### **Critical hand ischaemia after transradial cardiac catheterisation: an uncommon complication of a common procedure**

Rademakers LM\*, Laarman GJ

Neth Heart J. 2012 Sep;20(9):372-5

We describe a case of critical hand ischaemia after transradial cardiac catheterisation. The patient presented with hand ischaemia 5 days after transradial coronary angiography. Urgent angiography demonstrated radial artery occlusion with embolisation to the palmar arch and digital arteries. The ischaemia was refractory to an extensive thrombolytic regimen, and subsequently, the patient was referred to the vascular surgeon for urgent thrombectomy and patch angioplasty. The patient recovered slowly and no amputation was necessary, but complaints of right hand numbness and paresthesia of all digits remained.

*Impactfactor: 1.438*

### **Rademakers LM**

#### **Early double stent thrombosis associated with clopidogrel hyporesponsiveness**

Rademakers LM\*, Dewilde W\*, Kerkhof D van de\*

Neth Heart J. 2012 Jan;20(1):38-4. Epub 2011 May 21

A 57-year-old male patient without cardiovascular history suffered an acute myocardial infarction and underwent drug-eluting stent implantation in the left anterior descending artery. A few days later, the right coronary artery was also stented (drug-eluting stent). Three days later, he was re-admitted to our hospital in cardiogenic shock. Emergent coronary angiography showed total occlusion of both stents.

Platelet function analysis (PFA) showed attenuated platelet inhibition in response to clopidogrel treatment. The patient was the carrier of a loss-of-function polymorphism in the CYP2C19 gene, which has been associated with increased incidence of adverse thrombotic events. Antiplatelet therapy was switched to prasugrel and PFA revealed an adequate antiplatelet effect.

*Impactfactor: 1.438*

Sels JE

**Deep proteome profiling of circulating granulocytes reveals bactericidal/permeability-increasing protein as a biomarker for severe atherosclerotic coronary stenosis**

Bleijerveld OB, Wijten P, Cappadona S, McClellan EA, Polat AN, Raijmakers R, Sels JW\*, Colle L, Grasso S, Toorn HW van den, van Breukelen B, Stubbs A, Pasterkamp G, Heck AJ, Hoefler IE, Scholten A

J Proteome Res. 2012 Nov 2;11(11):5235-44. Epub 2012 Oct 11

Coronary atherosclerosis represents the major cause of death in Western societies. As atherosclerosis typically progresses over years without giving rise to clinical symptoms, biomarkers are urgently needed to identify patients at risk. Over the past decade, evidence has accumulated suggesting cross-talk between the diseased vasculature and cells of the innate immune system. We therefore employed proteomics to search for biomarkers associated with severe atherosclerotic coronary lumen stenosis in circulating leukocytes. In a two-phase approach, we first performed in-depth quantitative profiling of the granulocyte proteome on a small pooled cohort of patients suffering from chronic (sub)total coronary occlusion and matched control patients using stable isotope peptide labeling, two-dimensional LC-MS/MS and data-dependent decision tree fragmentation. Over 3000 proteins were quantified, among which 57 candidate biomarker proteins remained after stringent filtering. The most promising biomarker candidates were subsequently verified in the individual samples of the discovery cohort using label-free, single-run LC-MS/MS analysis, as well as in an independent verification cohort of 25 patients with total coronary occlusion (CTO) and 19 matched controls. Our data reveal bactericidal/permeability-increasing protein (BPI) as a promising biomarker for severe atherosclerotic coronary stenosis, being downregulated in circulating granulocytes of CTO patients.

*Impactfactor: 5.113*

Sels JE

**Fractional flow reserve is not associated with inflammatory markers in patients with stable coronary artery disease**

Sels JW\*, Elsenberg EH, Hoefler IE, Zonneveld AJ van, Kuiper J, Jukema JW, Pijls NH\*, Pasterkamp G

PLoS One. 2012;7(10):e46356 Epub 2012 Oct 16

**BACKGROUND:** Atherosclerosis is an inflammatory condition and increased blood levels of inflammatory biomarkers have been observed in acute coronary syndromes. In addition, high expression of inflammatory markers is associated with worse prognosis of coronary artery disease. The presence and extent of inducible ischemia in patients with stable angina has previously been shown to have strong prognostic value. We hypothesized that evidence of inducible myocardial ischemia by local lesions, as measured by fractional flow reserve (FFR), is associated with increased levels of blood based inflammatory biomarkers.

**METHODS:** Whole blood samples of 89 patients with stable angina pectoris and 16 healthy controls were analyzed. The patients with stable angina pectoris underwent coronary angiography and FFR of all coronary lesions. We analyzed plasma levels of cytokines IL-6, IL-8 and TNF- and membrane expression of Toll-like receptor 2 and 4, CD11b, CD62L and CD14 on monocytes and granulocytes as markers of inflammation. Furthermore, we quantified the severity of hemodynamically significant coronary artery disease by calculating Functional Syntax Score (FSS), an extension of the Syntax Score.

RESULTS: For the majority of biomarkers, we observed lower levels in the healthy control group compared with patients with stable angina who underwent coronary catheterization. We found no difference for any of the selected biomarkers between patients with a positive FFR ( $d < 0.75$ ) and negative FFR ( $> 0.80$ ). We observed no relationship between the investigated biomarkers and FSS.

CONCLUSION: The presence of local atherosclerotic lesions that result in inducible myocardial ischemia as measured by FFR in patients with stable coronary artery disease is not associated with increased plasma levels of IL-6, IL-8 and TNF- or increased expression of TLR2 and TLR4, CD11b, CD62L and CD14 on circulating leukocytes.

*Impactfactor: --*

## **Sels JE**

### **Functional measurement of coronary stenosis**

Pijls NH\*, Sels JW\*

J Am Coll Cardiol. 2012 Mar 20;59(12):1045-57

*Voor abstract zie: Cardiologie - Pijls NH*

*Impactfactor: 14.156*

## **Tonino WA**

### **Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease**

De Bruyne B, Pijls NH\*, Kalesan B, Barbato E, Tonino PA\*, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF; FAME 2 Trial Investigators

N Engl J Med. 2012 Sep 13;367(11):991-1001

*Voor abstract zie: Cardiologie - Pijls NH*

*Impactfactor: 53.298*

## **Tonino WA**

### **The impact of sex differences on fractional flow reserve-guided percutaneous coronary intervention: a FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) substudy**

Kim HS, Tonino PA\*, Bruyne B de, Yong AS, Tremmel JA, Pijls NH\*, Fearon WF; FAME Study Investigators

JACC Cardiovasc Interv. 2012 Oct;5(10):1037-42

OBJECTIVES: This study sought to evaluate the impact of sex differences on fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI).

BACKGROUND: The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study demonstrated that FFR-guided PCI improves outcomes compared with an angiography-guided strategy. The role of FFR-guided PCI in women versus men has not been evaluated.

METHODS: We analyzed 2-year data from the FAME study in the 744 men and 261 women with multivessel coronary disease, who were randomized to angiography- or FFR-guided PCI. Statistical comparisons based on sex were stratified by treatment method.

RESULTS: Although women were older and had significantly higher rates of hypertension than men did, there were no differences in the rates of major adverse cardiac events (20.3% vs. 20.2%,  $p = 0.923$ ) and its individual components at 2 years. FFR values were significantly higher in women than in men ( $0.75 \pm 0.18$  vs.  $0.71 \pm 0.17$ ,  $p = 0.001$ ). The proportion of

functionally significant lesions (FFR  $\leq$  0.80) was lower in women than in men for lesions with 50% to 70% stenosis (21.1% vs. 39.5%,  $p < 0.001$ ) and for lesions with 70% to 90% stenosis (71.9% vs. 82.0%,  $p = 0.019$ ). An FFR-guided strategy resulted in similar relative risk reductions for death, myocardial infarction, and repeat revascularization in men and in women. There were no interactions between sex and treatment method for any outcome variables.

**CONCLUSIONS:** In comparison with men, angiographic lesions of similar severity are less likely to be ischemia-producing in women. An FFR-guided PCI strategy is equally beneficial in women as it is in men.

*Impactfactor: --*

### **Veer M van 't**

#### **Circadian and weekly variation and the influence of environmental variables in acute myocardial infarction**

Wijnbergen I\*, Veer M van 't\*, Pijls NH\*, Tijssen J

Neth Heart J. 2012 Sep;20(9):354-9

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 1.438*

### **Veer M van 't**

#### **Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

*Voor abstract zie: Cardiologie - Wijnbergen I*

*Impactfactor: 6.800*

### **Veer M van 't**

#### **Instantaneous wave-free ratio or fractional flow reserve without hyperemia: novelty or nonsense?**

Pijls NH\*, Veer M van 't\*, Oldroyd KG, Berry C, Fearon WF, Kala P, Bocek O, Witt N, De Bruyne B, Pyxaras S

J Am Coll Cardiol. 2012 May 22;59(21):1916-7; author reply 1917-8

Comment on: Development and validation of a new adenosine-independent index of stenosis severity from coronary wave-intensity analysis: results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) study. [J Am Coll Cardiol. 2012]

*Impactfactor: 14.156*

**Veer M van 't**

**The impact of downstream coronary stenoses on fractional flow reserve assessment of intermediate left main disease**

Daniels DV, Veer M van 't\*, Pijls NH\*, Horst A van der, Yong AS, De Bruyne B, Fearon WF

JACC Cardiovasc Interv. 2012 Oct;5(10):1021-5

**OBJECTIVES:** The aim of this study was to assess the validity of measuring fractional flow reserve (FFR) of the left main (LM) coronary artery in the setting of concomitant left anterior descending (LAD) or left circumflex (LCX) stenoses.

**BACKGROUND:** The theoretical impact of a stenosis in the LAD on the FFR assessment of intermediate LM disease with the pressure wire in an unobstructed LCX is currently unknown.

**METHODS:** A previously validated in vitro model of the coronary circulation was used to create a fixed intermediate stenosis of the LM and a variable downstream LAD or LCX stenosis. The true LM FFR (FFR(LM true)), with no concomitant downstream disease, was compared to the apparent LM FFR (FFR (LM apparent)), with concomitant downstream disease measured with different degrees of LAD or LCX disease. Additionally, an equation based on a resistors model was derived to predict the effect of downstream stenosis on LM FFR (FFR(LM predicted)).

**RESULTS:** In the setting of isolated moderate LM disease (FFR  $0.72 \pm 0.08$ ), mild to moderate proximal LAD or LCX lesions did not significantly affect LM FFR. Lesions with a composite FFR (LM + downstream disease)  $e 0.65$  resulted in an FFR(LM apparent) that was not significantly different from FFR(LM true) ( $0.76 \pm 0.06$  vs.  $0.76 \pm 0.05$ ,  $p = 0.124$ ). Our equation for FFR(LM predicted) accurately modeled the effects of concomitant disease ( $r = 0.95$ ,  $p < 0.001$ ).

**CONCLUSIONS:** These data suggest that in the presence of proximal mild to moderate LAD or LCX disease, LM FFR can be reliably measured with the pressure wire placed in the uninvolved epicardial artery.

*Impactfactor: --*

**Veer M van 't**

**Variation of cardiac troponin I and T measured with sensitive assays in emergency department patients with noncardiac chest pain**

Scharnhorst V\*, Krasznai K\*, Veer M van 't\*, Michels RH\*

Clin Chem. 2012 Aug;58(8):1208-14

*Voor abstract zie: Algemeen Klinisch Laboratorium - Scharnhorst V*

*Impactfactor: 7.905*

**Vermeulen Windsant IC $\infty$**

**Blood transfusions increase circulating plasma free hemoglobin levels and plasma nitric oxide consumption: a prospective observational pilot study**

Vermeulen Windsant IC\*, Wit NC de, Sertorio JT, Beckers EA, Tanus-Santos JE, Jacobs MJ, Buurman WA

Crit Care. 2012 May 25;16(3):R95

**ABSTRACT:** Introduction: The increasing number of reports on the relation between transfusion of stored red blood cells (RBCs) and adverse patient outcome has sparked an intense debate on the benefits and risks of blood transfusions. Meanwhile, the pathophysiological mechanisms underlying this postulated relation remain unclear.

The development of hemolysis during storage might contribute to this mechanism by release of free hemoglobin (fHb), a potent nitric oxide (NO) scavenger, which may impair vasodilation and microcirculatory perfusion after transfusion. The objective of this prospective observational pilot study was to establish whether RBC transfusion results in increased circulating fHb levels and plasma NO consumption. In addition, the relation between increased fHb values and circulating haptoglobin, its natural scavenger, was studied.

**METHODS:** Thirty patients electively received 1 stored packed RBC unit (n = 8) or 2 stored packed RBC units (n = 22). Blood samples were drawn to analyze plasma levels of fHb, haptoglobin, and NO consumption prior to transfusion, and 15, 30, 60 and 120 minutes and 24 hours after transfusion. Differences were compared using Pearson's chi-square test or Fisher's exact test for dichotomous variables, or an independent-sample t test or Mann-Whitney U test for continuous data. Continuous, multiple-timepoint data were analyzed using repeated one-way analysis of variance or the Kruskal-Wallis test. Correlations were analyzed using Spearman or Pearson correlation.

**RESULTS:** Storage duration correlated significantly with fHb concentrations and NO consumption within the storage medium ( $r = 0.51$ ,  $P < 0.001$  and  $r = 0.62$ ,  $P = 0.002$ ). fHb also significantly correlated with NO consumption directly ( $r = 0.61$ ,  $P = 0.002$ ). Transfusion of 2 RBC units significantly increased circulating fHb and NO consumption in the recipient ( $P < 0.001$  and  $P < 0.05$ , respectively), in contrast to transfusion of 1 stored RBC unit. Storage duration of the blood products did not correlate with changes in fHb and NO consumption in the recipient. In contrast, pre-transfusion recipient plasma haptoglobin levels inversely influenced post-transfusion fHb concentrations.

**CONCLUSION:** These data suggest that RBC transfusion can significantly increase post-transfusion plasma fHb levels and plasma NO consumption in the recipient. This finding may contribute to the potential pathophysiological mechanism underlying the much-discussed adverse relation between blood transfusions and patient outcome. This observation may be of particular importance for patients with substantial transfusion requirements.

*Impactfactor: 4.607*

### **Vermeulen Windsant IC<sup>∞</sup>**

#### **Circulating intestinal fatty acid-binding protein as an early marker of intestinal necrosis after aortic surgery: a prospective observational cohort study**

Vermeulen Windsant IC\*, Hellenthal FA, Derikx JP, Prins MH, Buurman WA, Jacobs MJ, Schurink GW

Ann Surg. 2012 Apr;255(4):796-803

**OBJECTIVE:** This study evaluated the usefulness of plasma intestinal fatty-acid binding protein (IFABP) levels in the early identification of intestinal necrosis (IN) in patients undergoing different types of aortic surgery.

**BACKGROUND:** Intestinal compromise greatly contributes to postoperative adverse outcome. IN is the most detrimental form of intestinal compromise and is notoriously difficult to diagnose. IFABP is a small protein exclusively expressed by mature enterocytes and a promising marker of intestinal damage.

**METHODS:** Plasma IFABP concentrations were measured in blood samples taken perioperatively from 55 patients undergoing open thoracic or thoracoabdominal aneurysm repair [OR-TAA(A)], 25 patients undergoing conventional open abdominal aneurysm repair (OR-abdominal aortic aneurysm [AAA]), and 16 patients undergoing endovascular aneurysm repair (EVAR). Data were compared with perioperative changes in arterial pH and serum lactate levels.

RESULTS: IFABP levels increased in all patients undergoing OR-TAA(A) and OR-AAA reaching peak levels shortly after surgery;  $281 \pm 33$  to  $2,298 \pm 490$  pg/mL ( $P < 0.001$ ) and  $187 \pm 31$  to  $641 \pm 176$  pg/mL ( $P < 0.05$ ) respectively. IFABP levels were significantly higher in patients undergoing OR-TAA(A) ( $P < 0.001$ ). IFABP levels in EVAR patients remained at baseline concentrations throughout the study. Four patients [2 OR-AAA, 2 OR-TAA(A)] developed fatal postoperative intestinal ischemia on day 2 or 3. High levels of plasma IFABP at the end of surgery had 100% sensitivity and 98.1% specificity for the identification of patients developing IN. In OR-AAA patients, arterial pH and lactate levels were of additional discriminating value. Complete discrimination between patients with and without IN using plasma IFABP could be made on the first postoperative day.

CONCLUSIONS: Analysis of plasma IFABP levels is of additional value to other current plasma markers in the diagnosis of IN, and it enables early identification of patients with IN after aortic surgery days before clinical diagnosis.

*Impactfactor: 7.492*

### **Vermeulen Windsant IC<sup>∞</sup>**

#### **Hemolysis compromises nitric oxide-dependent vasodilatory responses in patients undergoing major cardiovascular surgery**

Hanssen SJ, Poll MC van de, Houben AJ, Vermeulen Windsant IC\*, Snoeijs MG, Bekers O, Buurman WA, Jacobs MJ

Thorac Cardiovasc Surg. 2012 Jun;60(4):255-61

BACKGROUND: The hemolytic products cell-free oxyhemoglobin (Fhb) and arginase-1 reduce nitric oxide (NO) bioavailability by scavenging NO and by degrading the NO precursor arginine to ornithine, respectively. In this study we evaluated the relevance of hemolysis to NO-dependent blood flow in patients undergoing cardiovascular surgery.

METHODS: Plasma Fhb, arginase-1, and amino acid concentrations were measured perioperatively. Forearm blood flow (FBF) responses to the intra-arterial administered NO-donor sodium nitroprusside (SNP) and the endothelium-dependent vasodilator acetylcholine (ACh) were measured by venous occlusion plethysmography.

RESULTS: When peak values plasma Fhb and arginase-1 were found, vascular dilatation to SNP, but not ACh, was significantly reduced compared with 1 day postoperatively, when Fhb had returned to baseline levels ( $p < 0.05$ ). Interestingly, plasma Fhb concentration was inversely correlated to FBF responses to SNP ( $r -0.93$ ,  $p < 0.001$ ). In contrast, the increase in arginase-1 was not biologically relevant as the ratio of plasma arginine to ornithine remained constant.

CONCLUSION: We conclude that hemolysis with concomitant release of Fhb during cardiovascular surgery is associated with impaired NO-dependent forearm blood flow.

*Impactfactor: 0.882*

### **Vermeulen Windsant IC<sup>∞</sup>**

#### **The impact of selective visceral perfusion on intestinal macrohemodynamics and microhemodynamics in a porcine model of thoracic aortic cross-clamping**

Kalder J, Keschenau P, Hanssen SJ, Greiner A, Vermeulen Windsant IC\*, Kennes LN, Tolba R, Prinzen FW, Buurman WA, Jacobs MJ, Koepffel TA

J Vasc Surg. 2012 Jul;56(1):149-58

INTRODUCTION: Despite its presumed effectiveness and clinical use, the physiology of selective visceral perfusion combined with distal aortic perfusion during open thoracoabdominal aortic surgery has not been characterized. Thus, the aim of this study was

to establish a translatable model of thoracic aortic-clamping to assess the effect of selective visceral perfusion with added distal aortic perfusion on local intestinal macrohemodynamics and microhemodynamics, intestinal histopathology, and markers of inflammation and intestinal damage.

**METHODS:** A thoracotomy was performed in 15 pigs, and the aorta was exposed, including the origins of celiac trunk and superior mesenteric artery. The animals were divided into three cohorts: control (I), thoracic aortic cross-clamping (II), and thoracic aortic cross-clamping with selective visceral perfusion plus distal aortic perfusion using extracorporeal circulation (III). Macrocirculatory and microcirculatory blood flow was assessed by transit time ultrasound volume flow measurements and fluorescent microspheres. Intestinal ischemia-reperfusion injury was determined by the analysis of perioperative intestinal fatty acid-binding protein (IFABP) and interleukin-8 (IL-8) levels and correlated with histopathologic changes.

**RESULTS:** Severe intestinal tissue injury and an inflammatory response were observed in cohort II compared with cohort III for IL-8 (38.2 vs 3.56 pg/mL;  $P = .04$ ). The procedure in cohort III resulted in a flow and pressure-associated intestinal hypoperfusion compared with cohort I in the superior mesenteric artery (mean blood pressure,  $24.1 \pm 10.4$  vs  $67.2 \pm 7.4$  mm Hg;  $P < .0001$ ; mean flow rates:  $353.3 \pm 133.8$  vs  $961.7 \pm 310.8$  mL/min;  $P < .0001$ ). This was paralleled in cohort III vs cohort I by a significant mucosal injury (IFABP,  $713 \pm 307.1$  vs  $170 \pm 115.4$  pg/mL;  $P = .014$ ) despite a profound recruitment of intestinal microcirculation ( $338\% \pm 206.7\%$  vs  $135\% \pm 123.7\%$ ;  $P = .05$ ).

**CONCLUSIONS:** This study reports a novel large-animal model of thoracic aortic cross-clamping that allows the study of visceral perfusion strategies. However, we demonstrated with IL-8 and IFABP measurements that thoracoabdominal aortic aneurysm surgery with selective visceral perfusion and distal aortic perfusion is superior to the clamp-and-sew technique, even though small intestinal tissue damage cannot be completely avoided by selective visceral perfusion and distal aortic perfusion. In any case, this model seems to be a platform to evaluate and optimize measures for gut wall protection.

*Impactfactor: 3.153*

## **Verstappen CC**

### **Een verbeterd protocol voor het voorkomen en behandelen van flebitis. Beter voor de patiënt en leerzaam voor de professionals**

Gorkum P van, Verstappen C\*

Verpleegkunde : Nederlands-Vlaams wetenschappelijk tijdschrift voor verpleegkundigen 2012; 3:6-12

*Impactfactor: --*

## **Voort PH van der**

### **Chronic Q fever: Review of the literature and a proposal of new diagnostic criteria**

Wegdam-Blans MC\*, Kampschreur LM, Delsing CE, Bleeker-Rovers CP, Sprong T, Kasteren ME van, Notermans DW, Renders NH, Bijlmer HA, Lestrade PJ, Koopmans MP, Nabuurs-Franssen MH, Oosterheert JJ; The Dutch Q fever Consensus Group

J Infect. 2012 Mar;64(3):247-259. Epub 2011 Dec 23

*Voor abstract zie: Pamm - Wegdam-Blans MC*

*Impactfactor: 4.126*

## **Voort PH van der**

### **Posttraumatic stress 18 months following cardioverter defibrillator implantation: shocks, anxiety, and personality**

Habibovic M\*, Broek KC van den, Alings M, Voort PH van der \*, Denollet J

Health Psychol. 2012 Mar;31(2):186-93

*Voor abstract zie: Cardiologie - Habibovic M*

*Impactfactor: 3.873*

## **Voort PH van der**

### **Three-dimensional computed tomography overlay for pulmonary vein antrum isolation: Follow-up and clinical outcomes**

Voort PH van der\*, Stevenhagen J, Dekker LR\*, Bullens R, Meijer A\*

Neth Heart J. 2012 Aug;20(7-8):302-6. Epub 2012 Jun 1

**BACKGROUND:** To facilitate the creation of circumferential lines in pulmonary vein (PV) antrum isolation, three-dimensional (3D) navigation systems are used widely. Alternatively, 3D reconstructions of the left atrium (LA) can be superimposed directly on fluoroscopy to guide ablation catheters and to mark ablation sites.

**METHODS:** In 71 atrial fibrillation patients circumferential PV ablation was performed. 3D reconstructions of the LA were derived from contrast cardiac-computed tomography and circumferential PV isolation was performed. In subsequent ablation procedures, veins were re-isolated, and defragmentation or linear lesions were performed if necessary.

**RESULTS:** Adequate 3D reconstructions were formed and registered to fluoroscopy in all patients. All veins, except 2 in one single patient, could be isolated, resulting in freedom of AF in 45 patients (63 %). In 19 patients a second procedure was performed, in which 2.7 in 3 patients a third procedure was performed. After follow-up of 15 with paroxysmal and 10 (67 %) with persistent AF were free of AF.

**CONCLUSIONS:** The results of 3D overlay for circumferential PV isolation are good, although the reconnection rate and need for subsequent ablations remains high, and the outcomes of this technique appear to be equivalent to other mapping techniques.

*Impactfactor: 1.438*

## **Wijnbergen I**

### **Circadian and weekly variation and the influence of environmental variables in acute myocardial infarction**

Wijnbergen I\*, Veer M van 't\*, Pijls NH\*, Tijssen J

Neth Heart J. 2012 Sep;20(9):354-9

**OBJECTIVES:** The aim of our study was to investigate the circadian and weekly variation and assess the influence of environmental variables on the occurrence of acute myocardial infarction (AMI).

**METHODS:** Our study population consisted of 2983 consecutive patients admitted with AMI between January 2006 and May 2008. Data were abstracted from hospital records and partially from an electronic database. In patients with a known time of onset of AMI, circadian variation was analysed. In all patients, weekly variation of onset of AMI was analysed. Information on daily mean temperature, sunny hours, rainy hours, maximal humidity and mean atmospheric pressure was obtained from the KNMI database and the influence of these environmental variables on the incidence of AMI was analysed.

**RESULTS AND CONCLUSION:** Incidence of AMI shows a circadian pattern with an increase in

occurrence during daylight. AMI occurs equally on each day of the week and no relation was found between environmental variables and the occurrence of AMI.

*Impactfactor: 1.438*

## **Wijnbergen I**

### **Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: the Eindhoven reperfusion study**

Wijnbergen I\*, Helmes H\*, Tijssen J\*, Brueren G\*, Peels K\*, Dantzig JM van\*, Veer M van 't\*, Koolen JJ\*, Pijls NH\*, Michels R\*

JACC Cardiovasc Interv. 2012 Mar;5(3):313-22

**OBJECTIVES:** The goal of this study was to demonstrate superiority of sirolimus-eluting stents (SES) over bare-metal stents (BMS) and of abciximab over no abciximab in primary percutaneous coronary intervention (PCI)

**BACKGROUND:** Drug-eluting stents (DES) are increasingly used in primary PCI, but the recommendations for use in primary PCI are based on a few randomized controlled trials with selected patients. The usefulness of abciximab in primary PCI is not established.

**METHODS:** Nine hundred seven patients referred to the Catharina Hospital were randomized to SES or BMS, and to abciximab or no abciximab in a prospective, randomized, open 2 × 2 factorial trial with blinded evaluation. Primary endpoint was major adverse cardiac and cerebrovascular events (MACCE), defined as the composite of death, myocardial infarction (MI), stroke, repeat revascularization, and bleeding at 1 year (stent arm) and the composite of death, target vessel MI, target vessel revascularization (TVR), and bleeding at 30 days (abciximab arm).

**RESULTS:** At 1 year, the rate of MACCE was lower in the SES arm (16.5% vs. 25.8%,  $p = 0.001$ ), mainly driven by less repeat revascularization (9.8% vs. 16.8%;  $p = 0.003$ ) and without influencing the cumulative incidence of death and MI (5.2% vs. 5.8%;  $p = 0.68$ ). At 30 days, the rate of the composite of death, target vessel MI, TVR, and bleeding was lower in the abciximab arm (8.2% vs. 12.4%,  $p = 0.04$ ), mainly driven by less TVR due to less stent thrombosis (1.2% vs. 7.4%,  $p < 0.001$ ). However, bleeding complications occurred more frequently in the abciximab group (5.7% vs. 2.8%,  $p = 0.03$ ).

**CONCLUSIONS:** Primary PCI with SES reduces adverse events at 1 year, mainly by reduction of repeat revascularization, whereas abciximab reduces early stent thrombosis, at the expense of more bleeding complications. (Comparison of Drug Eluting and Bare Metal Stents With or Without Abciximab in ST Elevation Myocardial Infarction [DEBATER]; NCT00986050).

*Impactfactor: 6.800*

\* = Werkzaam in het Catharina Ziekenhuis

∞ = Ten tijde van publicatie werkzaam bij: European Vascular Center Aachen-Maastricht, Department of Surgery, AZM University Hospital Maastricht

## **Cardiothoracale chirurgie**

## **Berrekouw E**

### **Inability to ventilate after tube exchange postoperative to pneumonectomy**

Verstraeten SE\*, Straten AH van\*, Korsten HH\*, Weber EW\*, Wielders PL\*, Berrekouw E\*

Case Rep Anesthesiol. 2012;2012:801093. Epub 2012 Apr 5

Voor abstract zie: *Cardiothoracale chirurgie - Verstraeten SE*

Impactfactor: --

## **Boxtel AG van**

### **Perioperative serum aspartate aminotransferase level as a predictor of survival after coronary artery bypass grafting**

Boxtel AG van\*, Bramer S\*, Soliman Hamad MA\*, Straten AH van\*

Ann Thorac Surg. 2012 Nov;94(5):1492-8. Epub 2012 Jul 26

**BACKGROUND:** Elevated cardiac enzymes after coronary artery bypass grafting (CABG) surgery have been identified as a risk factor for worse postoperative outcome. Cardiac enzymes play an important role in the diagnosis of perioperative myocardial infarction. This study aims to investigate the predictive value of aspartate aminotransferase (AST) with respect to early and late mortality after CABG.

**METHODS:** Patients undergoing isolated CABG in a single center between January 1998 and December 2010 were prospectively enrolled in our database. Patients were arbitrarily divided into 4 groups according to the postoperative AST level: group 1 (AST < 50 U/L), group 2 (AST = 51 to 100 U/L), group 3 (AST = 101 to 200 U/L), group 4 (AST = 201 to 300 U/L), and group 5 (AST > 300 U/L). The impact of biomedical variables on early mortality was determined using univariate and multivariate logistic regression analyses. Risk factors for late mortality were identified using Cox proportional hazard regression analyses.

**RESULTS:** The study population consisted of 13,505 patients who underwent isolated CABG. Postoperative AST level was identified as a risk factor for early (odds ratio = 3.6 [2.5 to 5.4],  $p < 0.0001$ ) and late mortality (hazard ratio = 1.4 [1.2 to 1.7],  $p < 0.001$ ). After correction for other risk factors, AST level was an independent predictor of worse survival.

**CONCLUSIONS:** Elevated postoperative AST level is an independent predictor of early and late mortality after CABG. Although it is not a specific indicator for cardiac damage, it can reflect ischemic effects on the other organs as an indirect sign of depressed cardiac function.

Impactfactor: 3.741

## **Bramer S**

### **Perioperative serum aspartate aminotransferase level as a predictor of survival after coronary artery bypass grafting**

Boxtel AG van\*, Bramer S\*, Soliman Hamad MA\*, Straten AH van\*

Ann Thorac Surg. 2012 Nov;94(5):1492-8. Epub 2012 Jul 26

Voor abstract zie: *Cardiothoracale chirurgie - Boxtel AG van*

Impactfactor: 3.741

## **Elenbaas TW**

### **A rare case of diffuse mitral valve fibroelastoma**

Jonge M de\*, Straten A van\*, Dantzig JM van\*, Merrienboer F van\*, Elenbaas T\*

Ann Thorac Surg. 2012 Aug;94(2):e53

Impactfactor: 3.741

## **Elenbaas TW**

### **Can the EuroSCORE predict midterm survival after aortic valve replacement?**

Koene BM\*, Straten AH van\*, Geldorp MW van\*, Woorst JF ter\*, Elenbaas TW\*, Soliman Hamad MA\*

J Cardiothorac Vasc Anesth. 2012 Aug;26(4):617-23. Epub 2012 Mar 8

Voor abstract zie: *Cardiothoracale chirurgie - Koene BM*

Impactfactor: 1.640

## **Elenbaas TW**

### **Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter\*, Korsten EH\*, Borne BE van den\*, Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72. Epub 2012 May 25

Voor abstract zie: *Cardiothoracale chirurgie - Ponten JE*

Impactfactor: --

## **Elenbaas TW**

### **Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den\*, Woorst JF ter\*, Elenbaas TW\*, Dantzig JM van\*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

Voor abstract zie: *Cardiothoracale chirurgie - Straten AH van*

Impactfactor: 3.741

## **Geldorp MW van**

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Koene BM\*, Straten AH van\*, Geldorp MW van\*, Woorst JF ter\*, Elenbaas TW\*, Soliman Hamad MA\*

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Voor abstract zie: *Cardiothoracale chirurgie - Koene BM*

Impactfactor: 1.640

## **Jonge M de**

### **A rare case of diffuse mitral valve fibroelastoma**

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Ann Thorac Surg. 2012 Aug;94(2):e53

Impactfactor: 3.741

## **Koene BM**

### **Can the EuroSCORE predict midterm survival after aortic valve replacement?**

Koene BM\*, Straten AH van\*, Geldorp MW van\*, Woorst JF ter\*, Elenbaas TW\*, Soliman Hamad MA\*

J Cardiothorac Vasc Anesth. 2012 Aug;26(4):617-23. Epub 2012 Mar 8

OBJECTIVES: The EuroSCORE as a predictor for midterm survival after isolated aortic valve replacement (AVR) and combined AVR with coronary artery bypass graft (CABG) surgery was

tested. Survival in different risk-stratification groups also was compared to the survival of the general Dutch population.

DESIGN: A retrospective analysis of prospectively collected data.

SETTING: A single-center study performed in an educational hospital.

PARTICIPANTS: All patients (N = 1,652) who underwent AVR with (n = 711) or without (n = 941) CABG surgery from January 2004 through December 2009.

INTERVENTIONS: AVR with or without CABG surgery.

MEASUREMENTS AND MAIN RESULTS: Univariate Cox regression analyses were used to identify the additive and the logistic EuroSCOREs as independent predictors of midterm mortality. Kaplan-Meier survival curves were used to compare the survival of different patients' risk subgroups, based on both the additive and the logistic EuroSCOREs, with the normal Dutch population matched for age and sex.

Both additive and logistic EuroSCOREs were significant predictors of midterm mortality after isolated AVR and AVR with CABG surgery. This was also true for the different risk-stratification groups. Except for survival after AVR with CABG surgery in the high-risk group based on the additive EuroSCORE, no difference was found between survival after surgery and survival of the age- and sex-matched normal population.

CONCLUSIONS: Both EuroSCORE models can predict midterm survival after isolated AVR and combined AVR with CABG surgery. However, the EuroSCORE is not a predictor for midterm survival when comparing the patient groups with the general Dutch population matched for age and sex. Except for high-risk patients undergoing AVR with CABG surgery, other risk subgroups have similar midterm survival to that of their age- and sex-matched cohorts of the Dutch population.

*Impactfactor: 1.640*

## **Ozdemir HI**

### **Use of extended radial artery conduit for complete arterial revascularization**

Ozdemir HI\*, Soliman Hamad MA\*, Ter Woorst JF\*, Straten AH van\*

Interact Cardiovasc Thorac Surg. 2012 Jun;14(6):714-6. Epub 2012 Feb 27

We have developed a new technique to elongate the radial artery (RA) with the distal segment of the left internal thoracic artery (LITA). The left anterior descending (LAD) artery is examined to define the site of the LITA-LAD anastomosis and the length of LITA required to perform the anastomosis. The distal segment of the LITA beyond this length is divided in order to elongate the RA. This extended conduit is long enough to perform complete arterial revascularization and to reach the ascending aorta for the proximal anastomosis. Between January 1998 and December 2010, 113 patients were operated on using this technique. There was no early mortality among the whole group. Two patients (1.8%) had perioperative myocardial infarction. Three patients (3.5%) had re-interventions. We conclude that this technique makes the optimal use of both arterial conduits and could be a valuable alternative option for patients who are selected for complete arterial revascularization.

*Impactfactor: --*

**Ponten JE**

**Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter\*, Korsten EH\*, Borne BE van den\*, Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72 Epub 2012 May 25

Cardiac herniation after pneumonectomy is recognized as a rare complication. This case report describes two cases. The mortality rate of this complication remains high as reported in the literature; in early-recognized cases 50 % and in late or unrecognized cases 100 %. In the following two cases a pneumonectomy was performed as a treatment for lung cancer. Within 48 h after the initial operative treatment, the clinical situation of the patients got worse and radiographic examinations showed a strongly deviated heart. After suspicion of the diagnosis, the patients were immediately transferred to the operation theatre for emergency thoracotomy. Per-operative the diagnosis was confirmed and the heart was returned into its original position while the defect in the pericardial sac was closed with a bovine pericardial patch. Both patients survived these procedures and did not suffer from any further complication.

*Impactfactor: --*

**Salah K**

**Evolution of cerebral perfusion techniques in type a aortic dissection surgery: a single center experience**

Salah K\*, Straten AH van\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*

Perfusion. 2012 Sep;27(5):363-70. Epub 2012 May 18

BACKGROUND: The purpose of this study was to investigate the effect of using antegrade selective cerebral perfusion (ASCP) with moderate hypothermia on hospital mortality after surgery for acute type A aortic dissection (AAAD).

METHODS: Between January 1998 and December 2008, 142 consecutive patients were operated on for AAAD. Patients were divided into two subgroups: the cohort of patients operated on from January 1998 until December 2003 (without ASCP) (P1998-2003, n=64) and the cohort operated on from January 2004 until December 2008 (with ASCP)(P2004-2008, n=78). RESULTS: The difference in hospital mortality was statistically significant (P1998-2003: 42.2%; P2004 -2008: 14.1%,  $p < 0.0005$ ). Survival rates were  $51.6 \pm 6.2\%$  vs.  $75.1 \pm 5.5\%$  and  $45.9 \pm 6.2\%$  vs.  $69.7 \pm 7.3\%$  for one and four years, respectively ( $p = 0.001$ ). Multivariate logistic regression analysis revealed that ASCP was the only independent protective factor of hospital mortality ( $p = 0.047$ ).

CONCLUSION: In patients operated on for AAAD, antegrade selective cerebral perfusion with moderate hypothermia is a significant factor in decreasing hospital mortality.

*Impactfactor: 0.918*

**Schonberger JP**

**Prophylactic treatment with alkaline phosphatase in cardiac surgery induces endogenous alkaline phosphatase release**

Kats S, Brands R, Soliman Hamad MA\*, Seinen W, Scharnhorst V\*, Wulkan RW, Schönberger JP\*, Oeveren W van

Int J Artif Organs. 2012 Feb;35(2):144-51

Voor abstract zie: Cardiothoracale chirurgie - Soliman Hamad MA

*Impactfactor: 1.861*

**Soliman Hamad MA**

**Can the EuroSCORE predict midterm survival after aortic valve replacement?**

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Perfusion. 2012 Sep;27(5):363-70. Epub 2012 May 18

*Voor abstract zie: Cardiothoracale chirurgie - Salah K*

*Impactfactor: 0.918*

**Soliman Hamad MA**

**Fast-track practice in cardiac surgery: results and predictors of outcome**

Haanschoten MC\*, Straten AH van\*, Woorst JF ter\*, Stepaniak PS, Meer AD van der\*, Zundert AA van\*, Soliman Hamad MA\*

Interact Cardiovasc Thorac Surg. 2012 Dec;15(6):989-94. Epub 2012 Sep 5

*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*Impactfactor: --*

**Soliman Hamad MA**

**Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events**

Verberkmoes NJ\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*, Peels CH\*, Straten AH van\*

Neth Heart J. 2012 May;20(5):193-6. Epub 2012 Feb 11

*Voor abstract zie: Cardiothoracale chirurgie - Verberkmoes NJ*

*Impactfactor: 1.438*

**Soliman Hamad MA**

**Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den\*, Woorst JF ter\*, Elenbaas TW\*, Dantzig JM van\*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

*Voor abstract zie: Cardiothoracale chirurgie - Straten AH van*

*Impactfactor: 3.741*

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#### **Perioperative serum aspartate aminotransferase level as a predictor of survival after coronary artery bypass grafting**

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Kats S, Brands R, Soliman Hamad MA\*, Seinen W, Scharnhorst V\*, Wulkan RW, Schönberger JP\*, Oeveren W van

Int J Artif Organs. 2012 Feb;35(2):144-51

**INTRODUCTION:** Laboratory and clinical data have implicated endotoxin as an important factor in the inflammatory response to cardiopulmonary bypass. We assessed the effects of the administration of bovine intestinal alkaline phosphatase (bIAP), an endotoxin detoxifier, on alkaline phosphatase levels in patients undergoing coronary artery bypass grafting.

**METHODS:** A total of 63 patients undergoing coronary artery bypass grafting were enrolled and prospectively randomized. Bovine intestinal alkaline phosphatase (n=32) or placebo (n=31) was administered as an intravenous bolus followed by continuous infusion for 36 hours. The primary endpoint was to evaluate alkaline phosphatase levels in both groups and to find out if administration of bIAP to patients undergoing CABG would lead to endogenous alkaline phosphatase release. **RESULTS:** No significant adverse effects were identified in either group. In all the 32 patients of the bIAP-treated group, we found an initial rise of plasma alkaline phosphatase levels due to bolus administration ( $464.27 \pm 176.17$  IU/L). A significant increase of plasma alkaline phosphatase at 4-6 hours postoperatively was observed ( $354.97 \pm 95.00$  IU/L) as well. Using LHA inhibition, it was shown that this second peak was caused by the generation of tissue non specific alkaline phosphatase (TNSALP-type alkaline phosphatase). **CONCLUSIONS:** Intravenous bolus administration plus 8 hours continuous infusion of alkaline phosphatase in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass results in endogenous alkaline phosphatase release. This endogenous alkaline phosphatase may play a role in the immune defense system.

*Impactfactor: 1.861*

### **Soliman Hamad MA**

#### **Results of one-hundred and seventy patients after elective Bentall operation**

Verbakel KM\*, Straten AH van\*, Hamad MA\*, Tan ES\*, Woorst JF ter\*

Asian Cardiovasc Thorac Ann. 2012 Aug;20(4):418-25.

*Voor abstract zie: Cardiothoracale chirurgie - Verbakel KM*

*Impactfactor: --*

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*Voor abstract zie: Cardiothoracale chirurgie - Ozdemir HI*

*Impactfactor: --*

**Straten AH van**

**A pulmonary shadow after lobectomy: an unexpected diagnosis**

Crijns K\*, Jansen FH\*, Straten AH van\*, Borne BE van den\*

Neth J Med. 2012 Jun;70(5):232, 235

*Impactfactor: 2.072*

**Straten AH van**

**A rare case of diffuse mitral valve fibroelastoma**

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*Voor abstract zie: Cardiothoracale chirurgie - Koene BM*

*Impactfactor: 1.640*

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*Impactfactor: --*

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**Straten AH van**

**Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events**

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Impactfactor: 1.438

**Straten AH van**

**Inability to ventilate after tube exchange postoperative to pneumonectomy**

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Case Rep Anesthesiol. 2012;2012:801093. Epub 2012 Apr 5

Voor abstract zie: *Cardiothoracale chirurgie - Verstraeten SE*

Impactfactor: --

**Straten AH van**

**Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den \*, Woorst JF ter \*, Elenbaas TW\*, Dantzig JM van\*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

**BACKGROUND:** Following guidelines, aortic valve replacement (AVR) in asymptomatic patients with severe aortic valve stenosis is often postponed until symptoms do occur. Delaying AVR will inevitably lead to progression of left ventricular hypertrophy. We studied the relationship between septum wall thickness indexed for body surface area (SWTI) as a measure for LV hypertrophy and 30-day and late all-cause mortality after AVR.

**METHODS:** This study included the data of adult patients who underwent isolated AVR between January 2006 and December 2010 and in whom a reliable measurement of the septum wall thickness could be made. The patients were stratified into three groups according to their SWTI. The SWTI was less than 6 mm/m<sup>2</sup> in 136 patients, between 6 and 8 mm/m<sup>2</sup> in 307 patients, and more than 8 mm/m<sup>2</sup> in 126 patients.

**RESULTS:** Death occurred in 10 patients within 30 days (1.8%), and 41 patients died during follow-up (7.2%). Univariate logistic regression analysis revealed only endocarditis as predictor of early mortality. Multivariate Cox regression analyses revealed SWTI as a continuous variable as well as a categorical (group) variable to be a predictor of late mortality. Compared with the group SWTI less than 6 mm/m<sup>2</sup>, odds ratio for the group with SWTI 6 to 8 mm/m<sup>2</sup> was 3.4 (p = 0.046), and for the group with SWTI more than 8 mm/m<sup>2</sup>, it was 6.0 (p = 0.005).

**CONCLUSIONS:** In patients undergoing AVR, the SWTI was a strong predictor of late mortality. Whether avoidance of progression of left ventricular hypertrophy by early AVR leads to better outcome remains to be investigated.

Impactfactor: 3.741

**Straten AH van**

**Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death**

Houthuizen P\*, Garsse LA van, Poels TT, Jaegere P de, Boon RM van der, Swinkels BM, Berg JM ten, Kley F van der, SchaliJ MJ, Baan J Jr, Cocchieri R, Brueren GR\*, Straten AH van\*, Heijer P den, Bentala M, Ommen V van, Kluin J, Stella PR, Prins MH, Maessen JG, Prinzen FW

Circulation. 2012 Aug 7;126(6):720-8. Epub 2012 Jul 12

*Voor abstract zie: Cardiologie - Houthuizen P*

*Impactfactor: 14.739*

**Straten AH van**

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*Impactfactor: 3.741*

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*Voor abstract zie: Cardiothorale chirurgie - Ozdemir HI*

*Impactfactor: --*

**Tan ME**

**Clinical evaluation of the Sorin Xtra(R) Autotransfusion System**

Overdevest EP\*, Lanen PW,\* Feron JC\*, Hees JW van\*, Tan ME\*

Perfusion. 2012 Jul;27(4):278-83. Epub 2012 Mar 29

*Voor abstract zie: ECC - Overdevest EP*

*Impactfactor: 0.918*

**Tan ME**

**Evolution of cerebral perfusion techniques in type a aortic dissection surgery: a single center experience**

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*Voor abstract zie: CTC - Salah K*

*Impactfactor: 0.918*

## **Tan ME**

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*Voor abstract zie: Cardiothoracale chirurgie - Verberkmoes NJ*

*Impactfactor: 1.438*

## **Tan ME**

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*Voor abstract zie: Cardiothoracale chirurgie - Verbakel KM*

*Impactfactor: --*

## **Verbakel KM**

### **Results of one-hundred and seventy patients after elective Bentall operation**

Verbakel KM\*, Straten AH van\*, Hamad MA\*, Tan ES\*, Woorst JF ter\*

Asian Cardiovasc Thorac Ann. 2012 Aug;20(4):418-25

The aim of this study was to evaluate the short and long-term operative results of patients who underwent a Bentall procedure in a 12-year period. We retrospectively analyzed the data of 170 patients who underwent an elective Bentall procedure between January 1998 and July 2010. All pre- and perioperative variables were entered into a multivariate regression model to identify significant predictors of early and late mortality. The early mortality rate was 11.2% (19/170 patients). Multivariate logistic regression analysis identified prior cardiac operation and cardiopulmonary bypass time as independent risk factors for early mortality, with odds ratios of 5.75 (95% confidence interval: 1.850-17.874;  $p=0.003$ ) and 1.011 (95% confidence interval: 1.003-1.019;  $p=0.008$ ), respectively. The Kaplan-Meier curve shows an overall survival of 78%±4% at 5 years and 66%±10% at 10 years. Cox regression analysis revealed no independent risk factors for late mortality. The Bentall procedure is still the procedure of choice for aortic root replacement. Improvements in perioperative management in recent years has improved the early outcome, and in our experience, the late results of this technique were satisfactory.

*Impactfactor: --*

## **Verberkmoes NJ**

### **Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events**

Verberkmoes NJ\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*, Peels CH\*, Straten AH van\*

Neth Heart J. 2012 May;20(5):193-6. Epub 2012 Feb 11

**BACKGROUND:** The impact of meteorological conditions on the occurrence of various cardiovascular events has been reported internationally. Data about the Dutch situation are limited.

**OBJECTIVES:** We sought to find out a correlation between weather conditions and the incidence of major acute cardiovascular events such as type A acute aortic dissection (AAD),

acute myocardial infarction (AMI) and acutely presented abdominal aortic aneurysms (AAAA).

**METHODS:** Between January 1998 and February 2010, patients who were admitted to our hospital (Catharina Hospital, Eindhoven, the Netherlands) because of AAD (n AAAA (n by the Royal Dutch Meteorological Institute (KNMI) over the same period.

**RESULTS:** During the study period, a total number of 11,412 patients were admitted with AMI, 212 patients with AAD and 1593 patients with AAAA. A significant correlation was found between the daily temperature and the number of hospital admissions for AAD. The lower the daily temperature, the higher the incidence of AAD (p incidence of AMI (p of AAAA.

**CONCLUSIONS:** Cold weather is correlated with a higher incidence of AAD and AMI.

*Impactfactor: 1.438*

### **Verstraeten SE**

#### **Inability to ventilate after tube exchange postoperative to pneumonectomy**

Verstraeten SE\*, Straten AH van\*, Korsten HH\*, Weber EW\*, Wielders PL\*, Berreklouw E\*

Case Rep Anesthesiol. 2012;2012:801093. Epub 2012 Apr 5

We report a case of inability to ventilate a patient after completion of pneumonectomy, due to migrated tumor tissue to the contralateral side. This represents an unusual complication with a high mortality rate. We have managed to find the cause in time and were able to remove the obstructive tissue using bronchoscopy.

*Impactfactor: --*

### **Woorst FJ ter**

#### **Can the EuroSCORE predict midterm survival after aortic valve replacement?**

Koene BM\*, Straten AH van\*, Geldorp MW van\*, Woorst JF ter\*, Elenbaas TW\*, Soliman Hamad MA\*

J Cardiothorac Vasc Anesth. 2012 Aug;26(4):617-23. Epub 2012 Mar 8

*Voor abstract zie: Cardiothoracale chirurgie - Koene BM*

*Impactfactor: 1.640*

### **Woorst FJ ter**

#### **Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter\*, Korsten EH\*, Borne BE van den\*, Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72 Epub 2012 May 25

*Voor abstract zie: Cardiothoracale chirurgie - Ponten JE*

*Impactfactor: --*

### **Woorst FJ ter**

#### **David procedure during a reoperation for ongoing chronic Q fever infection of an ascending aortic prosthesis**

Wegdam-Blans MC\*, Woorst JF ter\*, Klompenhouwer EG\*, Teijink JA\*.

Eur J Cardiothorac Surg. 2012 Jul;42(1):e19-20. Epub 2012 May 24

*Voor abstract zie: Pamm - Wegdam-Blans MC*

*Impactfactor: 2.550*

**Woorst FJ ter****Evolution of cerebral perfusion techniques in type a aortic dissection surgery: a single center experience**

Salah K\*, Straten AH van\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*  
Perfusion. 2012 Sep;27(5):363-70. Epub 2012 May 18

*Voor abstract zie: CTC - Salah K*

*Impactfactor: 0.918*

**Woorst FJ ter****Fast-track practice in cardiac surgery: results and predictors of outcome**

Haanschoten MC\*, Straten AH van\*, Woorst JF ter\*, Stepaniak PS,  
Meer AD van der\*, Zundert AA van\*, Soliman Hamad MA\*  
Interact Cardiovasc Thorac Surg. 2012 Dec;15(6):989-94. Epub 2012 Sep 5

*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*Impactfactor: --*

**Woorst FJ ter****Impact of temperature and atmospheric pressure on the incidence of major acute cardiovascular events**

Verberkmoes NJ\*, Soliman Hamad MA\*, Woorst JF ter\*, Tan ME\*, Peels CH\*,  
Straten AH van\*

Neth Heart J. 2012 May;20(5):193-6. Epub 2012 Feb 11

*Voor abstract zie: Cardiothoracale chirurgie - Verberkmoes NJ*

*Impactfactor: 1.438*

**Woorst FJ ter****Increased septum wall thickness in patients undergoing aortic valve replacement predicts worse late survival**

Straten AH van\*, Soliman Hamad MA\*, Peels KC\*, Broek KC van den\*, Woorst JF ter\*,  
Elenbaas TW\*, Dantzig JM van \*

Ann Thorac Surg. 2012 Jul;94(1):66-71. Epub 2012 May 16

*Voor abstract zie: Cardiothoracale chirurgie - Straten AH van*

*Impactfactor: 3.741*

**Woorst FJ ter****Left ventricular endocardial pacing in cardiac resynchronisation therapy: Moving from bench to bedside**

Bracke FA\*, Gelder BM van\*, Dekker LR\*, Houthuizen P\*, Woorst JF ter\*, Teijink JA\*  
Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

*Voor abstract zie: Cardiologie - Bracke FA*

*Impactfactor: 1.438*

**Woorst FJ ter**

**Results of one-hundred and seventy patients after elective Bentall operation**

Verbakel KM\*, Straten AH van\*, Hamad MA\*, Tan ES\*, Woorst JF ter\*

Asian Cardiovasc Thorac Ann. 2012 Aug;20(4):418-25

*Voor abstract zie: Cardiothoracale chirurgie - Verbakel KM*

*Impactfactor: --*

**Woorst FJ ter**

**Use of extended radial artery conduit for complete arterial revascularization**

Ozdemir HI\*, Soliman Hamad MA\*, Woorst JF ter\*, Straten AH van\*

Interact Cardiovasc Thorac Surg. 2012 Jun;14(6):714-6. Epub 2012 Feb 27

*Voor abstract zie: Cardiothorale chirurgie - Ozdemir HI*

*Impactfactor: --*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Chirurgie**

**Bendermacher BL**

**Applicability of the ankle-brachial-index measurement as screening device for high cardiovascular risk: an observational study**

Bendermacher BL\*, Teijink JA\*, Willigendael EM\*, Bartelink ML, Peters RJ, Langenberg M, Büller HR, Prins MH

BMC Cardiovasc Disord. 2012 Jul 30;12:59

**BACKGROUND:** Screening with ankle-brachial index (ABI) measurement could be clinically relevant to avoid cardiovascular events in subjects with asymptomatic atherosclerosis. To assess the practical impact of guidelines regarding the use of ABI as a screening tool in general practice, the corresponding number needed to screen, including the required time investment, and the feasibility of ABI performance, was assessed.

**METHODS:** An observational study was performed in the setting of 955 general practices in the Netherlands. Overall, 13,038 subjects of e 55 years presenting with symptoms of intermittent claudication and/or presenting with e one vascular risk factor were included. Several guidelines recommend the ABI as an additional measurement in selected populations for risk assessment for cardiovascular morbidity.

**RESULTS:** Screening of the overall population of e 50 years results in H 862 subjects per general practice who should be screened, resulting in a time-requirement of approximately 6 weeks of full time work. Using an existing clinical prediction model, 247 patients per general practice should be screened for PAD by ABI measurement.

**CONCLUSION:** Screening the entire population of e 50 years will in our opinion not be feasible in general practice. A more rationale and efficient approach might be screening of subsets of the population of e 55 years based on a clinical prediction model.

*Impactfactor: 1.517*

**Bendermacher BL**

**EVAR reintervention management strategies in contemporary practice**

Bendermacher BL\*, Stokmans R\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Aug;53(4):411-8

It is known that following an endovascular aneurysm repair (EVAR) procedure, patients may experience endoleaks, device migration, stent fractures, graft deterioration, or aneurysm growth that might require a reintervention. In this review management strategies of reinterventions after EVAR in contemporary practice will be discussed. The current endovascular treatment options of Type I endoleak involve securing of the attachment site with percutaneous transluminal balloon angioplasty, stent-graft extension, or placement of a stent at the proximal attachment site. Moreover, the use of endostaples to secure the position of the proximal cuff to the primary endograft have been developed. Type II endoleaks can be managed conservatively if the aneurysm is shrinking or remains stable. Otherwise, reinterventions include transarterial embolization, translumbar embolization, transcaval embolization, direct thrombin injection, and endoscopic or open ligation of the lumbar and mesenteric arteries. There is little debate regarding the treatment of type III endoleaks, including deployment of additional stent graft components to bridge the defect. Endovascular treatment of endotension includes endovascular conversion stent or relining of the stent graft. Alternative options are puncture of the aneurysm sac and removal of the aneurysm sac content. In case of migration large balloon-expandable stents can be used to improve the seal between the components, or devices that deploy staples to secure endovascular grafts to the aortic wall to secure endovascular components together.

In conclusion, the first treatment options for reinterventions after EVAR are catheter based nowadays.

*Impactfactor: 1.559*

## **Berende CA**

### **Laparoscopic Sleeve Gastrectomy Feasible for Bariatric Revision Surgery**

Berende CA\*, Zoete JP de\*, Smulders JF\*, Nienhuijs SW\*

Obes Surg. 2012 Feb;22(2):330-4. Epub 2011 Aug 25

Bariatric revision surgery is associated with several complications that can be attributed to decreased quality of tissue and complexity of the surgery. A laparoscopic sleeve gastrectomy is a simple technique with potential advantages. Therefore, the results of this procedure were evaluated as a revisional option. Fifty-one patients underwent laparoscopic sleeve gastrectomy (LSG). Indications for the LSG were insufficient weight loss (34 patients, group 1) or vomiting (17 patients, group 2) following a laparoscopic adjustable gastric banding (LAGB) or vertical banded gastroplasty (VBG). Patient and procedure characteristics as well as outcome were collected prospectively. From October 2006 to June 2010, 51 patients with a failed prior bariatric procedure (VBG or LAGB) were converted to (L)SG. The conversion rate was zero. The median procedure time was 99 min (range 54-221) and hospital stay was 3 days (range 2-38). There was no mortality after 30 days. Complications included bleeding (six) and leakage of the staple line (seven). Mean follow-up was 13.8 (2-46) months. LSG as revision surgery for insufficient weight loss resulted in extra weight loss of 52.7%, and the overall extra weight loss was 49.3%. When LSG was performed because of vomiting, 82% was able to eat solid food at follow-up. Of the 65 pre-existent co-morbidities, 21 were resolved and 18 improved. LSG as a revision procedure is feasible. An additional weight loss and further resolution of co-morbidity seem achievable, however, at the cost of a high number of complications. Therefore, revision bariatric surgery should be limited to expert tertiary bariatric centers.

*Impactfactor: 3.286*

## **Brinkman WM**

### **Criterion-based laparoscopic training reduces total training time**

Brinkman WM\*, Buzink SN\*, Alevizos L, Hingh IH de\*, Jakimowicz JJ\*

Surg Endosc. 2012 Apr;26(4):1095-101. Epub 2011 Nov 1

**INTRODUCTION:** The benefits of criterion-based laparoscopic training over time-oriented training are unclear. The purpose of this study is to compare these types of training based on training outcome and time efficiency.

**METHODS:** During four training sessions within 1 week (one session per day) 34 medical interns (no laparoscopic experience) practiced on two basic tasks on the Symbionix LAP Mentor virtual-reality (VR) simulator: 'clipping and grasping' and 'cutting'. Group C (criterion-based) (N = 17) trained to reach predefined criteria and stopped training in each session when these criteria were met, with a maximum training time of 1 h. Group T (time-based) (N = 17) trained for a fixed time of 1 h each session. Retention of skills was assessed 1 week after training. In addition, transferability of skills was established using the Haptica ProMIS augmented-reality simulator.

**RESULTS:** Both groups improved their performance significantly over the course of the training sessions (Wilcoxon signed ranks,  $P < 0.05$ ). Both groups showed skill transferability and skill retention. When comparing the performance parameters of group C and group T, their performances in the first, the last and the retention training sessions did not differ significantly (Mann-Whitney U test,  $P > 0.05$ ). The average number of repetitions needed to

meet the criteria also did not differ between the groups. Overall, group C spent less time training on the simulator than did group T (74:48 and 120:10 min, respectively;  $P < 0.001$ ). Group C performed significantly fewer repetitions of each task, overall and in session 2, 3 and 4.

**CONCLUSIONS:** Criterion-based training of basic laparoscopic skills can reduce the overall training time with no impact on training outcome, transferability or retention of skills. Criterion-based should be the training of choice in laparoscopic skills curricula.

*Impactfactor: 4.013*

## **Brinkman WM**

### **Novice surgeons versus experienced surgeons in laparoendoscopic single-site (LESS) surgery: a comparison of performances in a surgical simulator**

Alevizos L, Brinkman W\*, Fingerhut A, Jakimowicz J\*, Leandros E

World J Surg. 2012 May;36(5):939-44

**INTRODUCTION:** During the past years, there has been increasing interest in simulation-based training of technical skills especially in laparoscopy. The purpose of this study was to compare the performances of novice and experienced laparoscopic surgeons on a LESS simulator.

**METHODS:** The study recruited 20 surgeons classified into two groups: group NS consisted of ten residents without any laparoscopic experience, and group ES consisted of ten surgeons with experience in conventional laparoscopy (performed >90 laparoscopic cholecystectomies) but without any experience in LESS surgery. Both groups completed a mini-trainee course that included four repetitions of a standardized task of circle pattern cutting (CIRCLE). Time, path length, and economy of movement were measured and compared.

**RESULTS:** Group ES presented significantly better time scores than group NS in all four repetitions. Economy of movement did not differ significantly between the two groups, whereas path length was shorter for beginners at the forth effort. Moreover, group ES failed to improve path length and economy of movement scores, whereas group NS improved their performance significantly in these parameters.

**CONCLUSIONS:** It seems that previous laparoscopic experience in conventional laparoscopy may not necessarily be an advantage in all parameters of LESS surgery and the learning process can be longer than expected even for experienced surgeons.

*Impactfactor: 2.362*

## **Buth J**

### **The influence of smoking on endovascular abdominal aortic aneurysm repair**

Koole D, Moll FL, Buth J\*, Hobo R\*, Zandvoort H, Pasterkamp G, Herwaarden JA van; EUROSTAR collaborators

J Vasc Surg. 2012 Jun;55(6):1581-6. Epub 2012 Feb 9

**OBJECTIVES:** The main purpose of this study was to evaluate the influence of smoking on perioperative outcomes of endovascular aneurysm repair (EVAR), aneurysm sac behavior, abdominal aortic aneurysm (AAA) neck growth after EVAR, and its effect on stent graft migration during follow-up.

**METHODS:** Baseline characteristics and follow-up data were collected prospectively by patient record forms. Follow-up visits were scheduled at 1, 3, 6, 12, 18, and 24 months, and annually thereafter and included a clinical examination and imaging studies. Patients were stratified in three groups according to their smoking status as nonsmokers, former smokers, and smokers.

RESULTS: This study analyzed the data for 4176 nonsmokers, 2406 former smokers, and 2056 smokers who were enrolled prospectively in the European Collaborators on Stent-Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) database. Compared with nonsmokers, smokers required more percutaneous transluminal angioplasty and stent placements during EVAR ( $P < .001$ ) and stent graft migration occurred more often (hazard ratio, 1.45; 95% confidence interval, 1.03-2.05;  $P = .033$ ). Nonsmokers had more late type II endoleaks than former smokers and smokers (58.5%, 55.9%, and 35.5%, respectively;  $P < .001$ ). Smoking had no effect on aneurysm sac behavior or AAA neck growth after EVAR.

CONCLUSIONS: Smokers need more percutaneous transluminal angioplasty procedures and stents during EVAR. They have fewer late type II endoleaks during follow-up; however, smokers should be closely monitored because they have an increased risk of stent graft migration.

*Impactfactor: 3.153*

## **Buzink SN**

### **Criterion-based laparoscopic training reduces total training time**

Brinkman WM\*, Buzink SN\*, Alevizos L, Hingh IH de\*, Jakimowicz JJ\*

Surg Endosc. 2012 Apr;26(4):1095-101. Epub 2011 Nov 1

*Voor abstract zie: Chirurgie - Brinkman WM*

*Impactfactor: 4.013*

## **Buzink SN**

### **Laparoscopic Surgical Skills programme: preliminary evaluation of Grade I Level 1 courses by trainees**

Buzink S\*, Soltes M, Radonak J, Fingerhut A, Hanna G, Jakimowicz J\*

Wideochir Inne Tech Malo Inwazyjne. 2012 Aug;7(3):188-92

INTRODUCTION: New training models are needed to maintain safety and quality of surgical performance. A simulated setting using virtual reality, synthetic, and/or organic models should precede traditional supervised training in the operating room.

AIM: The aim of the paper is to describe the Laparoscopic Surgical Skills (LSS) programme and to provide information about preliminary evaluation of Grade I Level 1 courses, including overall quality, applicability of the course content in practice and the balance between theory and hands-on training modules, by participating trainees.

MATERIAL AND METHODS: During 5 accredited LSS Grade I Level 1 courses held in Eindhoven (the Netherlands), Kosice (Slovak Republic), and Lisbon (Portugal) between April 2011 and January 2012, demographic data and pre-course surgical experience in laparoscopic surgery of the participants were recorded. The final course evaluation form was completed by each participant after the course (anonymous) to evaluate course progress, course materials, assessment, staff, location and overall impression of the course on a 1-10 scale to obtain feedback information.

RESULTS: Forty-seven surgeons of 5 different nationalities were enrolled in an LSS Grade I Level 1 programme. Most participants were first or second year residents ( $n = 25$ ), but also already established surgeons took part ( $n = 6$ ). The mean age of the participants was 31.2 years ( $SD = 2.86$ ), the male/female ratio was 32/15, and previous experience with laparoscopic surgery was limited. Overall impression of the course was rated with 8.7 points ( $SD = 0.78$ ). The applicability of the course content in practice and the balance between theory and hands-on training were also rated very well - mean 8.8 ( $SD = 1.01$ ) and 8.1 points ( $SD = 0.80$ ) respectively.

CONCLUSIONS: Laparoscopic Surgical Skills Grade I Level 1 courses are evaluated as well balanced, with content applicable in clinical practice, meeting the expectations of individual participants. International interest in the programme suggests that LSS might become the future European standard in surgical education in laparoscopic surgery. Further conclusions concerning success of the programme may be drawn after the completion of clinical assessment of enrolled participants.

*Impactfactor:--*

### **Cuypers Ph W**

#### **EVAR reintervention management strategies in contemporary practice**

Bendermacher BL\*, Stokmans R\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*  
J Cardiovasc Surg (Torino). 2012 Aug;53(4):411-8

*Voor abstract zie: Chirurgie - Bendermacher BL*

*Impactfactor: 1.559*

### **Cuypers Ph W**

#### **No differences in perioperative outcome between symptomatic and asymptomatic AAAs after EVAR: an analysis from the ENGAGE Registry**

Stokmans RA\*, Teijink JA\*, Cuypers PW\*, Riambau V, Sambeek MR van\*  
Eur J Vasc Endovasc Surg. 2012 Jun;43(6):667-73. Epub 2012 Mar 21

*Voor abstract zie: Chirurgie - Stokmans RA*

*Impactfactor: 2.991*

### **Cuypers Ph W**

#### **Systematic approach to ruptured abdominal aortic aneurysm in the endovascular era: Intention-to-treat eEVAR protocol**

Willigendael EM\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*  
J Cardiovasc Surg (Torino). 2012 Feb;53(1):77-82

*Voor abstract zie: Chirurgie - Willigendael EM*

*Impactfactor: 1.559*

### **Dalen HC van**

#### **Supervised exercise therapy for intermittent claudication: current status and future perspectives**

Lauret GJ\*, Dalen DC van\*, Willigendael EM\*, Hendriks EJ, Bie RA de, Spronk S, Teijink JA\*

Vascular. 2012 Feb;20(1):12-9. Epub 2012 Feb 10

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: 0.891*

### **Dalen HC van**

#### **When is supervised exercise therapy considered useful in peripheral arterial occlusive disease? A nationwide survey among vascular surgeons**

Lauret GJ\*, Dalen HC van\*, Hendriks HJ, Sterkenburg SM van, Koelemay MJ, Zeebregts CJ, Peters RJ, Teijink JA\*

Eur J Vasc Endovasc Surg. 2012 Mar;43(3):308-12. Epub 2012 Jan 10

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: --*

## **Dudink RL**

### **Focus on extralevator perineal dissection in supine position for low rectal cancer has led to better quality of surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D,\* Nieuwenhuijzen GA\*,  
Lijnschoten I van\*, Martijn H, Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P,  
Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Dudink RL**

### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*,  
Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 2.499*

## **Dudink RL**

### **T3+ and T4 Rectal Cancer Patients Seem to Benefit From the Addition of Oxaliplatin to the Neoadjuvant Chemoradiation Regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*,  
Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de,  
Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Fokkenrood HJ**

### **Multidisciplinary treatment for peripheral arterial occlusive disease and the role of eHealth and mHealth**

Fokkenrood HJ\*, Lauret GJ\*, Scheltinga MR, Spreeuwenberg C, Bie RA de, Teijink JA

J Multidiscip Healthc. 2012;5:257-63 Epub 2012 Oct 8

Increasingly unaffordable health care costs are forcing care providers to develop economically viable and efficient health care plans. Currently, only a minority of all newly diagnosed peripheral arterial occlusive disease (PAOD) patients receive efficient and structured conservative treatment for their disease. The aim of this article is to introduce an innovative effective treatment model termed ClaudicatioNet. This concept was launched in The Netherlands as a means to combat treatment shortcomings and stimulate cohesion and collaboration between stakeholders. The overall goal of ClaudicatioNet is to stimulate quality and transparency of PAOD treatment by optimizing multidisciplinary health care chains on a national level. Improved quality is based on stimulating both a theoretical and practical knowledge base, while eHealth and mHealth technologies are used to create clear insights of provided care to enhance quality control management, in addition these technologies can be used to increase patient empowerment, thereby increasing efficacy of PAOD treatment. This online community consists of a web portal with public and personal

information supplemented with a mobile application. By connecting to these tools, a social community is created where patients can meet and keep in touch with fellow patients, while useful information for supervising health care professionals is provided. The ClaudicatioNet concept will likely create more efficient and cost-effective PAOD treatment by improving the quality of supervised training programs, extending possibilities and stimulating patient empowerment by using eHealth and mHealth solutions. A free market principle is introduced by introducing transparency to provided care by using objective and subjective outcome parameters. Cost-effectiveness can be achieved using supervised training programs, which may substitute for or postpone expensive invasive vascular interventions.

*Impactfactor: --*

### **Geldorp MW van**

#### **Clinical course of patients diagnosed with severe aortic stenosis in the Rotterdam area: insights from the AVARIJN study**

Heuvelman HJ, Geldorp MW van\*, Kappetein AP, Geleijnse ML, Galema TW, Bogers AJ, Takkenberg JJ

Neth Heart J. 2012 Dec;20(12):487-93

**OBJECTIVE:** To prospectively evaluate the clinical course of patients with severe aortic stenosis (AS) and identify factors associated with treatment selection and patient outcome.

**METHODS:** Patients diagnosed with severe AS in the Rotterdam area were included between June 2006 and May 2009. Patient characteristics, echocardiogram, brain natriuretic peptide (NT-proBNP), and treatment strategy were assessed at baseline, and after 6, 12, and 24 months. Endpoints were aortic valve replacement (AVR) / transcatheter aortic valve implantation (TAVI) and death.

**RESULTS:** The study population comprised 191 patients, 132 were symptomatic and 59 asymptomatic at study entry. Two-year cumulative survival of symptomatic patients was 89.8 % (95 % CI 79.8-95.0 %) after AVR/TAVI and 72.6 % (95 % CI 59.7-82.0 %) with conservative treatment. Two-year cumulative survival of asymptomatic patients was 91.5 % (95 % CI 80.8-96.4 %). Two-year cumulative incidence of AVR/TAVI was 55.9 % (95 % CI 47.5-63.5 %) in symptomatic patients. Sixty-eight percent of asymptomatic patients developed symptoms, median time to symptoms was 13 months; AVR/TAVI cumulative incidence was 38.3 % (95 % CI 23.1-53.3 %). Elderly symptomatic patients with multiple comorbidities were more likely to receive conservative treatment.

**CONCLUSIONS:** In contemporary Dutch practice many symptomatic patients do not receive invasive treatment of severe AS. Two-thirds of asymptomatic patients develop symptoms within 2 years, illustrating the progressive nature of severe AS. Treatment optimisation may be achieved through careful individualised assessment in a multidisciplinary setting.

*Impactfactor: 1.438*

### **Geldorp MW van**

#### **Progression of aortic valve stenosis in adults: a systematic review**

Heuvelman HJ, Geldorp MW van\*, Eijkemans MJ, Rajamannan NM, Bogers AJ, Roos-Hesselink JW, Takkenberg JJ

J Heart Valve Dis. 2012 Jul;21(4):454-62

Published reports on the progression of aortic valve stenosis (AS) over time are usually small, with widely varying AS progression rate estimates. Reliable estimates of AS progression are important for surveillance scheduling and optimal timing of surgical or interventional treatment. This systematic review presents an overview of published evidence on AS progression over time in adult patients with AS.

**METHODS:** A systematic review using PubMed and Embase was performed to assess AS progression over time in adult patients with AS measured by echocardiography. A total of 27 reports (15 prospective, 12 retrospective, total 4,921 patients, pooled age 69 years) was included in which the baseline and progression rates of the hemodynamic variables were pooled. Subgroup analyses were performed to investigate factors associated with AS progression and sources of heterogeneity.

**RESULTS:** Pooled annual AS progression was 3.70 mmHg per year (SE = 0.10) for randomized controlled trials, and 6.03 mmHg per year (SE = 0.10) for observational studies. A large variability in observed AS progression was found between studies, as well as a wide variety of methods employed to measure AS.

**CONCLUSION:** The observed large individual variability in measuring AS progression among the selected studies calls for the implementation of a universal method of AS assessment. This will facilitate an insight into the determinants of AS progression and allow for an evidence-based tailoring of treatment.

*Impactfactor: 0.811*

### **Grossmann I**

#### **Evaluation of the use of decision-support software in carcino-embryonic antigen (CEA)-based follow-up of patients with colorectal cancer**

Verberne CJ, Nijboer CH, Bock GH de, Grossmann I\*, Wiggers T, Havenga K

BMC Med Inform Decis Mak. 2012 Mar 5;12:14

**BACKGROUND:** The present paper is a first evaluation of the use of "CEAwatch", a clinical support software system for surgeons for the follow-up of colorectal cancer (CRC) patients. This system gathers Carcino-Embryonic Antigen (CEA) values and automatically returns a recommendation based on the latest values.

**METHODS:** Consecutive patients receiving follow-up care for CRC fulfilling our in- and exclusion criteria were identified to participate in this study. From August 2008, when the software was introduced, patients were asked to undergo the software-supported follow-up. Safety of the follow-up, experiences of working with the software, and technical issues were analyzed.

**RESULTS:** 245 patients were identified. The software-supported group contained 184 patients; the control group contained 61 patients. The software was safe in finding the same amount of recurrent disease with fewer outpatient visits, and revealed few technical problems. Clinicians experienced a decrease in follow-up workload of up to 50% with high adherence to the follow-up scheme.

**CONCLUSION:** CEAwatch is an efficient software tool helping clinicians working with large numbers of follow-up patients. The number of outpatient visits can safely be reduced, thus significantly decreasing workload for clinicians.

*Impactfactor: 1.477*

### **Hingh IH de**

#### **Acute neurological disorders following intraperitoneal administration of cisplatin**

Simkens GA\*, Hanse MC\*, Hingh IH de\*

Int J Gynaecol Obstet. 2012 Dec 13. pii: S0020-7292(12)00587-5

*Impactfactor: 2.045*

**Hingh IH de**

**Centralisatie pancreaschirurgie reduceert postoperatieve sterfte in Nederland  
[Centralisation of pancreaticoduodenectomy in the Netherlands has reduced post-operative mortality]**

Wilde RF de, Besselink MG, Borel Rinkes IH, Hingh IH de\*, Eijck CH van, Dejong CH, Porte RJ, Gouma DJ, Busch OR, Molenaar IQ

Ned Tijdschr Geneesk. 2012;156(32):A4791

OBJECTIVE: To analyse the extent of centralisation of pancreaticoduodenectomy (Whipple procedure) and changes in in-hospital mortality rates in the Netherlands.

DESIGN: Retrospective analysis.

METHODS: Data on patients who had undergone pancreaticoduodenectomy (PD) during the 2004-2009 period was acquired from the Kiwa Prismant registry. Based on the number of procedures performed annually, hospitals were divided into 4 volume-categories: very-low (<5), low (5-10), medium (11-19) and high (≥ 20). Changes in volume and in-hospital mortality were analysed per volume category. A subgroup analysis based on age was also performed.

RESULTS: 2155 patients who had undergone PD were included. The number of hospitals performing PD decreased from 48 in 2004 to 30 in 2009 ( $p = 0.01$ ). The proportion of patients who had undergone PD in a medium- or high-volume hospital increased from 52.9% to 91.2% ( $p < 0.001$ ). Post-operative mortality rates decreased from 9.8% to 5.1% ( $p = 0.04$ ). Average mortality was 14.7%, 9.8%, 6.3% and 3.3% in very low-, low-, medium-, and high-volume hospitals, respectively ( $p < 0.001$ ). The difference in mortality between medium- and high-volume hospitals was statistically significant ( $p = 0.004$ ). The mortality rate in patients ≥ 70 years was 10.4% compared with 4.4% in younger patients ( $p < 0.001$ ).

CONCLUSION : Nationwide centralisation of PD is occurring in Netherlands, and this is associated with a decrease in in-hospital mortality. Further centralisation is likely to further decrease in-hospital mortality, especially in the elderly.

*Impactfactor: --*

**Hingh IH de**

**Criterion-based laparoscopic training reduces total training time**

Brinkman WM\*, Buzink SN\*, Alevizos L, Hingh IH de\*, Jakimowicz JJ\*

Surg Endosc. 2012 Apr;26(4):1095-101. Epub 2011 Nov 1

*Voor abstract zie: Chirurgie - Brinkman WM*

*Impactfactor: 4.013*

**Hingh IH de**

**Early- and long-term outcome data of patients with pseudomyxoma peritonei from appendiceal origin treated by a strategy of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy**

Chua TC, Moran BJ, Sugarbaker PH, Levine EA, Glehen O, Gilly FN, Baratti D, Deraco M, Elias D, Sardi A, Liauw W, Yan TD, Barrios P, Gómez Portilla A, Hingh IH de\*, Ceelen WP, Pelz JO, Piso P, González-Moreno S, Speeten K van der, Morris DL

J Clin Oncol. 2012 Jul 10;30(20):2449-56. Epub 2012 May 21

PURPOSE: Pseudomyxoma peritonei (PMP) originating from an appendiceal mucinous neoplasm remains a biologically heterogeneous disease. The purpose of our study was to evaluate outcome and long-term survival after cytoreductive surgery (CRS) and

hyperthermic intraperitoneal chemotherapy (HIPEC) consolidated through an international registry study.

**PATIENTS AND METHODS:** A retrospective multi-institutional registry was established through collaborative efforts of participating units affiliated with the Peritoneal Surface Oncology Group International.

**RESULTS:** Two thousand two hundred ninety-eight patients from 16 specialized units underwent CRS for PMP. Treatment-related mortality was 2% and major operative complications occurred in 24% of patients. The median survival rate was 196 months (16.3 years) and the median progression-free survival rate was 98 months (8.2 years), with 10- and 15-year survival rates of 63% and 59%, respectively. Multivariate analysis identified prior chemotherapy treatment ( $P < .001$ ), peritoneal mucinous carcinomatosis (PMCA) histopathologic subtype ( $P < .001$ ), major postoperative complications ( $P = .008$ ), high peritoneal cancer index ( $P = .013$ ), debulking surgery (completeness of cytoreduction [CCR], 2 or 3;  $P < .001$ ), and not using HIPEC ( $P = .030$ ) as independent predictors for a poorer progression-free survival. Older age ( $P = .006$ ), major postoperative complications ( $P < .001$ ), debulking surgery (CCR 2 or 3;  $P < .001$ ), prior chemotherapy treatment ( $P = .001$ ), and PMCA histopathologic subtype ( $P < .001$ ) were independent predictors of a poorer overall survival.

**CONCLUSION:** The combined modality strategy for PMP may be performed safely with acceptable morbidity and mortality in a specialized unit setting with 63% of patients surviving beyond 10 years. Minimizing nondefinitive operative and systemic chemotherapy treatments before definitive cytoreduction may facilitate the feasibility and improve the outcome of this therapy to achieve long-term survival. Optimal cytoreduction achieves the best outcomes.

*Impactfactor: 18.372*

### **Hingh IH de**

#### **Higher prevalence of sexual dysfunction in colon and rectal cancer survivors compared with the normative population: A population-based study**

Oudsten BL den, Traa MJ, Thong MS, Martijn H\*, Hingh IH de\*, Bosscha K, Poll-Franse LV van de

Eur J Cancer. 2012 Nov;48(17):3161-70. Epub 2012 May 17

*Voor abstract zie: Radiotherapie - Martijn H*

*Impactfactor: 1.171*

### **Hingh IH de**

#### **Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality**

Wilde RF de, Besselink MG, Tweel I van der, Hingh IH de\*, Eijck CH van, Dejong CH, Porte RJ, Gouma DJ, Busch OR, Molenaar IQ; for the Dutch Pancreatic Cancer Group

Br J Surg. 2012 Mar;99(3):404-10. Epub 2012 Jan 11

**BACKGROUND:** The impact of nationwide centralization of pancreaticoduodenectomy (PD) on mortality is largely unknown. The aim of this study was to analyse changes in hospital volumes and in-hospital mortality after PD in the Netherlands between 2004 and 2009.

**METHODS:** Nationwide data on International Classification of Diseases, ninth revision (ICD-9) code 5-526 (PD, including Whipple), patient age, sex and mortality were retrieved from the independent nationwide KiwaPrismant registry. Based on established cut-off points of annually performed PDs, hospitals were categorized as very low (fewer than 5), low (5-10), medium (11-19) or high (at least 20) volume. A subgroup analysis based on a cut-off age of 70 years was also performed.

RESULTS: Some 2155 PDs were included. The number of hospitals performing PD decreased from 48 in 2004 to 30 in 2009 (P = 0.011). In these specific years, the proportion of patients undergoing PD in a medium- or high-volume centre increased from 52.9 to 91.2 per cent (P < 0.001). Nationwide mortality rates after PD decreased from 9.8 to 5.1 per cent (P = 0.044). The mortality rate during the 6-year period was 14.7, 9.8, 6.3 and 3.3 per cent in very low-, low-, medium- and high-volume hospitals respectively (P < 0.001). The difference in mortality between medium- and high-volume centres was statistically significant (P = 0.004). The volume-outcome relationship was not influenced by age (P = 0.467). The mortality rate after PD in patients aged at least 70 years was 10.4 per cent compared with 4.4 per cent in younger patients (P < 0.001).

CONCLUSION: With nationwide centralization of PD, the in-hospital mortality rate after this procedure decreased. Further centralization of PD is likely to decrease mortality further, especially in the elderly.

*Impactfactor: 4.606*

### **Hingh IH de**

#### **Intraoperative versus early postoperative intraperitoneal chemotherapy after cytoreduction for colorectal peritoneal carcinomatosis: an experimental study**

Klaver YL\*, Hendriks T, Lomme RM, Rutten HJ\*, Bleichrodt RP, Hingh IH de\*

Ann Surg Oncol. 2012 Jul;19 Suppl 3:S475-82. Epub 2011 Aug 12

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

### **Hingh IH de**

#### **Is the use of autologous platelet-rich plasma gels in gynecologic, cardiac, and general, reconstructive surgery beneficial?**

Everts PA, Hoogbergen MM\* Weber TA, Devilee RJ\*, Monftort G van\*, Hingh IH de\*

Curr Pharm Biotechnol. 2012 Jun;13(7):1163-72. Epub 2011 Jul 8

*Voor abstract zie: Plastische Chirurgie - Hoogbergen MM*

*Impactfactor: 2.805*

### **Hingh IH de**

#### **Nationwide improvement of only short-term survival after resection for pancreatic cancer in the Netherlands**

Nienhuijs SW\*, Akker SA van den, Vries E de, Hingh IH de\*, Visser O, Lemmens VE

Pancreas. 2012 Oct;41(7):1063-6

*Voor abstract zie: Chirurgie - Nienhuijs SW*

*Impactfactor: 2.386*

### **Hingh IH de**

#### **Outcomes of colorectal cancer patients with peritoneal carcinomatosis treated with chemotherapy with and without targeted therapy**

Klaver YL\*, Simkens LH, Lemmens VE, Koopman M, Teerenstra S, Bleichrodt RP,

Hingh IH de\*, Punt CJ

Eur J Surg Oncol. 2012 Jul;38(7):617-23. Epub 2012 May 8

*Voor abstract zie: Chirurgie - Klaver YL*

*Impactfactor: 2.499*

**Hingh IH de**

**Outcomes of elderly patients undergoing cytoreductive surgery and perioperative intraperitoneal chemotherapy for colorectal cancer peritoneal carcinomatosis**

Klaver YL\*, Chua TC, Hingh IH de\*, Morris DL

J Surg Oncol. 2012 Feb;105(2):113-8. Epub 2011 Jul 20

Voor abstract zie: *Chirurgie - Klaver YL*

*Impactfactor: 2.100*

**Hingh IH de**

**Pancreatitis of biliary origin, optimal timing of cholecystectomy (PONCHO trial): study protocol for a randomized controlled trial**

Bouwense SA, Besselink MG, Brunschot S van, Bakker OJ, Santvoort HC van, Schepers NJ, Boermeester MA, Bollen TL, Bosscha K, Brink MA, Bruno MJ, Consten EC, Dejong CH, Duijvendijk P van, Eijck CH van, Gerritsen JJ, Goor H van, Heisterkamp J,

Hingh IH de\*, Kruij PM, Molenaar IQ, Nieuwenhuijs VB, Rosman C, Schaapherder AF, Scheepers JJ, Spanier MB, Timmer R, Weusten BL, Witteman BJ, Ramshorst B van, Gooszen HG, Boerma D; for the Dutch Pancreatitis Study Group

Trials. 2012 Nov 26;13(1):225

**BACKGROUND:** After an initial attack of biliary pancreatitis, cholecystectomy minimizes the risk of recurrent biliary pancreatitis and other gallstone-related complications. Guidelines advocate performing cholecystectomy within 2 to 4 weeks after discharge for mild biliary pancreatitis. During this waiting period, the patient is at risk of recurrent biliary events. In current clinical practice, surgeons usually postpone cholecystectomy for 6 weeks due to a perceived risk of a more difficult dissection in the early days following pancreatitis and for logistical reasons. We hypothesize that early laparoscopic cholecystectomy minimizes the risk of recurrent biliary pancreatitis or other complications of gallstone disease in patients with mild biliary pancreatitis without increasing the difficulty of dissection and the surgical complication rate compared with interval laparoscopic cholecystectomy.

**METHODS/DESIGN:** PONCHO is a randomized controlled, parallel-group, assessor-blinded, superiority multicenter trial. Patients are randomly allocated to undergo early laparoscopic cholecystectomy, within 72 hours after randomization, or interval laparoscopic cholecystectomy, 25 to 30 days after randomization. During a 30-month period, 266 patients will be enrolled from 18 hospitals of the Dutch Pancreatitis Study Group. The primary endpoint is a composite endpoint of mortality and acute readmissions for biliary events (that is, recurrent biliary pancreatitis, acute cholecystitis, symptomatic/obstructive choledocholithiasis requiring endoscopic retrograde cholangiopancreatography including cholangitis (with/without endoscopic sphincterotomy), and uncomplicated biliary colics) occurring within 6 months following randomization. Secondary endpoints include the individual endpoints of the composite endpoint, surgical and other complications, technical difficulty of cholecystectomy and costs.

**DISCUSSION:** The PONCHO trial is designed to show that early laparoscopic cholecystectomy (within 72 hours) reduces the combined endpoint of mortality and re-admissions for biliary events as compared with interval laparoscopic cholecystectomy (between 25 and 30 days) after recovery of a first episode of mild biliary pancreatitis.

*Impactfactor: 2.496*

**Hingh IH de**

**Peritoneal carcinomatosis of colorectal origin: incidence, prognosis and treatment options**

Klaver YL\*, Lemmens VE, Nienhuijs SW\*, Luyer MD\*, Hingh IH de\*

World J Gastroenterol. 2012 Oct 21;18(39):5489-94

Voor abstract zie: Chirurgie - Klaver YL

Impactfactor: 2.471

**Hingh IH de**

**Surgical techniques for parastomal hernia repair: a systematic review of the literature**

Hansson BM, Slater NJ, Velden AS van der, Groenewoud HM, Buyne OR, Hingh IH de\*, Bleichrodt RP

Ann Surg. 2012 Apr;255(4):685-95

**BACKGROUND:** Parastomal hernias are a frequent complication of enterostomies that require surgical treatment in approximately half of patients. This systematic review aimed to evaluate and compare the safety and effectiveness of the surgical techniques available for parastomal hernia repair.

**METHODS:** Systematic review was performed in accordance with PRISMA. Assessment of methodological quality and selection of studies of parastomal hernia repair was done with a modified

**MINORS.** Subgroups were formed for each surgical technique. Primary outcome was recurrence after at least 1-year follow-up. Secondary outcomes were mortality and postoperative morbidity. Outcomes were analyzed using weighted pooled proportions and logistic regression.

**RESULTS:** Thirty studies were included with the majority retrospective. Suture repair resulted in a significantly increased recurrence rate when compared with mesh repair (odds ratio [OR] 8.9, 95% confidence interval [CI] 5.2-15.1;  $P < 0.0001$ ). Recurrence rates for mesh repair ranged from 6.9% to 17% and did not differ significantly. In the laparoscopic repair group, the Sugarbaker technique had less recurrences than the keyhole technique (OR 2.3, 95% CI 1.2-4.6;  $P = 0.016$ ). Morbidity did not differ between techniques. The overall rate of mesh infections was low (3%, 95% CI 2) and comparable for each type of mesh repair.

**CONCLUSIONS:** Suture repair of parastomal hernia should be abandoned because of increased recurrence rates. The use of mesh in parastomal hernia repair significantly reduces recurrence rates and is safe with a low overall rate of mesh infection. In laparoscopic repair, the Sugarbaker technique is superior over the keyhole technique showing fewer recurrences.

Impactfactor: 7.492

**Hingh IH de**

**The hospital standardized mortality ratio fallacy: a narrative review**

Gestel YR van, Lemmens VE, Lingsma HF, Hingh IH de\*, Rutten HJ\*, Coebergh JW

Med Care. 2012 Aug;50(8):662-7

**BACKGROUND:** Outcome measures, like hospital standardized mortality ratios (HSMRs), are increasingly used to assess quality of care. The validity of HSMRs and their accuracy to reflect quality of care is heavily contested.

**OBJECTIVE:** We explored apparent and potential shortcomings and adverse effects of the HSMR in the assessment of quality of care.

RESEARCH DESIGN AND METHODS: For this narrative review, relevant articles were collected from Medline databases using the following search terms: "hospital standardized mortality ratio," "standardized mortality ratio," "HSMR," "quality of care," and "in-hospital mortality." In addition, other important articles were subtracted from the reference lists of the primary articles.

RESULTS: The current literature exhibits important shortcomings of the HSMR that in particular affect hospitals providing specialized care of a certain level of complexity. Because of the lack or insufficiency of data concerning case-mix, coding variation between hospitals, disease severity, referral bias, end-of life care, and place of death, the current HSMR model is not able to adjust adequately for these aspects. This leads to incomparability of HSMRs between hospitals. Instead of separate aspects of continuity of care, all factors contributing to quality of care should be considered.

CONCLUSIONS: Given the several shortcomings, use of the HSMR as an indicator of quality of care can be considered as a fallacy. Publication of the HSMR is not likely to lead to improvement of quality of care and might harm both hospitals and patients.

*Impactfactor: 3.411*

### **Hingh IH de**

#### **To Sleeve or NOT to Sleeve in Bariatric Surgery?**

Rutte PW van\*, Luyer MD\*, Hingh IH de\*, Nienhuijs SW\*

ISRN Surg. 2012;2012:674042. Epub 2012 Aug 16

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: --*

### **Hobo R**

#### **The influence of smoking on endovascular abdominal aortic aneurysm repair**

Koole D, Moll FL, Buth J\*, Hobo R\*, Zandvoort H, Pasterkamp G, Herwaarden JA van; EUROSTAR collaborators

J Vasc Surg. 2012 Jun;55(6):1581-6. Epub 2012 Feb 9

*Voor abstract zie: Chirurgie - Buth J*

*Impactfactor: 3.153*

### **Holman F**

#### **Perineal hernia repair after abdominoperineal rectal excision**

Martijnse IS\*, Holman F\*, Nieuwenhuijzen GA\*, Rutten HJ\*, Nienhuijs SW\*

Dis Colon Rectum. 2012 Jan;55(1):90-5

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 3.132*

### **Jakimowicz JJ**

#### **Criterion-based laparoscopic training reduces total training time**

Brinkman WM\*, Buzink SN\*, Alevizos L, Hingh IH de\*, Jakimowicz JJ\*

Surg Endosc. 2012 Apr;26(4):1095-101. Epub 2011 Nov 1

*Voor abstract zie: Chirurgie - Brinkman WM*

*Impactfactor: 4.013*

### **Jakimowicz JJ**

#### **Laparoscopic Surgical Skills programme: preliminary evaluation of Grade I Level 1 courses by trainees**

Buzink S\*, Soltes M, Radonak J, Fingerhut A, Hanna G, Jakimowicz J\*

Wideochir Inne Tech Malo Inwazyjne. 2012 Aug;7(3):188-92

*Voor abstract zie: Chirurgie - Buzink SN*

*Impactfactor: --*

### **Jakimowicz JJ**

#### **Novice surgeons versus experienced surgeons in laparoendoscopic single-site (LESS) surgery: a comparison of performances in a surgical simulator**

Alevizos L, Brinkman W\*, Fingerhut A, Jakimowicz J\*, Leandros E

World J Surg. 2012 May;36(5):939-44

*Voor abstract zie: Chirurgie - Brinkman*

*Impactfactor: 2.362*

### **Jakimowicz JJ**

#### **Single versus multimodality training basic laparoscopic skills**

Brinkman WM\*, Havermans SY\*, Buzink SN, Botden SM, Jakimowicz JJ\*, Schoot BC\*

Surg Endosc. 2012 Aug;26(8):2172-8. Epub 2012 Feb 21

*Voor abstract zie: Urologie - Brinkman WM*

*Impactfactor: 4.013*

### **Klaver YL**

#### **Intraoperative versus early postoperative intraperitoneal chemotherapy after cytoreduction for colorectal peritoneal carcinomatosis: an experimental study**

Klaver YL\*, Hendriks T, Lomme RM, Rutten HJ\*, Bleichrodt RP, Hingh IH de\*

Ann Surg Oncol. 2012 Jul;19 Suppl 3:S475-82. Epub 2011 Aug 12

**BACKGROUND:** Perioperative intraperitoneal chemotherapy is used as an adjunct to cytoreductive surgery (CS) for peritoneal carcinomatosis (PC) in order to prolong survival. Worldwide, hyperthermic intraperitoneal chemotherapy (HIPEC), early postoperative intraperitoneal chemotherapy (EPIC), and combinations of the two are used. It remains unclear which regimen is most beneficial. **METHODS:** The rat colon carcinoma cell line CC-531 was injected into the peritoneal cavity of 80 WAG/ Rij rats to induce PC. Animals were randomized into four treatment groups (n = 20): CS only, CS followed by HIPEC (mitomycin 35 mg/m<sup>2</sup>) at 41.5°C, CS followed by EPIC during 5 days (i.p. injection of mitomycin on day 1 and 5-fluorouracil on days 2-5), and CS followed by HIPEC plus EPIC. Primary outcome was survival. **RESULTS:** In rats treated with CS only, median survival was 53 days (95% confidence interval (CI) 49-57 days). In rats treated with CS followed by HIPEC, survival was significantly (P = 0.001) increased (median survival 94 days, 95% CI 51-137 days). In the group treated with EPIC after CS, 12 out of 20 rats were still alive at the end of the experiment (P < 0.001 as compared with CS only). In the group receiving both treatments, 11 rats died of toxicity, and therefore this group was not included in the survival analysis. **CONCLUSIONS:** Both EPIC and HIPEC were effective in prolonging survival. The beneficial effect of EPIC on survival seemed to be more pronounced than that of HIPEC. Further research is indicated to evaluate and compare the possible benefits and adverse effects associated with both treatments.

*Impactfactor: 4.166*

**Klaver YL**

**Outcomes of colorectal cancer patients with peritoneal carcinomatosis treated with chemotherapy with and without targeted therapy**

Klaver YL\*, Simkens LH, Lemmens VE, Koopman M, Teerenstra S, Bleichrodt RP, Hingh IH de\*, Punt CJ

Eur J Surg Oncol. 2012 Jul;38(7):617-23. Epub 2012 May 8

**BACKGROUND:** Although systemic therapies have shown to result in survival benefit in patients with metastatic colorectal cancer (mCRC), outcomes in patients with peritoneal carcinomatosis (PC) are poor. No data are available on outcomes of current chemotherapy schedules plus targeted agents in mCRC patients with PC.

**METHODS:** Previously untreated mCRC patients treated with chemotherapy in the CAIRO study and with chemotherapy and targeted therapy in the CAIRO2 study were included and retrospectively analysed according to presence or absence of PC at randomisation. Patient demographics, primary tumour characteristics, progression-free survival (PFS), overall survival (OS), and occurrence of toxicity were evaluated.

**RESULTS:** Thirty-four patients with PC were identified in the CAIRO study and 47 patients in the CAIRO2 study. Median OS was decreased for patients with PC compared with patients without PC (CAIRO: 10.4 versus 17.3 months, respectively ( $p = 0.001$ ); CAIRO2: 15.2 versus 20.7 months, respectively ( $p < 0.001$ )). Median number of treatment cycles did not differ between patients with or without PC in both studies. Occurrence of major toxicity was more frequent in patients with PC treated with sequential chemotherapy in the CAIRO study as compared to patients without PC. This was not reflected in reasons to discontinue treatment. In the CAIRO2 study, no differences in major toxicity were observed.

**CONCLUSION:** Our data demonstrate decreased efficacy of current standard chemotherapy with and without targeted agents in mCRC patients with PC. This suggests that the poor outcome cannot be explained by undertreatment or increased susceptibility to toxicity, but rather by relative resistance to treatment.

*Impactfactor: 2.499*

**Klaver YL**

**Outcomes of elderly patients undergoing cytoreductive surgery and perioperative intraperitoneal chemotherapy for colorectal cancer peritoneal carcinomatosis**

Klaver YL\*, Chua TC, Hingh IH de\*, Morris DL

J Surg Oncol. 2012 Feb;105(2):113-8. Epub 2011 Jul 20

**BACKGROUND:** The combined treatment of cytoreductive surgery (CRS) and perioperative chemotherapy (PIC) for colorectal peritoneal carcinomatosis (PC) is a rigorous surgical treatment most suited for fit and young patients. With technical maturity and improved perioperative care, we examined the outcomes of elderly patients undergoing CRS and PIC for colorectal PC.

**METHODS:** All consecutive patients treated in two tertiary centers for PC of colorectal cancer who were 70 years of age or older at the time of surgery were included. Data on patient characteristics, concomitant diseases, operation details, perioperative course, and follow-up were retrieved from medical charts. Primary outcomes were perioperative morbidity and mortality. Secondary outcomes were disease-free and overall survival.

**RESULTS:** Twenty-four patients (11 male) were included in this study (mean age 73.5 years). In eight patients major complications occurred. In six patients the postoperative course was complicated by minor adverse events. There was no perioperative mortality. Median overall survival was 35 months with a 6, 12, and 18 months survival rate of 94%, 83%, and 68%, respectively.

CONCLUSIONS: CRS and PIC for colorectal PC may be safely performed with acceptable morbidity in selected elderly patients. When considering patients for surgery, performance status, and the disease extent should be used as eligibility criteria rather than age.

*Impactfactor: 2.100*

#### **Klaver YL**

#### **Peritoneal carcinomatosis of colorectal origin: Incidence, prognosis and treatment options**

Klaver YL\*, Lemmens VE, Nienhuijs SW\*, Luyer MD\*, Hingh IH de\*

World J Gastroenterol. 2012 Oct 21;18(39):5489-94

Peritoneal carcinomatosis (PC) is one manifestation of metastatic colorectal cancer (CRC). Tumor growth on intestinal surfaces and associated fluid accumulation eventually result in bowel obstruction and incapacitating levels of ascites, which profoundly affect the quality of life for affected patients. PC appears resistant to traditional 5-fluorouracil-based chemotherapy, and surgery was formerly reserved for palliative purposes only. In the absence of effective treatment, the historical prognosis for these patients was extremely poor, with an invariably fatal outcome.

These poor outcomes likely explain why PC secondary to CRC has received little attention from oncologic researchers. Thus, data are lacking regarding incidence, clinical disease course, and accurate treatment evaluation for patients with PC. Recently, population-based studies have revealed that PC occurs relatively frequently among patients with CRC. Risk factors for developing PC have been identified: right-sided tumor, advanced T-stage, advanced N-stage, poor differentiation grade, and younger age at diagnosis.

During the past decade, both chemotherapeutical and surgical treatments have achieved promising results in these patients. A chance for long-term survival or even cure may now be offered to selected patients by combining radical surgical resection with intraperitoneal instillation of heated chemotherapy. This combined procedure has become known as hyperthermic intraperitoneal chemotherapy. This editorial outlines recent advancements in the medical and surgical treatment of PC and reviews the most recent information on incidence and prognosis of this disease. Given recent progress, treatment should now be considered in every patient presenting with PC.

*Impactfactor: 2.471*

#### **Kusters M**

#### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*, Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 2.499*

## **Kusters M**

### **T3+ and T4 rectal cancer patients seem to benefit from the addition of oxaliplatin to the neoadjuvant chemoradiation regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*  
Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Lauret GJ**

### **Multidisciplinary treatment for peripheral arterial occlusive disease and the role of eHealth and mHealth**

Fokkenrood HJ\*, Lauret GJ\*, Scheltinga MR, Spreeuwenberg C, Bie RA de, Teijink JA\*  
J Multidiscip Healthc. 2012;5:257-63 Epub 2012 Oct 8

*Voor abstract zie: Chirurgie - Fokkenrood HJ*

*Impactfactor: --*

## **Lauret GJ**

### **Supervised exercise therapy for intermittent claudication: current status and future perspectives**

Lauret GJ\*, Dalen DC van\*, Willigendael EM\*, Hendriks EJ, Bie RA de, Spronk S, Teijink JA\*

Vascular. 2012 Feb;20(1):12-9. Epub 2012 Feb 10

Intermittent claudication (IC) has a high prevalence in the older population and is closely associated with cardiovascular and cerebrovascular disease. High mortality rates are reported due to ongoing atherosclerotic disease. Because of these serious health risks, treatment of IC should address reduction of cardiovascular events (and related morbidity/mortality) and improvement of the poor health-related quality of life (QoL) and functional capacity. In several randomized clinical trials and systematic reviews, supervised exercise therapy (SET) is compared with non-supervised exercise, usual care, placebo, walking advice or vascular interventions. The current evidence supports SET as the primary treatment for IC. SET improves maximum walking distance and health-related QoL with a marginal risk of comorbidity or mortality. This is also illustrated in contemporary international guidelines. Community-based SET appears to be at least as efficacious as programs provided in a clinical setting. In the Netherlands, a national integrated care network (ClaudicationNet) providing specialized care for patients with IC is currently being implemented. Besides providing a standardized form of SET, the specialized physical therapists stimulate medication compliance and perform lifestyle coaching. Future research should focus on the influence of co-morbidities on prognosis and effect of SET outcome and the potential beneficial effects of SET combined with a vascular intervention.

*Impactfactor: 0.891*

**Lauret GJ**

**The ClaudicatioNet concept: design of a national integrated care network providing active and healthy aging for patients with intermittent claudication**

Lauret GJ\*, Gijsbers HJ, Hendriks EJ, Bartelink ML, Bie RA de, Teijink JA\*

Vasc Health Risk Manag. 2012;8:495-503

**INTRODUCTION:** Intermittent claudication (IC) is a manifestation of peripheral arterial occlusive disease (PAOD). Besides cardiovascular risk management, supervised exercise therapy (SET) should be offered to all patients with IC. Outdated guidelines, an insufficient number of specialized physiotherapists (PTs), lack of awareness of the importance of SET by referring physicians, and misguided financial incentives all seriously impede the availability of a structured SET program in The Netherlands. **DESCRIPTION OF CARE PRACTICE:** By initiating regional care networks, ClaudicatioNet aims to improve the quality of care for patients with IC. Based on the chronic care model as a conceptual framework, these networks should enhance the access, continuity, and (cost) efficiency of the health care system. With the aid of a national database, health care professionals will be able to benchmark patient results while ClaudicatioNet will be able to monitor quality of care by way of functional and patient reported outcome measures.

**DISCUSSION:** The success of ClaudicatioNet is dependent on several factors. Vascular surgeons, general practitioners and coordinating central caregivers will need to team up and work in close collaboration with specialized PTs. A substantial task in the upcoming years will be to monitor the quality, volume, and distribution of ClaudicatioNet PTs. Finally, misguided financial incentives within the Dutch health care system need to be tackled.

**CONCLUSION:** With ClaudicatioNet, integrated care pathways are likely to improve in the upcoming years. This should result in the achievement of optimal quality of care for all patients with IC.

*Impactfactor: --*

**Lauret GJ**

**When is supervised exercise therapy considered useful in peripheral arterial occlusive disease? A nationwide survey among vascular surgeons**

Lauret GJ\*, Dalen HC van\*, Hendriks HJ, Sterkenburg SM van, Koelemay MJ, Zeebregts CJ, Peters RJ, Teijink JA\*

Eur J Vasc Endovasc Surg. 2012 Mar;43(3):308-12. Epub 2012 Jan 10

**OBJECTIVES:** Although international guidelines state that supervised exercise therapy (SET) should be offered to all patients with intermittent claudication (IC), SET appears to be underutilised in clinical practice. The aim of this study was to document current opinions of Dutch vascular surgeons on SET as treatment option for peripheral arterial occlusive disease (PAOD).

**MATERIALS AND METHODS:** Vascular surgeons and fellows in vascular surgery were asked to complete a 24-question survey either at the 2011 Annual Meeting of the Dutch Society for Vascular Surgery or online.

**RESULTS:** Ninety-one participants, including 83 vascular surgeons (51% of all Dutch vascular surgeons), completed the survey. The respondents would refer 75.4% of newly diagnosed patients with IC for SET. SET was considered less useful in patients with IC and major (cardiopulmonary) comorbidity or a significant iliac artery stenosis. In critical limb ischaemia, the combination of SET and angioplasty was considered useful in 71.9%. Respondents regarded patient satisfaction (63.3%) and improvement in pain-free or maximal walking ability (26.6%) as clinically most relevant goals of SET. Most (84.4%) agreed that SET should also include lifestyle management.

CONCLUSION: Although the vast majority of Dutch vascular surgeons consider SET as an important treatment option for PAOD, SET should receive more emphasis in clinical practice since arguments not to refer for SET are outdated. Furthermore, vascular surgeons agree that lifestyle management should be integrated in SET.

*Impactfactor: --*

## **Luyer MD**

### **Enteric neuroprotection**

Luyer MD\*

J Physiol. 2012 Jun 15;590(Pt 12):2827

*Impactfactor: --*

## **Luyer MD**

### **Peritoneal carcinomatosis of colorectal origin: Incidence, prognosis and treatment options**

Klaver YL\*, Lemmens VE, Nienhuijs SW\*, Luyer MD\*, Hingh IH de\*

World J Gastroenterol. 2012 Oct 21;18(39):5489-94

*Voor abstract zie: Chirurgie - Klaver YL*

*Impactfactor: 2.471*

## **Luyer MD**

### **Risk of anastomotic leakage with non-steroidal anti-inflammatory drugs in colorectal surgery**

Gorissen KJ, Benning D, Berghmans T, Snoeijs MG, Sosef MN, Hulsewe KW, Luyer MD\*

Br J Surg. 2012 May;99(5):721-7

BACKGROUND: With the implementation of multimodal analgesia regimens in fast-track surgery programmes, non-steroidal anti-inflammatory drugs (NSAIDs) are being prescribed routinely. However, doubts have been raised concerning the safety of NSAIDs in terms of anastomotic healing.

METHODS: Data on patients who had undergone primary colorectal anastomosis at two teaching hospitals between January 2008 and December 2010 were analysed retrospectively. Exact use of NSAIDs was recorded. Rates of anastomotic leakage were compared between groups and corrected for known risk factors in both univariable and multivariable analyses.

RESULTS: A total of 795 patients were divided into four groups according to NSAID use: no NSAIDs (471 patients), use of non-selective NSAIDs (201), use of selective cyclo-oxygenase (COX) 2 inhibitors (79), and use of both selective and non-selective NSAIDs (44). The overall leak rate was 9.9 per cent (10.0 per cent for right colonic, 8.7 per cent for left colonic and 12.4 per cent for rectal anastomoses). Known risk factors such as smoking and use of steroids were not significantly associated with anastomotic leakage. Stapled anastomosis was identified as an independent predictor of leakage in multivariable analysis (odds ratio (OR) 2.22, 95 per cent confidence interval 1.30 to 3.80;  $P = 0.003$ ). Patients on NSAIDs had higher anastomotic leakage rates than those not on NSAIDs (13.2 versus 7.6 per cent; OR 1.84, 1.13 to 2.98;  $P = 0.010$ ). This effect was mainly due to non-selective NSAIDs (14.5 per cent; OR 2.13, 1.24 to 3.65;  $P = 0.006$ ), not selective COX-2 inhibitors (9 per cent; OR 1.16, 0.49 to 2.75;  $P = 0.741$ ). The overall mortality rate was 4.2 per cent, with no significant difference between groups ( $P = 0.438$ ).

CONCLUSION: Non-selective NSAIDs may be associated with anastomotic leakage.

*Impactfactor: 4.606*

## **Luyer MD**

### **Stimulation of the autonomic nervous system in colorectal surgery: a study protocol for a randomized controlled trial**

Berghmans TM, Hulsewé KW, Buurman WA, Luyer MD\*

Trials. 2012 Jun 27;13:93

**BACKGROUND:** Postoperative ileus (POI) is a well-known complication of abdominal surgery and is considered to be caused by a local inflammation in the gut. Previously it has been shown that both local and systemic inflammation can be reduced by stimulation of the autonomic nervous system via lipid rich nutrition. Stimulation of the autonomic nervous system releases acetylcholine from efferent vagal nerve endings that binds to nicotinic receptors located on the inflammatory cells leading to a decrease of proinflammatory mediators. Besides administration of nutrition there are other ways of stimulating the autonomic nervous system such as gum chewing.

**METHODS/DESIGN:** This prospective, placebo-controlled randomized trial will include 120 patients undergoing colorectal surgery which are randomized for gum chewing preoperatively and in the direct postoperative phase or a placebo. Postoperative ileus will be assessed both clinically by time to first flatus and time to first defecation and by determination of gastric motility using ultrasound to measure dimensions of the antrum. Furthermore the inflammatory response is quantified by analyzing proinflammatory mediators. Finally, markers of gut barrier integrity will be measured as well as occurrence of postoperative complications.

**DISCUSSION:** We hypothesize that chewing gum preoperatively and in the direct postoperative phase in patients undergoing colorectal surgery dampens local and systematic inflammation, via activation of the autonomic nervous system. Down-regulation of the inflammatory cascade via stimulation of the vagus nerve will ameliorate POI and enhance postoperative recovery.

*Impactfactor: 2.496*

## **Luyer MD**

### **To Sleeve or NOT to Sleeve in Bariatric Surgery?**

Rutte PW van\*, Luyer MD\*, Hingh IH de\*, Nienhuijs SW\*

ISRN Surg. 2012;2012:674042. Epub 2012 Aug 16

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: --*

## **Maaskant-Braat AJ**

### **Axillary and systemic treatment of patients with breast cancer and micrometastatic disease or isolated tumor cells in the sentinel lymph node**

Maaskant-Braat AJ\*, Voogd AC, Poll-Franse LV van de, Coebergh JW,

Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):524-8

**BACKGROUND:** After introduction of sentinel node biopsy (SNB) in patients with breast cancer a higher proportion of micrometastases and isolated tumor cells are being detected. Prognostic impact and clinical relevance of this minimal nodal involvement is under debate and substantial variation in the use of axillary surgery and/or systemic adjuvant treatment could be expected.

**METHODS:** Data from the population-based Eindhoven Cancer Registry were used on all (n = 9038) women who underwent SNB for invasive breast cancer from 1996 to 2008 and medical

files were studied to determine the role of minimal nodal involvement in the decision to use adjuvant systemic treatment.

**RESULTS:** Forty-five percent of 172 patients with isolated tumor cells and 76% of 605 patients with micrometastases received adjuvant systemic treatment. Thirty-five of 59 patients with isolated tumor cells and 153 of 193 patients with micrometastases received systemic therapy based on primary tumor characteristics. The remainder probably received adjuvant therapy based on presence of minimal nodal involvement. Thirty-seven percent of the patients with isolated tumor cells underwent an axillary lymph node dissection compared to 75% when micrometastases were present. Multivariate analyses showed a significantly higher chance of receiving systemic treatment when isolated tumor cells (OR 1.5 (95% CI, 1.05-2.15)) or micrometastases (OR 10.7 (95% CI, 8.56-13.27)) were present, compared to a negative lymph node status.

**CONCLUSION:** The debate on necessity of performing completion ALND and administration of systemic therapy in patients with minimal nodal involvement is reflected by the treatment patterns observed in our population-based study.

**SYNOPSIS:** Describing time-trends and predictors of axillary and systemic treatment of patients with breast cancer and micrometastases or isolated tumor cells in their sentinel lymph node(s).

*Impactfactor: 2.491*

## **Maaskant-Braat AJ**

### **Lymphatic mapping after previous breast surgery**

Maaskant-Braat AJ\*, Bruijn SZ de, Woensdregt K\*, Pijpers H\*, Voogd AC, Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):444-8. Epub 2011 Nov 21

**BACKGROUND:** To assess the feasibility of lymphatic mapping and determine the lymphatic drainage pathways in patients previously treated with breast conserving therapy (BCT).

**METHODS:** We included patients without current breast cancer that previously received BCT with sentinel node biopsy (SNB) and/or axillary lymph node dissection (ALND) for primary breast cancer. The study population consisted of 44 patients and was divided into two groups according to previous surgical treatment of the axilla: 22 patients after previous SNB and 22 patients after previous ALND. Standard lymphatic mapping was performed and the lymphatic drainage pattern was registered. Drainage located outside the ipsilateral axilla was recorded as aberrant.

**RESULTS:** Lymphoscintigraphy revealed a drainage pattern in 17 of 44 patients (39%). The identification rate in the SNB-group was 41% and 36% in the ALND-group (P=0.760). 8 patients (18%) showed aberrant drainage, which tended to be more frequent in the ALND-group than in the SNB-group (27% versus 9%, P=0.122). Lymphatic drainage to the contralateral axilla was observed in 2 patients, both previously treated with ALND.

**CONCLUSIONS:** Lymphatic mapping seems feasible after previous BCT with axillary treatment, in spite of a relatively low identification rate. Aberrant drainage tends to be more frequent after previous treatment with ALND.

*Impactfactor: 2.491*

## **Martijnse IS**

### **Focus on extralevator perineal dissection in supine position for low rectal cancer has led to better quality of surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D\*, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

**BACKGROUND:** After abdominoperineal excision (APE), the presence of tumor cells in the circumferential resection margin (R1) and iatrogenic tumor perforations are still frequent and result in an increased rate of local recurrences. In this study, a standardized supine APE with an increased focus on the perineal dissection (sPPD) is compared to the customary supine APE.

**METHODS:** From 2000 to 2010, a total of 246 patients underwent APE for rectal cancer (sPPD and customary supine APE). All patients were staged with preoperative magnetic resonance imaging (MRI) and received neoadjuvant treatment (n = 203) when margins were involved or threatened (cT3 + and T4). As a result of a quality improvement program in 2006, the surgical technique was modified: it became standardized, emphasis was placed on the perineal dissection, and pelvic dissection was limited to avoid false routes when following the total mesorectal excision planes deep into the pelvis.

**RESULTS:** Overall, the percentage of involved circumferential resection margins (CRMs) was 10%. In the period before introducing sPPD, the R1 percentages for cT0-3 and cT4 tumors were 6.8 and 30.2%, compared to 2.2 and 5.7% after introduction of sPPD (P = 0.001). Risk factors for R1 resection were preoperative T4 tumors (14.9%, P = 0.011), tumor perforation (33.3%, P = 0.002), fistulating tumors (35.7%, P = 0.002), mucus-producing tumors (23.1%, P = 0.006), or bulky tumors (66.7%, P < 0.001).

**CONCLUSIONS:** The objective of surgical treatment of low rectal cancer is to obtain negative resection margins and subsequently reduce the risk of local recurrence. A combination of the appropriate preoperative treatment and standardized surgical technique such as sPPD can achieve this goal.

*Impactfactor: 4.166*

## **Martijnse IS**

### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*, Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

**INTRODUCTION:** Lymph node involvement is one of the most important prognostic factors in rectal cancer. After neoadjuvant treatment the number of retrieved lymph nodes is often reported to be low which impairs reliable tumour staging. This study examines the effect of patent blue staining on the number of harvested lymph nodes and evaluates whether a higher number of retrieved lymph nodes is of prognostic significance.

**PATIENTS AND METHODS:** Between March 2007 and December 2010, 295 consecutive patients with locally advanced rectal cancer following neoadjuvant treatment were included. Specimens were either not stained (NB), injected with patent blue into the mesorectum (MB) or directly into the inferior mesenteric artery (AB). Data were retrieved from a prospective database.

**RESULTS:** The number of evaluated lymph nodes was significantly higher in the stained specimens: mean 6.8 in the NB group (n=89), 11.5 in the MB group (n=86) and 17.4 in the AB

group (n=106) ( $p < 0.001$ ). The percentage of patients with a minimum of 12 lymph nodes increased from 15.5% (NB) to 44.2% (MB) to 74.5% (AB) ( $p < 0.001$ ). The three-year cancer specific survival for the lymph node ratio (LNR) was 95% (0), 94.4% (0.01-0.1), 80.1% (0.11-0.4) and 63.7% (0.41-1).

**CONCLUSION:** The use of patent blue in patients who underwent rectal cancer surgery after neoadjuvant treatment significantly enhanced lymph node harvest. Injection into the inferior mesenteric artery was most effective. This relatively simple and generally applicable method can help to improve lymph node detection which lowers the LNR and allows adequate tumour staging.

*Impactfactor: 2.499*

## **Martijnse IS**

### **Perineal hernia repair after abdominoperineal rectal excision**

Martijnse IS\*, Holman F\*, Nieuwenhuijzen GA\*, Rutten HJ\*, Nienhuijs SW\*

Dis Colon Rectum. 2012 Jan;55(1):90-5

**BACKGROUND:** : A perineal hernia can severely disable everyday activities. Its repair is a surgical challenge, and guidance by the literature is limited. The series described so far are small or encompass a long period in which even nonmesh techniques were used.

**OBJECTIVE:** : The aim of this study was to review recent results of a perineal mesh-based repair.

**PATIENTS:** : Medical charts of patients with a symptomatic perineal hernia after abdominoperineal resection due to rectal cancer were reviewed.

**MAIN OUTCOME MEASURES:** : Data included patients' characteristics, operative details, recurrence, and complications.

**RESULTS:** : In total, 29 patients underwent repair of a symptomatic perineal hernia after an abdominoperineal resection due to rectal cancer. The majority was male (66%), and the median age was 59 years (range, 41-83). All patients received neoadjuvant treatment. From 2003 until 2006, polytetrafluoroethylene or Vypro mesh and Prolene 2.0 sutures were used for perineal hernia repair. All 8 repairs failed; repeated repair using various methods was successful in 63%. After 2006, the surgical technique was changed into a high-tension repair with the use of a nonabsorbable mesh. This technique was successful for 20 of 21 patients (95%). Complications encountered in the entire group of 29 patients were urinary retention (n = 2), wound infection, seroma, and fistula (n = 1 each).

**LIMITATIONS:** : Even though this is the largest group described in the literature, the results are limited because of the small number of patients.

**CONCLUSION:** : Repair of perineal hernia remains challenging and only a few reports offer advice on how to manage this unusual problem. However, superior results have been shown with the new meshbased technique through perineal approach with only 5% recurrence.

*Impactfactor: 3.132*

## **Martijnse IS**

### **T3+ and T4 Rectal Cancer Patients Seem to Benefit From the Addition of Oxaliplatin to the Neoadjuvant Chemoradiation Regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

**BACKGROUND:** To achieve T-downstaging and better resectability in locally advanced rectal cancer, neoadjuvant radiochemotherapy (RCT) has become the current standard of

treatment. A variety of schemes have been used. This study investigates which scheme had the best effect on these parameters.

**METHODS:** Our institution is a referral center for locally advanced rectal cancer. Different neoadjuvant radiochemotherapy regimens were administered: long course radiotherapy (RTH), 5-FU and leucovorin (5FUBolus), a combination of capecitabine and oxaliplatin (CORE), and capecitabine only (CAP). Selection of patients for 1 of the regimens was based on hospital policy rather than patient or tumor characteristics.

**RESULTS:** The data of 504 consecutive patients (n = 181 T3+, n = 323 T4) without metastatic disease (cM0) who underwent surgery for advanced rectal carcinoma between 1994 and 2010 were reviewed. The RTH, 5FUBolus, CORE, and CAP scheme were administered to 106, 137, 155, and 106 patients, respectively. Odds ratios for downstaging were less effective for RTH, 5FUBolus, and CAP (0.31, 0.44, and 0.31; P < .0001) when compared with the CORE scheme. Odds ratios for a R1 resection (3.74, 1.94, 1.14; P = .003) or CRM+ resection (3.78, 2.73, 1.34; P = .001) were also in favor of the CORE. Hazard ratios for CSS were significantly better for the CORE scheme.

**CONCLUSIONS:** Downstaging with neoadjuvant treatment results in an increased number of radical resections. In our study, the combination of capecitabine and oxaliplatin appears to be the most effective regimen for locally advanced rectal cancer tumors. However, longer follow-up will be necessary to confirm this conclusion.

*Impactfactor: 4.166*

### **Montfort G van**

#### **Is the use of autologous platelet-rich plasma gels in gynecologic, cardiac, and general, reconstructive surgery beneficial?**

Everts PA, Hoogbergen MM\*, Weber TA, Devilee RJ\*, Monftort G van\*, Hingh IH de\*  
Curr Pharm Biotechnol. 2012 Jun;13(7):1163-72. Epub 2011 Jul 8

*Voor abstract zie: Plastische Chirurgie - Hoogbergen MM*

*Impactfactor: 2.805*

### **Nienhuijs SW**

#### **Bariatric surgery with operating room teams that stayed fixed during the day: a multicenter study analyzing the effects on patient outcomes, teamwork and safety climate, and procedure duration**

Stepaniak PS\*, Heij C, Buise MP\*, Mannaerts GH, Smulders F, Nienhuijs SW\*

Anesth Analg. 2012 Dec;115(6):1384-92. Epub 2012 Nov 9

*Voor abstract zie: Anesthesiologie - Stepaniak PS*

*Impactfactor: 3.286*

### **Nienhuijs SW**

#### **Indications and Short-Term Outcomes of Revisional Surgery After Failed or Complicated Sleeve Gastrectomy**

Rutte PW van\*, Smulders JF\*, Zoete JP de\*, Nienhuijs SW\*

Obes Surg. 2012 Dec;22(12):1903-8. Epub 2012 Sep 22

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: 3.286*

## **Nienhuijs SW**

### **Intervention techniques for chronic postherniorrhaphy pain**

Thomassen I\*, Suijlekom HA van \*, Gaag A van der \*, Nienhuijs SW\*

European Surgery 2012;44(3):132-7

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: 0.283*

## **Nienhuijs SW**

### **Laparoscopic Sleeve Gastrectomy Feasible for Bariatric Revision Surgery**

Berende CA\*, Zoete JP de\*, Smulders JF\*, Nienhuijs SW\*

Obes Surg. 2012 Feb;22(2):330-4. Epub 2011 Aug 25

*Voor abstract zie: Chirurgie - Berende CA*

*Impactfactor: 3.286*

## **Nienhuijs SW**

### **Nationwide improvement of only short-term survival after resection for pancreatic cancer in the Netherlands**

Nienhuijs SW\*, Akker SA van den, Vries E de, Hingh IH de\*, Visser O, Lemmens VE

Pancreas. 2012 Oct;41(7):1063-6

**OBJECTIVES:** Evaluation of incidence, treatment, and survival trends after resection of pancreatic cancer at a national level.

**METHODS:** Using data on patient and tumor characteristics from the nationwide Netherlands Cancer Registry trends were analyzed for the period 1989-2008.

**RESULTS:** A total of 30,025 patients diagnosed with pancreatic cancer were included. The incidence remained stable over the 20-year study period at approximately 9 per 100,000 inhabitants. Resection rates increased from 8% in 1989 to 12% in 2008, adjuvant chemotherapy rates increased from 7% to 29%, and palliative chemotherapy rates increased from 5% to 19% ( $P < 0.0001$  each). Relative survival proportions did not change over time; besides a minimal, nonsignificant increase at 3 months from 53% to 55%, these remained 34% at 6 months and 4.5% at 3 years. Among the patients undergoing tumor resection, relative survival increased from 82% to 93% at 3 months and from 51% to 63% at 1 year after diagnosis. However, no improvement was seen after 3 years (23%).

**CONCLUSIONS:** The increased short-term survival among patients who underwent resection probably reflects decreased postoperative mortality driven by ongoing centralization efforts. However, longer-term survival remained poor irrespective of the changes in management in the past decades.

*Impactfactor: 2.386*

## **Nienhuijs SW**

### **Pathogenesis of the epigastric hernia**

Ponten JE\*, Somers KY\*, Nienhuijs SW\*

Hernia. 2012 Dec;16(6):627-33. Epub 2012 Jul 24

*Voor abstract zie: Chirurgie - Ponten JE*

*Impactfactor: 1.843*

## **Nienhuijs SW**

### **Perineal hernia repair after abdominoperineal rectal excision**

Martijnse IS\*, Holman F\*, Nieuwenhuijzen GA\*, Rutten HJ\*, Nienhuijs SW\*

Dis Colon Rectum. 2012 Jan;55(1):90-5

Voor abstract zie: *Chirurgie - Maaskant Braat AJ*

*Impactfactor: 3.132*

## **Nienhuijs SW**

### **Peritoneal carcinomatosis of colorectal origin: Incidence, prognosis and treatment options**

Klaver YL\*, Lemmens VE, Nienhuijs SW\*, Luyer MD\*, Hingh IH de\*

World J Gastroenterol. 2012 Oct 21;18(39):5489-94

Voor abstract zie: *Chirurgie - Klaver YL*

*Impactfactor: 2.471*

## **Nienhuijs SW**

### **Randomized controlled multicenter international clinical trial of self-gripping Parietex" ProGrip" polyester mesh versus lightweight polypropylene mesh in open inguinal hernia repair: interim results at 3 months**

Kingsnorth A, Gingell-Littlejohn M, Nienhuijs S\*, Schüle S, Appel P, Ziprin P, Eklund A, Miserez M, Smeds S

Hernia. 2012 Jun;16(3):287-94. Epub 2012 Mar 28

**PURPOSE:** To compare clinical outcomes following sutureless Parietex" ProGrip" mesh repair to traditional Lichtenstein repair with lightweight polypropylene mesh secured with sutures.

**METHODS:** This is a 3-month interim report of a 1-year multicenter international study. Three hundred and two patients were randomized; 153 were treated with Lichtenstein repair (L group) and 149 with Parietex" ProGrip" precut mesh (P group) with or without fixation. The primary outcome measure was postoperative pain using the visual analog scale (VAS, 0-150 mm); other outcomes were assessed prior to surgery and up to 3 months postoperatively.

**RESULTS:** Compared to baseline, pain score was lower in the P group at discharge (-10%) and at 7 days (-13%), while pain increased in the L group at discharge (+39%) and at 7 days (+21%). The difference between groups was significant at both time points ( $P = 0.007$  and  $P = 0.039$ , respectively). In the P group, patients without fixation suffered less pain compared to those with single-suture fixation (1 month: -20.9 vs. -6.15%,  $P = 0.02$ ; 3 months: -24.3 vs. -7.7%,  $P = 0.01$ ). The infection rate was significantly lower in the P group during the 3-month follow-up (2.0 vs. 7.2%,  $P = 0.032$ ). Surgery duration was significantly shorter in the P group (32.4 vs. 39.1 min;  $P < 0.001$ ). No recurrence was observed at 3 months in both groups.

**CONCLUSIONS:** Surgery duration, early postoperative, pain and infection rates were significantly reduced with self-gripping polyester mesh compared to Lichtenstein repair with polypropylene mesh. The use of fixation increased postoperative pain in the P group. The absence of early recurrence highlights the gripping efficiency effect.

*Impactfactor: 1.843*

## **Nienhuijs SW**

### **Steroid use is associated with clinically irrelevant biopsies in patients with suspected giant cell arteritis**

Thomassen I\*, Brok AN den, Konings CJ\*, Nienhuijs SW\*, Poll MC van de\*

Am Surg. 2012 Dec;78(12):1362-8

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: 1.285*

## **Nienhuijs SW**

### **To Sleeve or NOT to Sleeve in Bariatric Surgery?**

Rutte PW van\*, Luyer MD\*, Hingh IH de\*, Nienhuijs SW\*

ISRN Surg. 2012;2012:674042. Epub 2012 Aug 16

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: --*

## **Nienhuijs SW**

### **Uncommon complications of biliary stones**

Janssen S\*, Mierlo I van\*, Gilissen LP\*, Nienhuijs SW\*, Heemskerk J

Open Journal of Internal Medicine, 2012, 2, 19-26

*Voor abstract zie: Maag-darm-leverziekten - Janssen SJ*

*Impactfactor: --*

## **Nieuwenhuijzen GA**

### **Acute cholecystitis in high risk surgical patients: percutaneous cholecystostomy versus laparoscopic cholecystectomy (CHOCOLATE Trial): Study protocol for a randomized controlled trial**

Kortram K, Ramshorst B van, Bollen TL, Besselink MG, Gouma DJ, Karsten T, Kruyt PM, Nieuwenhuijzen GA\*, Kelder JC, Tromp E, Boerma D

Trials. 2012 Jan 12;13(1):7

**BACKGROUND:** Laparoscopic cholecystectomy in acute calculous cholecystitis in high risk patients can lead to significant morbidity and mortality. Percutaneous cholecystostomy may be an alternative treatment option but the current literature does not provide the surgical community with evidence based advice.

**METHODS:** The CHOCOLATE trial is a randomised controlled, parallel-group, superiority multicenter trial. High risk patients, defined as APACHE-II score 7-14, with acute calculous cholecystitis will be randomised to laparoscopic cholecystectomy or percutaneous cholecystostomy. During a two year period 284 patients will be enrolled from 30 high volume teaching hospitals. The primary endpoint is a composite endpoint of major complications within three months following randomization and need for reintervention and mortality during the follow-up period of one year. Secondary endpoints include all other complications, duration of hospital admission, difficulty of procedures and total costs.

**DISCUSSION:** The CHOCOLATE trial is designed to provide the surgical community with an evidence based guideline in the treatment of acute calculous cholecystitis in high risk patients.

*Impactfactor: 2.496*

## **Nieuwenhuijzen GA**

### **An abnormal screening mammogram causes more anxiety than a palpable lump in benign breast disease**

Keyzer-Dekker CM, Esch L van, Vries J de, Ernst MF, Nieuwenhuijzen GA\*, Roukema JA, Steeg AF van der

Breast Cancer Res Treat. 2012 Jul;134(1):253-8. Epub 2012 Mar 21

Being recalled for further diagnostic procedures after an abnormal screening mammogram (ASM) can evoke a high state anxiety with lowered quality of life (QoL). We examined whether these adverse psychological consequences are found in all women with benign breast disease (BBD) or are particular to women referred after ASM. In addition, the influence of the anxiety as a personality characteristic (trait anxiety) was studied. Between September 2002 and February 2010 we performed a prospective longitudinal study in six Dutch hospitals. Women referred after ASM or with a palpable lump in the breast (PL), who were subsequently diagnosed with BBD, were included. Before diagnosis (at referral) and during follow-up, questionnaires were completed examining trait anxiety (at referral), state anxiety, depressive symptoms (at referral, one, three and 6 months after diagnosis), and QoL (at referral and 12 months). Women referred after ASM (N=363) were compared with women with PL (N=401). A similar state anxiety score was found in both groups, but a lower psychological QoL score at 12 months was seen in the ASM group. In women with not-high trait anxiety those in the ASM group were more anxious with more depressive symptoms at referral, and reported impaired psychological QoL at referral and at 12 months compared with the PL group. No differences were found between ASM and PL in women with high trait anxiety, but this group scored unfavorably on anxiety, depressive symptoms and QoL compared with women with not-high trait anxiety. ASM evokes more anxiety and depressive symptoms and lowered QoL compared with women referred with PL, especially in women who are not prone to anxiety. Women should be fully informed properly about the risks and benefits of breast cancer screening programs. We recommend identifying women at risk of reduced QoL using a psychometric test.

*Impactfactor: 5.245*

## **Nieuwenhuijzen GA**

### **Anxiety after an abnormal screening mammogram is a serious problem**

Keyzer-Dekker CM, Vries J de, Esch L van, Ernst MF, Nieuwenhuizen GA\*, Roukema JA, Steeg AF van der

Breast. 2012 Feb;21(1):83-8. Epub 2011 Sep 15

**PURPOSE:** The aim of this study was to analyze the possible negative psychological consequences of a false positive screening mammogram (FPSM). We compared anxiety evoked by first (FSM) versus repeat screening mammogram (RSM). Questionnaires were completed prior to the diagnosis and during follow up.

**RESULTS:** No differences in anxiety, depressive symptoms, and Quality of Life (QoL) were found between FSM (N = 186) or RSM (N = 296) groups. All women experienced high anxiety before diagnosis was known. High trait anxiety was predictive for more anxiety, depressive symptoms, and lower QoL. Women with low score on trait anxiety were more momentary anxious in FSM group compared with RSM group ( $p = 0.048$ ).

**CONCLUSION:** Negative psychological consequences after an FPSM are seen in all women. These effects are strengthened by personality and timing of the screening mammogram. All women should receive correct information concerning the negative psychological effects and should be offered psychosocial support if needed.

*Impactfactor: 2.491*

## **Nieuwenhuijzen GA**

### **Axillary and systemic treatment of patients with breast cancer and micrometastatic disease or isolated tumor cells in the sentinel lymph node**

Maaskant-Braat AJ\*, Voogd AC, Poll-Franse LV van de, Coebergh JW, Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):524-8

*Voor abstract zie: Chirurgie - Maaskant-Braat AJ*

*Impactfactor: 2.491*

## **Nieuwenhuijzen GA**

### **Combined anxiety and depressive symptoms before diagnosis of breast cancer**

Esch L van, Roukema JA, Ernst MF, Nieuwenhuijzen GA\*, Vries J de

J Affect Disord. 2012 Feb;136(3):895-901. Epub 2011 Oct 4

**PURPOSE:** To determine the relationship between pre-diagnosis state anxiety, depressive symptoms, and combined state anxiety and depressive symptoms (CADS) with quality of life (QOL), fatigue, state anxiety and depressive symptoms one and two years after surgery in women with breast cancer.

**METHODS:** Women with breast problems referred to a Dutch outpatient clinic were recruited for the study. Participants (N=428) completed a set of questionnaires before diagnosis (Time0) and the women with breast cancer subsequently received questionnaires at 12 (Time1) and 24months (Time2) after surgical treatment. The questionnaire set consisted of questionnaires on demographics, state anxiety, depressive symptoms, fatigue, QOL, neuroticism, and trait anxiety. Chi-square tests, independent samples T-tests, and multivariate linear regression analyses were used to do the analyses.

**RESULTS:** Before their diagnosis of breast cancer, 111 women (28%) had CADS. Of the CADS-group, a higher percentage had elevated levels of anxiety, depressive symptoms, and CADS at all follow-up moments than of the non-CADS-group. CADS-score at before diagnosis and neuroticism were the most important predictors of outcome measures at Time1 and Time2.

**CONCLUSIONS:** More than one in four women, who later received the diagnosis breast cancer, had elevated levels of both state anxiety and depressive symptoms (CADS) just before diagnosis. This factor was also a major predictor of QOL, state anxiety, depressive symptoms, and fatigue 12 and 24months after surgery. This implies that women with a higher score on both state anxiety and depressive symptoms should be identified as soon as possible in the process of diagnosis and treatment of breast cancer using validated questionnaires or screening instruments. Only by identifying this group of patients, tailored psychological care can be accomplished.

*Impactfactor: 3.517*

## **Nieuwenhuijzen GA**

### **Focus on extralevator perineal dissection in supine position for low rectal cancer has led to better quality of surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D\*, Nieuwenhuijzen GA\*,

Lijnschoten I van\*, Martijn H\*, Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Nieuwenhuijzen GA**

### **Hormone treatment without surgery for patients aged 75 years or older with operable breast cancer**

Wink CJ, Woensdregt K\*, Nieuwenhuijzen GA\*, Sangen MJ van der\*,

Hutschemaekers S, Roukema JA, Tjan-Heijnen VC, Voogd AC

Annals of Surgical Oncology 2012 Apr;19(4):1185-91. Epub 2011 Oct 27

Voor abstract zie: *Chirurgie - Woensdregt K*

*Impactfactor: 4.166*

## **Nieuwenhuijzen GA**

### **Increased incidence and survival for oesophageal cancer but not for gastric cardia cancer in the Netherlands**

Dikken JL, Lemmens VE, Wouters MW, Wijnhoven BP, Siersema PD, Nieuwenhuijzen

GA\*, Sandick JW van, Cats A, Verheij M, Coebergh JW, Velde CJ van de

Eur J Cancer. 2012 Jul;48(11):1624-32. Epub 2012 Feb 6

INTRODUCTION: A worldwide increasing incidence is seen for oesophageal adenocarcinoma, but not for oesophageal squamous cell carcinoma (SCC) and gastric cardia adenocarcinoma. Purposes of the current study were to evaluate the changing incidence rates of oesophageal and gastric cardia cancer, and to assess survival trends.

PATIENTS AND METHODS: Patients diagnosed with oesophageal adenocarcinoma (N=12,195) or SCC (N=9046), or gastric cardia adenocarcinoma (N=9900) between 1989 and 2008 in the Netherlands were included. Changes in European Standard Population (ESP) and relative survival over time were evaluated.

RESULTS: Incidence rates for oesophageal adenocarcinoma increased in males (+7.5%,  $P<0.001$ ) and females (+5.2%,  $P<0.001$ ), while the incidence for oesophageal SCC remained stable in males (-0.2%,  $P=0.6$ ) and slightly increased in females (+1.7%,  $P=0.001$ ). The incidence for gastric cardia cancer decreased in males (-1.2%,  $P<0.006$ ), and remained stable in females (-0.2%,  $P=0.7$ ). Five-year survival for both M0 and M1 oesophageal carcinoma doubled over the last 20years. No significant changes in survival were found for M0 and M1 gastric cardia carcinoma.

DISCUSSION: In the Netherlands, a rising incidence is seen for oesophageal adenocarcinoma, but not for gastric cardia adenocarcinoma. This finding most likely reflects true changes in disease burden, rather than being the result of changes in diagnosis or classification. The increased survival for oesophageal carcinoma can be attributed to centralisation of surgery, and an increased use of multimodality therapy, factors hardly acknowledged for gastric cancer.

*Impactfactor: 5.536*

## **Nieuwenhuijzen GA**

### **Increased Resection Rates and Survival Among Patients Aged 75 Years and Older with Esophageal Cancer: A Dutch Nationwide Population-Based Study**

Faiz Z, Lemmens VE, Siersema PD, Nieuwenhuijzen GA\*, Wouters MW, Rozema T,

Coebergh JW, Wijnhoven BP

World J Surg. 2012 Dec;36(12):2872-8

BACKGROUND: The incidence of esophageal cancer has grown over the recent decades and 30 % of esophageal cancer patients are now 75 years or older at the time of diagnosis. The aim of this study was to evaluate trends in management and survival of patients aged 75 years or older with esophageal cancer.

**METHODS:** In the Netherlands cancer registry, we identified all patients aged 75 years or older who were diagnosed with esophageal cancer between 1989 and 2008. Trends in management and survival were analyzed by time period (1989-2001 vs. 2002-2008), TNM stage, and age (75-79, 80-84, and 85+ years). (2) testing was used to analyze time trends in treatment, Kaplan-Meier analysis and log-rank testing to estimate survival, and Cox regression model to calculate hazard ratios for death.

**RESULTS:** Some 7,253 patients were included in the study. The surgical resection rate increased over the 1989-2008 period from 8.9 to 12.6 % ( $p = 0.028$ ), especially among patients aged 75-79 years (44.6 vs. 55.4 %,  $p < 0.001$ ) and patients with TNM stage I disease (12.7 vs. 22.0 %,  $p < 0.001$ ). The use of definitive chemoradiotherapy (CRT) also increased (0.19 vs. 2.20 %,  $p < 0.001$ ). Whereas the use of chemotherapy as a single-modality treatment more than doubled (0.64 vs. 1.54 %,  $p = 0.004$ ), that of radiotherapy alone decreased (38.1 vs. 31.6 %,  $p < 0.001$ ). Although median survival time was marginally higher in the 2002-2008 period than in 1989-2001, overall 5 year survival rates remained low at 6 and 5 %, respectively ( $p < 0.001$ ). Five-year survival rate after surgery increased from 16 to 30 % ( $p < 0.001$ ).

**CONCLUSIONS:** In patients of 75 years or older, surgical treatment and use of definitive CRT have increased between 1989 and 2008. Also, an increase in the use of chemotherapy as a single modality was noted. Overall 5 year survival for all cancer patients was stable but remained poor, while survival of patients who underwent esophagectomy improved significantly in the Netherlands since 1989.

*Impactfactor: 2.362*

## **Nieuwenhuijzen GA**

### **Lymphatic mapping after previous breast surgery**

Maaskant-Braat AJ\*, Bruijn SZ de, Woensdregt K\*, Pijpers H\*, Voogd AC, Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):444-8. Epub 2011 Nov 21

*Voor abstract zie: Chirurgie - Maaskant Braat AJ*

*Impactfactor: 2.491*

## **Nieuwenhuijzen GA**

### **Lymphatic mapping after previous breast surgery**

Maaskant-Braat AJ\*, Bruijn SZ de, Woensdregt K\*, Pijpers H\*, Voogd AC, Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):444-8. Epub 2011 Nov 21

*Voor abstract zie: Chirurgie - Maaskant Braat AJ*

*Impactfactor: 2.491*

## **Nieuwenhuijzen GA**

### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*, Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 2.499*

## **Nieuwenhuijzen GA**

### **Perineal hernia repair after abdominoperineal rectal excision**

Martijnse IS\*, Holman F\*, Nieuwenhuijzen GA\*, Rutten HJ\*, Nienhuijs SW\*

Dis Colon Rectum. 2012 Jan;55(1):90-5

Voor abstract zie: *Chirurgie - Maaskant Braat AJ*

*Impactfactor: 3.132*

## **Nieuwenhuijzen GA**

### **Preoperative chemoradiotherapy for esophageal or junctional cancer**

Hagen P van, Hulshof MC, Lanschot JJ van, Steyerberg EW, Berge Henegouwen MI van, Wijnhoven BP, Richel DJ, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Kate FJ ten, Creemers GJ\*, Punt CJ, Plukker JT, Verheul HM, Spillenaar Bilgen EJ, Dekken H van, Sangen MJ van der\*, Rozema T, Biermann K, Beukema JC, Piet AH, Rij CM van, Reinders JG, Tilanus HW, Gaast A van der; CROSS Group

N Engl J Med. 2012 May 31;366(22):2074-84

**BACKGROUND:** The role of neoadjuvant chemoradiotherapy in the treatment of patients with esophageal or esophagogastric-junction cancer is not well established. We compared chemoradiotherapy followed by surgery with surgery alone in this patient population.

**METHODS:** We randomly assigned patients with resectable tumors to receive surgery alone or weekly administration of carboplatin (doses titrated to achieve an area under the curve of 2 mg per milliliter per minute) and paclitaxel (50 mg per square meter of body-surface area) for 5 weeks and concurrent radiotherapy (41.4 Gy in 23 fractions, 5 days per week), followed by surgery.

**RESULTS:** From March 2004 through December 2008, we enrolled 368 patients, 366 of whom were included in the analysis: 275 (75%) had adenocarcinoma, 84 (23%) had squamous-cell carcinoma, and 7 (2%) had large-cell undifferentiated carcinoma. Of the 366 patients, 178 were randomly assigned to chemoradiotherapy followed by surgery, and 188 to surgery alone. The most common major hematologic toxic effects in the chemoradiotherapy-surgery group were leukopenia (6%) and neutropenia (2%); the most common major nonhematologic toxic effects were anorexia (5%) and fatigue (3%). Complete resection with no tumor within 1 mm of the resection margins (R0) was achieved in 92% of patients in the chemoradiotherapy-surgery group versus 69% in the surgery group ( $P < 0.001$ ). A pathological complete response was achieved in 47 of 161 patients (29%) who underwent resection after chemoradiotherapy. Postoperative complications were similar in the two treatment groups, and in-hospital mortality was 4% in both. Median overall survival was 49.4 months in the chemoradiotherapysurgery group versus 24.0 months in the surgery group. Overall survival was significantly better in the chemoradiotherapy-surgery group (hazard ratio, 0.657; 95% confidence interval, 0.495 to 0.871;  $P = 0.003$ ).

**CONCLUSIONS:** Preoperative chemoradiotherapy improved survival among patients with potentially curable esophageal or esophagogastric-junction cancer. The regimen was associated with acceptable adverse-event rates.

*Impactfactor: 53.298*

## **Nieuwenhuijzen GA**

### **T3+ and T4 rectal cancer patients seem to benefit from the addition of oxaliplatin to the neoadjuvant chemoradiation regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE van de, Velde CJ, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Nieuwenhuijzen GA**

### **The effect of socioeconomic status on staging and treatment decisions in esophageal cancer**

Bus P, Aarts MJ, Lemmens VE, Oijen MG van, Creemers GJ\*, Nieuwenhuijzen GA\*, Baal JW van, Siersema PD

J Clin Gastroenterol. 2012 Nov;46(10):833-9

*Voor abstract zie: Inwendige geneeskunde - Creemers GJ*

*Impactfactor: 3.159*

## **Poll MC van den**

### **Een jongen met pijn rechts in de onderbuik. [13-Year old boy with abdominal pain]**

Thomassen I\*, Klinkhamer PJ\*, Poll MC van den\*

Ned Tijdschr Geneeskd. 2012;156(18):A3566

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: --*

## **Poll MC van den**

### **Steroid use is associated with clinically irrelevant biopsies in patients with suspected giant cell arteritis**

Thomassen I\*, Brok AN den, Konings CJ\*, Nienhuijs SW\*, Poll MC van de\*

Am Surg. 2012 Dec;78(12):1362-8

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: 1.285*

## **Ponten JE**

### **Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter \*, Korsten EH\*, Borne BE van den\*, Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72. Epub 2012 May 25

Cardiac herniation after pneumonectomy is recognized as a rare complication. This case report describes two cases. The mortality rate of this complication remains high as reported in the literature; in early-recognized cases 50 % and in late or unrecognized cases 100 %. In the following two cases a pneumonectomy was performed as a treatment for lung cancer. Within 48 h after the initial operative treatment, the clinical situation of the patients got worse and radiographic examinations showed a strongly deviated heart. After suspicion of the diagnosis, the patients were immediately transferred to the operation theatre for

emergency thoracotomy. Per-operative the diagnosis was confirmed and the heart was returned into its original position while the defect in the pericardial sac was closed with a bovine pericardial patch. Both patients survived these procedures and did not suffer from any further complication.

*Impactfactor: --*

## **Ponten JE**

### **Pathogenesis of the epigastric hernia**

Ponten JE\*, Somers KY\*, Nienhuijs SW\*

Hernia. 2012 Dec;16(6):627-33. Epub 2012 Jul 24

**PURPOSE:** Epigastric herniation is a rather common condition with a reported prevalence up to 10 %. Only a minority is symptomatic, presumably the reason for the scarce literature on this subject. Epigastric hernias have specific characteristics for which several anatomical theories have been developed. Whether these descriptions of pathological mechanisms still hold with regard to the characteristics of epigastric hernia is the subject of this review.

**METHODS:** A multi-database research was performed to reveal relevant literature by free text word and subject headings 'epigastric hernia', 'linea alba', 'midline' and 'abdominal wall'. Reviewed were studies on anatomical theories describing the pathological mechanism of epigastric herniation, incidence, prevalence and female-to-male ratio and possible explanatory factors.

**RESULTS:** Three different theories have been described of which two have not been confirmed by other studies. The attachment of the diaphragm causing extra tension in the epigastric region is the one still standing. Around 1.6-3.6 % of all abdominal hernias and 0.5-5 % of all operated abdominal hernias is an epigastric hernia. Epigastric hernias are 2-3 times more common in men, with a higher incidence in patients from 20 to 50 years. Some cadaver studies show an epigastric hernia rate of 0.5-10 %. These specific features of the epigastric hernias (the large asymptomatic proportion, male predominance, only above umbilical level) are discussed with regard to the general theories.

**CONCLUSIONS:** The epigastric hernia is a very common condition, mostly asymptomatic. Together with general factors for hernia formation, the theory of extra tension in the epigastric region by the diaphragm is the most likely theory of epigastric hernia formation.

*Impactfactor: 1.843*

## **Rutte PW van**

### **Indications and short-term outcomes of revisional surgery after failed or complicated sleeve gastrectomy**

Rutte PW van\*, Smulders JF\*, Zoete JP de\*, Nienhuijs SW\*

Obes Surg. 2012 Dec;22(12):1903-8. Epub 2012 Sep 22

**BACKGROUND:** Sleeve gastrectomy (SG) is an upcoming primary treatment modality for morbid obesity. The aim of this study was to report the indications for and the outcomes of revisional surgery after SG.

**METHODS:** Four hundred sixteen individuals underwent a SG between August 2006 and July 2010 with a minimum follow-up of 12 months. The patients that needed revision were identified from our prospective registry. Patients were subdivided in a first group undergoing revision as part of a two-step procedure, a second group with failure of a secondary SG, and a third group with failure of a primary SG.

**RESULTS:** Twenty-three patients (5.5 %) had an unplanned revision. Fourteen (3.4 %) had a two-step procedure because of super obesity. A significant additional weight loss was achieved after revision; no complications occurred in this group. Five patients with failure of

a secondary SG had no significant additional weight loss after revision. Reflux disease was cured. Eighteen patients in the third group showed significant additional weight loss and remission of diabetes and hypertension. Both reflux disease and dysphagia did not heal in all affected patients after revision. The early complication rate in the whole cohort was 23.4 %; staple line leakage was 5.4 %, and bleeding was 8.1 %. Revision-related mortality was 0 %.

CONCLUSION: In a large series of sleeve gastrectomies, the unplanned revision rate was 5.5 %. Revision of a sleeve gastrectomy is feasible in patients that do not achieve sufficient weight loss and in those patients developing complications after the initial sleeve gastrectomy.

*Impactfactor: 3.286*

## **Rutte PW van**

### **To sleeve or NOT to sleeve in bariatric surgery?**

Rutte PW van\*, Luyer MD\*, Hingh IH de\*, Nienhuijs SW\*

ISRN Surg. 2012;2012:674042. Epub 2012 Aug 16

Morbid obesity has become a global epidemic during the 20th century. Until now bariatric surgery is the only effective treatment for this disease leading to sustained weight loss and improvement of comorbidities. The sleeve gastrectomy is becoming a promising alternative for the gold standard the gastric bypass and it is gaining popularity as a stand-alone procedure. The effect of the laparoscopic sleeve gastrectomy is based on a restrictive mechanism, but a hormonal effect also seems to play an important role. Similar results are achieved in terms of excess weight loss and resolution of comorbidities compared to the gastric bypass. Inadequate weight loss or weight regain can be treated by revisional surgery. Complication rates after LSG appear to be lower compared with gastric bypass. General guidelines recommend bariatric surgery between the age of 18 and 65. However bariatric surgery in the elderly seems safe with respect to weight loss and resolution of comorbidities. At the same time weight loss surgery is more often performed in adolescent patients failing weight loss attempts. Even though more studies are needed describing long-term effects, there is already enough evidence that this technique is an effective single procedure for a considerable proportion of obese patients.

*Impactfactor: --*

## **Rutten HJ**

### **Comparison of magnetic resonance imaging and histopathological response to chemoradiotherapy in locally advanced rectal cancer**

Patel UB, Brown G, Rutten HJ\*, West N, Sebag-Montefiore D, Glynne-Jones R, Rullier E, Peeters M, Cutsem E van, Ricci S, Velde C van de, Kjell P, Quirke P

Ann Surg Oncol. 2012 Sep;19(9):2842-52

BACKGROUND: Magnetic resonance imaging (MRI) methods for chemoradiotherapy (CRT) response assessment of rectal cancer include posttreatment T staging (ymrT), tumor regression grading (mrTRG), volume reduction posttreatment, and modified RECIST measurement. We compared these methods in identifying good versus poor responders with the histopathological standards of T stage (ypT) and tumor regression grading (TRG).

METHODS: A total of 86 patients underwent CRT in a prospective phase II trial for MRI-defined locally advanced rectal cancer. Two readers independently assessed MRIs for ymrT, mrTRG, volume change, and RECIST. Parameters for each case were categorized as good or poor response and analyzed against ypT and TRG by univariate logistic regression.

RESULTS: A total of 83 patients had evaluable imaging, and 78 had final pathology (five did not undergo surgery). Of these, 34 patients had good response (ypT0-3a) and 44 had poor

response (>ypT3a). Also, 27 patients had favorable pathologic TRG (predominant fibrosis) and 51 had unfavorable TRG (predominant tumor). Good mrTRG and ymr <T3b stage were both significantly (P = 0.001) associated with favorable pathology odds ratio [OR] = 16.11 (95 % confidence interval [95 % CI]: 3.36-77.29) and 17.50 (95 % CI: 5.38-56.89), respectively. RECIST measurements and volumereduction of >80 % showed an OR of 3.23 (95 % CI: 1.14-9.17), 4.25 (95 % CI: 0.92-15.45), respectively, for a good ypT score (P = 0.028), but there was no association for histopathological TRG.

CONCLUSION: Favorable and unfavorable histopathology are predicted by both ymrT and mrTRG, and we recommend these parameters for post-treatment assessment of rectal cancers treated with CRT.

*Impactfactor: 4.166*

## **Rutten HJ**

### **Focus on Extralevator Perineal Dissection in Supine Position for Low Rectal Cancer Has Led to Better Quality of Surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D,\* Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H,\* Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Rutten HJ**

### **Increased adjuvant treatment and improved survival in elderly stage III colon cancer patients in The Netherlands**

Steenbergen LN van, Lemmens VE, Rutten HJ\*, Wymenga AN, Nortier JW, Janssen-Heijnen ML

Ann Oncol. 2012 Nov;23(11):2805-11. Epub 2012 May 4

Background We determined to what extent patients with colon cancer stage III e 75 years received adjuvant chemotherapy and the impact on overall and disease-specific survival. Patients and methods Data from The Netherlands Cancer Registry on all 8051 patients with colon cancer stage III e 75 years diagnosed in 1997-2009 were included. Trends in adjuvant chemotherapy administration were analysed and multivariable overall and disease-specific survival analyses were performed. Results The proportion of stage III colon cancer patients e 75 years who received adjuvant chemotherapy increased from 12% in 1997-2000 to 23% in 2007-2009 (P < 0.0001), with a marked age gradient and large geographic variation. Five-year overall survival increased over time from 28% in 1997-2000 to 35% in 2004-2006 (P < 0.0001). Sixty percent of patients died of colorectal cancer. Adjuvant chemotherapy was the strongest positive predictor of survival in this retrospective study (hazard ratio = 0.5; 95% confidence interval: 0.4 -0.5). Conclusion There has been an increase in administration of adjuvant chemotherapy to elderly patients with stage III colon cancer in The Netherlands since 1997. Survival of elderly patients with stage III colon cancer increased over time, at least partly due to stage migration. The large effect of adjuvant chemotherapy on survival in this study is likely to be associated with the selection of fitter patients for adjuvant treatment.

*Impactfactor: 6.425*

## **Rutten HJ**

### **Intraoperative versus early postoperative intraperitoneal chemotherapy after cytoreduction for colorectal peritoneal carcinomatosis: an experimental study**

Klaver YL\*, Hendriks T, Lomme RM, Rutten HJ\*, Bleichrodt RP, Hingh IH de\*

Ann Surg Oncol. 2012 Jul;19 Suppl 3:S475-82. Epub 2011 Aug 12

Voor abstract zie: *Chirurgie - Klaver YL*

Impactfactor: 4.166

## **Rutten HJ**

### **Local application of gentamicin-containing collagen implant in the prophylaxis and treatment of surgical site infection**

Rutten HJ\*

Int J Surg. 2012;10 Suppl 1:S1

Impactfactor: --

## **Rutten HJ**

### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*, Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

Voor abstract zie: *Chirurgie - Martijnse IS*

Impactfactor: 2.499

## **Rutten HJ**

### **Perineal hernia repair after abdominoperineal rectal excision**

Martijnse IS\*, Holman F\*, Nieuwenhuijzen GA\*, Rutten HJ\*, Nienhuijs SW\*

Dis Colon Rectum. 2012 Jan;55(1):90-5

Voor abstract zie: *Chirurgie - Maaskant Braat AJ*

Impactfactor: 3.132

## **Rutten HJ**

### **T3+ and T4 Rectal Cancer Patients Seem to Benefit From the Addition of Oxaliplatin to the Neoadjuvant Chemoradiation Regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

Voor abstract zie: *Chirurgie - Martijnse IS*

Impactfactor: 4.166

## **Rutten HJ**

### **The hospital standardized mortality ratio fallacy: a narrative review**

Gestel YR van, Lemmens VE, Lingsma HF, Hingh IH de\*, Rutten HJ\*, Coebergh JW

Med Care. 2012 Aug;50(8):662-7

Voor abstract zie: *Chirurgie - Hingh IH de*

Impactfactor: 3.411

**Sambeek MR van**

**Early results from the ENGAGE Registry: Real-world Performance of the Endurant Stent Graft for Endovascular AAA Repair in 1262 patients**

Stokmans RA\*, Teijink JA\*, Forbes TL, Böckler D, Peeters PJ, Riambau V, Hayes PD, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Oct;44(4):369-75. Epub 2012 Jul 24

*Voor abstract zie: Chirurgie - Stokmans RA*

*Impactfactor: 2.991*

**Sambeek MR van**

**EVAR reintervention management strategies in contemporary practice**

Bendermacher BL\*, Stokmans R\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Aug;53(4):411-8

*Voor abstract zie: Chirurgie - Bendermacher BL*

*Impactfactor: 1.559*

**Sambeek MR van**

**No differences in perioperative outcome between symptomatic and asymptomatic AAAs after EVAR: an analysis from the ENGAGE Registry**

Stokmans RA\*, Teijink JA\*, Cuypers PW\*, Riambau V, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Jun;43(6):667-73. Epub 2012 Mar 21

*Voor abstract zie: Chirurgie - Stokmans RA*

*Impactfactor: 2.991*

**Sambeek MR van**

**Systematic approach to ruptured abdominal aortic aneurysm in the endovascular era: Intention-to-treat eEVAR protocol**

Willigendael EM\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Feb;53(1):77-82

*Voor abstract zie: Chirurgie - Willigendael EM*

*Impactfactor: 1.559*

**Sambeek MR van**

**Systematic review of guidelines on abdominal aortic aneurysm screening**

Ferket BS, Grootenboer N, Colkesen EB, Visser JJ, Sambeek MR van\*, Spronk S, Steyerberg EW, Hunink MG

J Vasc Surg. 2012 May;55(5):1296-1304. Epub 2011 Feb 16

**OBJECTIVES:** Usually, physicians base their practice on guidelines, but recommendations on the same topic may vary across guidelines. Given the uncertainties regarding abdominal aortic aneurysm (AAA) screening, physicians should be able to identify systematically and transparently developed recommendations. We performed a systematic review of AAA screening guidelines to assist physicians in their choice of recommendations.

**METHODS:** Guidelines in English published between January 1, 2003 and February 26, 2010 were retrieved using MEDLINE, CINAHL, the National Guideline Clearinghouse, the National Library for Health, the Canadian Medication Association Infobase, and the G-I-N International Guideline Library. Guidelines developed by national and international medical societies from Western countries, containing recommendations on AAA screening were

included. Three reviewers independently assessed rigor of guideline development using the Appraisal of Guidelines Research and Evaluation (AGREE) instrument. Two independent reviewers performed extraction of recommendations.

**RESULTS:** Of 2415 titles identified, seven guidelines were included in this review. Three guidelines were less rigorously developed based on AGREE scores below 40%. All seven guidelines contained a recommendation for one-time screening of elderly men by ultrasonography to select AAAs  $\geq$  5.5 cm for elective surgical repair. Four guidelines, of which three were less rigorously developed, contained disparate recommendations on screening of women and middle-aged men at elevated risk. There was no agreement on the management of smaller AAAs.

**CONCLUSION:** Consensus exists across guidelines on one-time screening of elderly men to detect and treat AAAs  $\geq$  5.5 cm. For other target groups and management of small AAAs, prediction models and cost-effectiveness analyses are needed to provide guidance.

*Impactfactor: 3.153*

### **Sambeek MR van**

#### **Treatment of post-implantation aneurysm growth by laparoscopic sac fenestration: long-term results**

Voûte MT, Bastos Gonçalves FM, Hendriks JM, Metz R, Sambeek MR van\*, Muhs BE, Verhagen HJ

Eur J Vasc Endovasc Surg. 2012 Jul;44(1):40-4. Epub 2012 May 22

**OBJECTIVES:** Sac growth after endovascular aneurysm repair (EVAR) is an important finding, which may influence prognosis. In case of a type II endoleak or endotension, clipping of side branches and subsequent sac fenestration has been presented as a therapeutic alternative. The long-term clinical efficacy of this procedure is unknown.

**METHODS:** The study included eight patients who underwent laparoscopic aortic collateral clipping and sac fenestration for enlarging aneurysms following EVAR. Secondary interventions and clinical outcome were retrieved from hospital records. Sac behaviour was evaluated measuring volumes on periodical computed tomography angiography (CTA) imaging using dedicated software.

**RESULTS:** Follow-up had a median length of 6.6 (range 0.6-8.6) years. During this time, only three patients successfully achieved durable aneurysm shrinkage ( $n = 2$ ) or stability ( $n = 1$ ). The remaining patients suffered persistent ( $n = 2$ ) or recurrent sac growth ( $n = 3$ ), all regarded as failure of fenestration. A total of six additional interventions were performed, comprising open conversion ( $n = 2$ ), relining ( $n = 1$ ) and implantation of iliac extensions ( $n = 3$ ). All additional interventions were successful at arresting further sac growth during the remainder of follow-up.

**CONCLUSIONS:** Despite being a less invasive alternative to conversion and open repair, the long-term outcome of sac fenestration is unpredictable and additional major procedures were often necessary to arrest sac growth.

*Impactfactor: 2.991*

### **Simkens GA**

#### **Acute neurological disorders following intraperitoneal administration of cisplatin**

Simkens GA\*, Hanse MC\*, Hingh IH de \*

Int J Gynaecol Obstet. 2012 Dec 13. pii: S0020-7292(12)00587-5

*Impactfactor: 2.045*

**Smulders JF**

**Indications and short-term outcomes of revisional surgery after failed or complicated sleeve gastrectomy**

Rutte PW van\*, Smulders JF\*, Zoete JP de\*, Nienhuijs SW\*

Obes Surg. 2012 Dec;22(12):1903-8. Epub 2012 Sep 22

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: 3.286*

**Smulders JF**

**Laparoscopic sleeve gastrectomy feasible for bariatric revision surgery**

Berende CA\*, Zoete JP de\*, Smulders JF\*, Nienhuijs SW\*

Obes Surg. 2012 Feb;22(2):330-4. Epub 2011 Aug 25

*Voor abstract zie: Chirurgie - Berende CA*

*Impactfactor: 3.286*

**Stokmans RA**

**Early results from the ENGAGE Registry: Real-world Performance of the Endurant Stent Graft for Endovascular AAA Repair in 1262 patients**

Stokmans RA\*, Teijink JA\*, Forbes TL, Böckler D, Peeters PJ, Riambau V, Hayes PD, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Oct;44(4):369-75. Epub 2012 Jul 24

**OBJECTIVE:** The ENGAGE registry was undertaken to examine the real-world outcome after endovascular abdominal aortic aneurysm (AAA) repair (EVAR) with the Endurant Stent Graft in a large, contemporary, global series of patients.

**METHODS:** From March 2009 to April 2011, 1262 AAA patients (89.6% men; mean age 73.1 years, range 43-93 years) were enrolled from 79 sites in 30 countries and treated with Endurant. Results are described following the reporting standards for EVAR. Follow-up data were tabulated for all 1262 patients at a 30-day follow-up and for the first 500 patients at a 1-year follow-up.

**RESULTS:** Intra-operative technical success was achieved in 99.0% of cases. Within 30 days, adverse events were reported in 3.9% of patients, including a 1.3% mortality rate. Type-I or -III endoleaks were identified in 1.5% of cases. Estimated overall survival, aneurysm-related survival and freedom from secondary interventions at 1 year were 91.6%, 98.6% and 95.1%, respectively. At 1 year, aneurysm size increased  $\leq 5$  mm in 2.8% and decreased  $\leq 5$  mm in 41.3% of cases.

**CONCLUSION:** Early results from this real world, global experience are promising and indicate that endovascular AAA repair with the Endurant Stent Graft is safe and effective across different geographies and standards of practice. Longer-term follow-up is necessary to assess durability of these results.

*Impactfactor: 2.991*

**Stokmans RA**

**EVAR reintervention management strategies in contemporary practice**

Bendermacher BL\*, Stokmans R\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Aug;53(4):411-8

*Voor abstract zie: Chirurgie - Bendermacher BL*

*Impactfactor: 1.559*

**Stokmans RA**

**No differences in perioperative outcome between symptomatic and asymptomatic AAAs after EVAR: an analysis from the ENGAGE Registry**

Stokmans RA\*, Teijink JA\*, Cuypers PW\*, Riambau V, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Jun;43(6):667-73. Epub 2012 Mar 21

AIM: This study aimed to compare the differences in perioperative outcome after endovascular repair of symptomatic abdominal aneurysms (S-AAAs) and elective non-symptomatic AAAs (E-AAAs). Data from the ENGAGE Registry were used for the analysis.

METHODS: Between March 2009 and December 2010, 1200 AAA patients were enrolled from 79 sites in 30 countries and treated with an Endurant Stent Graft. S-AAAs defined as AAAs accompanied by abdominal or back pain, without rupture, were present in 185 (15.4%) patients and E-AAAs in 1015 (84.6%) patients. Multivariate logistic regression was used to compare results.

RESULTS: At baseline, E-AAA patients had larger aneurysms on average ( $P = 0.006$ ) and scored higher ASA classification more often ( $P = 0.001$ ). Further analyses were corrected for baseline differences. Operation time and technical success were comparable, and S-AAAs were admitted to the Intensive Care Unit (ICU) as often as E-AAAs (35.7% vs. 33.4%,  $P = 0.479$ ). Post-operative hospitalisation was similar ( $4.83 \pm 5.29$  in E-AAAs and  $4.37 \pm 3.49$  in S-AAAs,  $P = 0.360$ ). No differences in the occurrence of major adverse events, including mortality, within the 30-day postimplantation were seen between S-AAA and E-AAA patients, respectively, 3.2% and 4.2% ( $P = 0.572$ ).

CONCLUSION: With contemporary devices and technical proficiency, there is no difference in outcome between symptomatic AAA and elective non-symptomatic AAA patients if treated with endovascular techniques.

*Impactfactor: 2.991*

**Teijink JA**

**Applicability of the ankle-brachial-index measurement as screening device for high cardiovascular risk: an observational study**

Bendermacher BL\*, Teijink JA\*, Willigendael EM\*, Bartelink ML, Peters RJ,

Langenberg M, Büller HR, Prins MH

BMC Cardiovasc Disord. 2012 Jul 30;12:59

*Voor abstract zie: Chirurgie - Bendermacher BL*

*Impactfactor: 1.517*

**Teijink JA**

**Chronic Q fever: Review of the literature and a proposal of new diagnostic criteria**

Wegdam-Blans MC\*, Kampschreur LM, Delsing CE, Bleeker-Rovers CP, Sprong T, Kasteren ME van, Notermans DW, Renders NH, Bijlmer HA, Lestrade PJ, Koopmans MP, Nabuurs-Franssen MH, Oosterheert JJ; The Dutch Q fever Consensus Group

J Infect. 2012 Mar;64(3):247-259. Epub 2011 Dec 23

*Voor abstract zie: Pamm - Wegdam-Blans MC*

*Impactfactor: 4.126*

## **Teijink JA**

### **Circulating biomarkers and abdominal aortic aneurysm size**

Hellenthal FA, Pulinx B, Welten RJ, Teijink JA\*, Dieijen-Visser MP van, Wodzig WK, Schurink GW

J Surg Res. 2012 Aug;176(2):672-8. Epub 2011 Oct 11

**BACKGROUND:** Abdominal aortic aneurysm (AAA) is a degenerative disease of the abdominal aorta leading to progressive dilatation, intra-luminal thrombus (ILT) formation, and rupture. Understanding the natural history of AAA is essential, because different processes and, therefore, different biomarkers, could be involved at each stage of disease progression. The purpose of the present study was to investigate the relationship between systemic expression of biomarkers of inflammation and extracellular matrix remodeling and aneurysm size in AAA patients.

**METHODS AND RESULTS:** All consecutive patients admitted to the (out-) patient clinic of the surgical department of two large community centers were prospectively included. Patients were divided into three groups based on their aneurysm diameter: small (30-44 mm; n = 59), medium-sized (45-54 mm; n = 64) or large (≥ 55 mm; n = 95) AAA. Linear regression modeling showed that age and serum hsCRP concentration were positively associated, whereas serum HDL and IgG concentrations were negatively associated with aneurysm size. This regression model was corrected for possible bias due to statin use and center of inclusion; and also indicated that in general men have larger aneurysms compared with women.

**CONCLUSIONS:** Different aneurysm sizes showed different expression pattern of HDL, IgG, and hsCRP. These biomarkers may be useful in predicting AAA progression.

*Impactfactor: 2.247*

## **Teijink JA**

### **David procedure during a reoperation for ongoing chronic Q fever infection of an ascending aortic prosthesis**

Wegdam-Blans MC\*, Woorst JF ter\*, Klompenhouwer EG\*, Teijink JA\*

Eur J Cardiothorac Surg. 2012 Jul;42(1):e19-20. Epub 2012 May 24

*Voor abstract zie: Pamm - Wegdam-Blans MC*

*Impactfactor: 2.550*

## **Teijink JA**

### **Early and mid-term results of a prospective observational study comparing emergency endovascular aneurysm repair with open surgery in both ruptured and unruptured acute abdominal aortic aneurysms**

Bosch JA ten, Willigendael EM\*, Kruidenier LM, Loos ER de, Prins MH, Teijink JA\*

Vascular. 2012 Apr;20(2):72-80. Epub 2012 Mar 27

The aim of the paper is to prospectively describe early and mid-term outcomes for emergency endovascular aneurysm repair (eEVAR) versus open surgery in acute abdominal aortic aneurysms (aAAAs), both unruptured (symptomatic) and ruptured. We enrolled all consecutive patients treated for aAAA at our center between April 2002 and April 2008. The main outcome parameters were 30-day, 6- and 12-month mortality (all-cause and aneurysm-related). Two hundred forty patients were enrolled in the study. In the unruptured aAAA group (n = 111), 47 (42%) underwent eEVAR. The 30-day, 6- and 12-month mortality rates were 6, 13 and 15% in the eEVAR group versus 11% (NS), 13% (NS) and 16% (NS) in the open group, respectively. In the ruptured aAAA group (n = 129), 25 (19%) underwent eEVAR

(mortality rates: 20, 28 and 36%, respectively) compared with 104 (81%) patients who underwent open surgery (mortality rates: 45% (P = 0.021), 60% (P = 0.004) and 63% (P = 0.014), respectively). In conclusion, the present study showed a reduced 30-day, 6- and 12-month mortality of eEVAR compared with open surgery in all patients with aAAA, mainly due to a lower mortality in the ruptured aAAA group. Late aneurysm-related mortality occurred only in the eEVAR group.

*Impactfactor: 0.891*

### **Teijink JA**

#### **Early results from the ENGAGE Registry: Real-world Performance of the Endurant Stent Graft for Endovascular AAA Repair in 1262 patients**

Stokmans RA\*, Teijink JA\*, Forbes TL, Böckler D, Peeters PJ, Riambau V, Hayes PD, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Oct;44(4):369-75.Epub 2012 Jul 24

*Voor abstract zie: Chirurgie - Stokmans RA*

*Impactfactor: 2.991*

### **Teijink JA**

#### **Effect of supervised exercise therapy for intermittent claudication in patients with diabetes mellitus**

Pul KM van, Kruidenier LM, Nicolai SP, Bie RA de, Nieman FH, Prins MH, Teijink JA\*

Ann Vasc Surg. 2012 Oct;26(7):957-63 Epub 2012 Aug 1

**BACKGROUND:** Primary treatment for patients with intermittent claudication is exercise therapy. Diabetes mellitus (DM) is a frequently occurring comorbidity in patients with intermittent claudication, and in these patients, exercise tolerance is decreased. However, there is little literature about the increase in walking distance after supervised exercise therapy (SET) in patients with both intermittent claudication and DM. The objective of this study was to determine the effectiveness of SET for intermittent claudication in patients with DM.

**METHODS:** Consecutive patients with intermittent claudication who started SET were included. Exclusion criteria were Rutherford stage 4 to 6 and the inability to perform the standardized treadmill test. SET was administered according to the guidelines of the Royal Dutch Society for Physiotherapy. At baseline and at 1, 3, and 6 months of follow-up, a standardized treadmill exercise test was performed. The primary outcome measurement was the absolute claudication distance (ACD).

**RESULTS:** We included 775 patients, of whom 230 had DM (29.7%). At 6 months of follow-up, data of 440 patients were available. Both ACD at baseline and at 6 months of follow-up were significantly lower in patients with DM (P < 0.001). However, increase in ACD after 6 months of SET did not differ significantly (P = 0.48) between the DM group and the non-DM group (270 m and 400 m, respectively).

**CONCLUSION:** In conclusion, SET for patients with intermittent claudication is equally effective in improving walking distance for both patients with and without DM, although ACD remains lower in patients with DM.

*Impactfactor: 1.035*

### **Teijink JA**

#### **Endovascular treatment of a hepatic artery pseudoaneurysm associated with gastrointestinal tract bleeding**

Vainas T\*, Klompenhouwer E\*, Duijm L\*, Tielbeek X\*, Teijink J\*

J Vasc Surg. 2012 Apr;55(4):1145-9. Epub 2012 Feb 25

*Voor abstract zie: Chirurgie - Vainas T*

*Impactfactor: 3.153*

### **Teijink JA**

#### **EVAR reintervention management strategies in contemporary practice**

Bendermacher BL\*, Stokmans R\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Aug;53(4):411-8

*Voor abstract zie: Chirurgie - Bendermacher BL*

*Impactfactor: 1.559*

### **Teijink JA**

#### **Left ventricular endocardial pacing in cardiac resynchronisation therapy: Moving from bench to bedside**

Bracke FA\*, Gelder BM van \*, Dekker LR\*, Houthuizen P\*, Woorst JF ter\*, Teijink JA\*

Neth Heart J. 2012 Mar;20(3):118-24. Epub 2011 Nov 9

*Voor abstract zie: Cardiologie - Bracke FA*

*Impactfactor: 1.438*

### **Teijink JA**

#### **Multidisciplinary treatment for peripheral arterial occlusive disease and the role of eHealth and mHealth**

Fokkenrood HJ\*, Lauret GJ\*, Scheltinga MR, Spreeuwenberg C, Bie RA de, Teijink JA\*

J Multidiscip Healthc. 2012;5:257-63 Epub 2012 Oct 8

*Voor abstract zie: Chirurgie - Fokkenrood HJ*

*Impactfactor: --*

### **Teijink JA**

#### **No differences in perioperative outcome between symptomatic and asymptomatic AAAs after EVAR: an analysis from the ENGAGE Registry**

Stokmans RA\*, Teijink JA\*, Cuypers PW\*, Riambau V, Sambeek MR van\*

Eur J Vasc Endovasc Surg. 2012 Jun;43(6):667-73. Epub 2012 Mar 21

*Voor abstract zie: Chirurgie - Stokmans RA*

*Impactfactor: 2.991*

### **Teijink JA**

#### **Plasma levels of Matrix Metalloproteinase-9: a possible diagnostic marker of successful endovascular aneurysm repair**

Hellenthal FA, Bosch JA, Pulinx B, Wodzig WK, Haan MW de, Prins MH, Welten RJ,

Teijink JA\*, Schurink GW

Eur J Vasc Endovasc Surg. 2012 Feb;43(2):171-2. Epub 2011 Dec 14

OBJECTIVE: The aim of the study was evaluating the diagnostic value of plasma matrix

metalloproteinase- (MMP)-2 and -9 and tissue inhibitor of MMP-1 (TIMP-1) for endoleak detection after endovascular aneurysm repair (EVAR).

REPORT: Consecutive EVAR patients (n = 17) with endoleak and matched controls without endoleak (n = 20) were prospectively enrolled. Increased levels of MMP-9 were observed in patients with endoleak (P < 0.001). Regression analysis showed no significant influence of age, sex or abdominal aortic aneurysm (AAA) size. The receiver operating characteristic (ROC) curve of plasma MMP-9 levels showed that a cut-off value of 55.18 ng ml(-1) resulted in 100% sensitivity and 96% specificity with an AUC value of 0.988 (P < 0.001) to detect endoleak.

CONCLUSIONS: Plasma MMP-9 levels appear to discriminate between patients with an without an endoleak with high sensitivity and specificity.

*Impactfactor: 2.942*

### **Teijink JA**

#### **Supervised exercise therapy for intermittent claudication: current status and future perspectives**

Lauret GJ\*, Dalen DC van\*, Willigendael EM\*, Hendriks EJ, Bie RA de, Spronk S, Teijink JA\*

Vascular. 2012 Feb;20(1):12-9. Epub 2012 Feb 10

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: 0.891*

### **Teijink JA**

#### **Systematic approach to ruptured abdominal aortic aneurysm in the endovascular era: Intention-to-treat eEVAR protocol**

Willigendael EM\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Feb;53(1):77-82

*Voor abstract zie: Chirurgie - Willigendael EM*

*Impactfactor: 1.559*

### **Teijink JA**

#### **The ClaudicatioNet concept: design of a national integrated care network providing active and healthy aging for patients with intermittent claudication**

Lauret GJ\*, Gijsbers HJ, Hendriks EJ, Bartelink ML, Bie RA de, Teijink JA\*

Vasc Health Risk Manag. 2012;8:495-503

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: --*

### **Teijink JA**

#### **Treatment for intermittent claudication and the effects on walking distance and quality of life**

Kruidenier LM, Viechtbauer W, Nicolai SP, Büller H, Prins MH, Teijink JA\*

Vascular. 2012 Feb;20(1):20-35. Epub 2012 Jan 23

The objective of the study was to provide an overview of the most common treatments for intermittent claudication and to determine the effectiveness in improving walking distance and quality of life based on a combination of direct and indirect evidence. We included trials that compared: angioplasty, surgery, exercise therapy or no treatment for intermittent claudication. Outcome measurements were walking distance (maximum, pain-free) and

quality of life (physical, mental). We used a network meta-analysis model for the combination of direct and indirect evidence. We included 42 studies, presenting 3106 participants. The network meta-analysis showed that supervised exercise therapy ( = 1.62, P < 0.01), angioplasty ( = 1.89, P < 0.01) and surgery ( = 2.72, P = 0.02) increased walking distance significantly more than no treatment. Furthermore, supervised exercise therapy ( = 0.60, P < 0.01), angioplasty ( = 0.91, P = 0.01) and surgery ( = 1.07, P < 0.01) increased physical quality of life more than no treatment. However, in the sensitivity analysis, only supervised exercise therapy had additional value over no symptomatic treatment ( = 0.66, P < 0.01). In conclusion, this network meta-analysis indicates that supervised exercise therapy is more effective in both increasing walking distance and physical quality of life, compared with no treatment. Angioplasty and surgery also increase walking distance, compared with no treatment, but results for physical quality of life are less convincing.

*Impactfactor: 0.891*

### **Teijink JA**

#### **When is Supervised Exercise Therapy Considered Useful in Peripheral Arterial Occlusive Disease? A Nationwide Survey among Vascular Surgeons**

Lauret GJ\*, Dalen HC van \*, Hendriks HJ, Sterkenburg SM van, Koelemay MJ, Zeebregts CJ, Peters RJ, Teijink JA\*.

Eur J Vasc Endovasc Surg. 2012 Mar;43(3):308-12. Epub 2012 Jan 10

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: 2.491*

### **Thomassen I**

#### **Een jongen met pijn rechts in de onderbuik . [13-Year old boy with abdominal pain]**

Thomassen I\*, Klinkhamer PJ\*, Poll MC van den\*

Ned Tijdschr Geneeskd. 2012;156(18):A3566

A 13-year old boy presents with pain in the lower right abdomen, showing clinical signs of appendicitis. During McBurney' incision an appendix sana was seen. Histologic examination showed penetrating enterobiasis. This was treated with mebendazol.

*Impactfactor: --*

### **Thomassen I**

#### **Intervention techniques for chronic postherniorrhaphy pain**

Thomassen I\*, Suijlekom HA van\*, Gaag A van der\*, Nienhuijs SW\*

European Surgery 2012;44(3):132-7

**BACKGROUND:** Chronic post-surgical pain is the main problem after inguinal hernia repair, frequently mandating treatment. Different treatment modalities are proposed. The aim of this review was to evaluate recent literature on different interventions to treat chronic inguinal pain after inguinal hernia repair and their outcomes.

**METHODS:** The Medline database, CINAHL, Embase, and Pubmed, including e-links to related articles, and the clinical trial registry of the Cochrane Collaboration were searched for relevant articles. Studies since 2001 reporting an intervention and their outcome to treat chronic postoperative inguinal pain in adult patients were selected. Study design, length of follow-up, number of included and evaluated patients, definition of chronic pain, description, as well as outcome of the intervention are extracted.

RESULTS: A total of 29 studies were included; eleven of them were prospective, the remaining retrospective. One study about pharmacological treatment (n = 2), two studies about peripheral nerve blockage (n = 9), three studies about pulsed radiofrequency (n = 12), four studies about neurostimulation (n = 7), one study about removal of staples or tackers (n = 1), one study about neuroablation (n = 10), and 17 studies about neurectomy (n = 733) were included.

CONCLUSIONS: This collective review shows the broad spectrum of interventions to treat chronic postoperative inguinal pain. Due to a wide range of pain definitions and outcome measurement a true comparison is difficult.

### **Thomassen I**

#### **Steroid use is associated with clinically irrelevant biopsies in patients with suspected giant cell arteritis**

Thomassen I\*, Brok AN den, Konings CJ\*, Nienhuijs SW\*, Poll MC van de\*  
Am Surg. 2012 Dec;78(12):1362-8

Temporal artery biopsy (TAB) is the diagnostic gold standard for giant cell arteritis (GCA). GCA is treated by high-dose corticosteroids. In cases of high clinical suspicion, steroids may be administered despite negative TAB, making TAB clinically irrelevant. We assessed the role of TAB in clinical decisionmaking in patients with suspected GCA and to identify factors associated with clinically irrelevant TAB. Charts of patients who underwent TAB from 2005 to 2010 were reviewed for clinical parameters potentially associated with GCA and clinically irrelevant TAB. We studied 143 patients with 99 negative (69%), 34 positive (24%), and 10 undefined (7%) TABs. Eventually 26 patients (18% of the entire cohort and 26% of the patients with a negative TAB) received steroid treatment for GCA despite negative TAB. The start of steroid treatment before TAB was associated with clinically irrelevant TABs. If clinical suspicion of GCA is high, a TAB can be considered clinically irrelevant.

*Impactfactor: 1.285*

### **Vainas T**

#### **Endovascular treatment of a hepatic artery pseudoaneurysm associated with gastrointestinal tract bleeding**

Vainas T\*, Klompenhouwer E\*, Duijm L\*, Tielbeek X\*, Teijink J\*  
J Vasc Surg. 2012 Apr;55(4):1145-9. Epub 2012 Feb 25

Hemosuccus pancreaticus is a rare cause of gastrointestinal bleeding from the pancreatic duct originating from aneurysms or pseudoaneurysms of peripancreatic arteries. It is a life-threatening cause of gastrointestinal bleeding that should always be considered in patients with prolonged or intermittent obscure gastrointestinal blood loss, or both, especially in patients with pancreatic disorders or prior pancreatic surgery. We demonstrate an endovascular treatment strategy in a patient with a common hepatic pseudoaneurysm and upper gastrointestinal tract bleeding, with preserved flow in the hepatic artery. This treatment consisted of a covered stent placement in the hepatic artery, followed by transcatheter coil embolization of collateral feeding arteries.

*Impactfactor: 3.153*

## **Vermeer TA**

### **T3+ and T4 rectal cancer patients seem to benefit from the addition of oxaliplatin to the neoadjuvant chemoradiation regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*  
Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Wasowicz DK**

### **Focus on extralevator perineal dissection in supine position for low rectal cancer has led to better quality of surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D,\* Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H,\* Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Wasowicz DK**

### **Patent blue staining as a method to improve lymph node detection in rectal cancer following neoadjuvant treatment**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Rutten HJ\*, Nieuwenhuijzen GA\*, Wasowicz-Kemps DK\*

Eur J Surg Oncol. 2012 Mar;38(3):252-8. Epub 2012 Jan 4

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 2.499*

## **Willigendael EM**

### **Applicability of the ankle-brachial-index measurement as screening device for high cardiovascular risk: an observational study**

Bendermacher BL\*, Teijink JA\*, Willigendael EM\*, Bartelink ML, Peters RJ, Langenberg M, Büller HR, Prins MH

BMC Cardiovasc Disord. 2012 Jul 30;12:59

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*Impactfactor: 1.517*

## **Willigendael EM**

### **Early and mid-term results of a prospective observational study comparing emergency endovascular aneurysm repair with open surgery in both ruptured and unruptured acute abdominal aortic aneurysms**

Bosch JA ten, Willigendael EM\*, Kruidenier LM, Loos ER de, Prins MH, Teijink JA\*

Vascular. 2012 Apr;20(2):72-80. Epub 2012 Mar 27

The aim of the paper is to prospectively describe early and mid-term outcomes for emergency endovascular aneurysm repair (eEVAR) versus open surgery in acute abdominal aortic aneurysms (aAAAs), both unruptured (symptomatic) and ruptured. We enrolled all

consecutive patients treated for aAAA at our center between April 2002 and April 2008. The main outcome parameters were 30-day, 6- and 12-month mortality (all-cause and aneurysm-related). Two hundred forty patients were enrolled in the study. In the unruptured aAAA group (n = 111), 47 (42%) underwent eEVAR. The 30-day, 6- and 12-month mortality rates were 6, 13 and 15% in the eEVAR group versus 11% (NS), 13% (NS) and 16% (NS) in the open group, respectively. In the ruptured aAAA group (n = 129), 25 (19%) underwent eEVAR (mortality rates: 20, 28 and 36%, respectively) compared with 104 (81%) patients who underwent open surgery (mortality rates: 45% (P = 0.021), 60% (P = 0.004) and 63% (P = 0.014), respectively). In conclusion, the present study showed a reduced 30-day, 6- and 12-month mortality of eEVAR compared with open surgery in all patients with aAAA, mainly due to a lower mortality in the ruptured aAAA group. Late aneurysm-related mortality occurred only in the eEVAR group.

*Impactfactor: 0.891*

### **Willigendael EM**

#### **Supervised exercise therapy for intermittent claudication: current status and future perspectives**

Lauret GJ\*, Dalen DC van\*, Willigendael EM\*, Hendriks EJ, Bie RA de, Spronk S, Teijink JA\*

Vascular. 2012 Feb;20(1):12-9. Epub 2012 Feb 10

*Voor abstract zie: Chirurgie - Lauret GJ*

*Impactfactor: 0.891*

### **Willigendael EM**

#### **Systematic approach to ruptured abdominal aortic aneurysm in the endovascular era: Intention-to-treat eEVAR protocol**

Willigendael EM\*, Cuypers PW\*, Teijink JA\*, Sambeek MR van\*

J Cardiovasc Surg (Torino). 2012 Feb;53(1):77-82

Emergency endovascular aneurysm repair (eEVAR) for ruptured abdominal aortic aneurysms (rAAA) is still a relatively new treatment option. A pre-defined strategy of an eEVAR first approach for rAAA is associated with improved mortality rates. After establishing and implementing the Intention-to-treat eEVAR protocol for rAAAs the mortality and morbidity rates improved significantly. The presented Intention-to-treat eEVAR protocol starts at the first telephone call to the ambulance department and lasts until the post-operative care unit. The protocol involves the close collaboration between the ambulance department, vascular surgeon, emergency department physicians, anaesthesiologists, operating room staff and radiology technicians. The availability of a variety of off-the-shelf stent-grafts, and an operating room that is adequately equipped to perform endovascular procedures is crucial in obtaining better outcomes. High volume centres that offer open surgical repair as well as eEVAR for rAAA show that the Intention-to-treat eEVAR protocol is achievable and appears to be associated with favorable mortality over open repair with appropriate case selection. Unstable or older patients with rAAA may particularly benefit by eEVAR.

*Impactfactor: 1.559*

## **Woensdregt K**

### **Hormone treatment without surgery for patients aged 75 years or older with operable breast cancer**

Wink CJ, Woensdregt K\*, Nieuwenhuijzen GA\*, Sangen MJ van der\*,  
Hutschemaekers S, Roukema JA, Tjan-Heijnen VC, Voogd AC

Annals of Surgical Oncology 2012 Apr;19(4):1185-91. Epub 2011 Oct 27

**PURPOSE:** To evaluate the trend in the use of primary endocrine treatment (PET) for elderly patients with operable breast cancer and to study mean time to response (TTR), local control, time to progression (TTP), and overall survival.

**METHODS:** Data of 184 patients aged  $\geq$  75 years, diagnosed with breast cancer in the south of the Netherlands between 2001 and 2008 and receiving PET, were analyzed.

**RESULTS:** The percentage of women  $\geq$  75 years with breast cancer receiving PET in the south of the Netherlands decreased from 23% in the period 1988-1992 to 12% in 1997-2000, and increased to 29% in 2005-2008. Mean age at diagnosis of 184 patients treated with PET in the period 2001-2008 was 84 years (range 75-89 years). Mean length of follow-up was 2.6 years. In 107 patients (58%), an initial response was achieved (mean TTR 7 months), 21 patients (12%) showed stable disease. A total of 64 patients (35%), with or without prior response, eventually displayed progression (mean TTP 20 months). No differences in TTR and TTP were observed between the patients starting with tamoxifen or an aromatase inhibitor. One hundred nineteen (65%) of 184 patients had died by January 1, 2010. In 17 patients (14%), breast cancer was the cause of death.

**CONCLUSIONS:** Tumor progression was observed in a substantial proportion of the cohort, but only a small number of patients died of breast cancer. Further research is needed on the safety and effectiveness of PET for elderly women with breast cancer to justify the current widespread use.

*Impactfactor: 4.166*

## **Zoete JP de**

### **Indications and short-term outcomes of revisional surgery after failed or complicated sleeve gastrectomy**

Rutte PW van\*, Smulders JF\*, Zoete JP de\*, Nienhuijs SW\*

Obes Surg. 2012 Dec;22(12):1903-8. Epub 2012 Sep 22

*Voor abstract zie: Chirurgie - Rutte PW van*

*Impactfactor: 3.286*

## **Zoete JP de**

### **Laparoscopic sleeve gastrectomy feasible for bariatric revision surgery**

Berende CA\*, Zoete JP de\*, Smulders JF\*, Nienhuijs SW\*

Obes Surg. 2012 Feb;22(2):330-4. Epub 2011 Aug 25

*Voor abstract zie: Chirurgie - Berende CA*

*Impactfactor: 3.286*

\* = *Werkzaam in het Catharina Ziekenhuis*

## **Dermatologie**

**Bouten H**

**Anogenital malignancies in women after renal transplantation over 40 years in a single center**

Meeuwis KA, Melchers WJ, Bouten H\*, Kerkhof PC van de, Hinten F, Quint WG, Massuger LF, Hoitsma AJ, Rossum MM van, Hullu JA de

Transplantation. 2012 May 15;93(9):914-22

BACKGROUND: Renal transplant recipients have an increased risk to develop human papillomavirus (HPV)-related anogenital malignancies. A clinical overview of female anogenital posttransplantation malignancies and possible multifocal premalignancies over a period of 40 years renal transplantation is presented. Additionally, the genotype-specific prevalence of HPV in these (pre)malignancies was investigated.

METHODS: Data of 1023 women, who underwent a renal transplantation between 1968 and 2008, were collected. Clinical data of all female renal transplant recipients who developed anogenital malignancies were retrospectively analyzed. The histology, cytology, and distribution of genotype-specific HPV infections were analyzed in all primary anogenital tumors and possible (multifocal) premalignancies.

RESULTS: Sixteen anogenital malignancies (1.6%) were found: vulva (n=6), cervix (n=5), and anus (n=5). Twelve of 16 patients never had a cervical smear before transplantation. The median interval between transplantation and diagnosis of malignancy was 136 months (range, 16-288 months). Highrisk HPV was detected in 91.7% of investigated lesions, HPV subtype 16 predominated (54.5%). Four of seven patients with two distinct anogenital lesions had different HPV types in the lesions.

CONCLUSIONS: A high number of anogenital malignancies developed in our cohort, which are nearly all caused by HPV. Multifocal lesions within one patient frequently contained different high-risk HPV genotypes in both lesions. Our results underline the importance of anogenital screening and monitoring before and periodically after renal transplantation to prevent morbidity and mortality from anogenital malignancies.

*Impactfactor: 4.003*

**Brand EJ**

**Imiquimod 5% Cream as Pre-Treatment of Mohs Micrographic Surgery for Nodular Basal Cell Carcinoma in the Face, A Prospective Randomized Controlled Study Imiquimod As Pre-Treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*, Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

**Geer S van der**

**Imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for nodular basal cell carcinoma in the face, a prospective randomized controlled study imiquimod as pre-treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*, Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

Background: Imiquimod 5% cream can reduce or clear superficial and small nodular basal cell carcinoma (BCC). It could be used as a pre-treatment of Mohs micrographic surgery (MMS) to decrease defect size.

Objective: after Mohs micrographic surgery. In addition, to study the effect on the number of Mohs stages and reconstruction time.

Methods and Materials:

the face were included. The imiquimod group used imiquimod 5% cream for 4 weeks, before MMS. The control group was treated with MMS only. Tumour and defect sizes were measured. We noted the number of Mohs-stages, reconstruction time and side-effects.

Results: increase in area from tumour size at baseline to the post-MMS defect for the imiquimod group was significantly less compared to the control group, 50% vs 147% ( $p=0.00$ ). A tendency towards less Mohs stages in the imiquimod group was observed and the reconstruction time was significantly shorter in this group (0.01).

Conclusion: tumour size in a primary nodular BCC and reduced the surgical defect size.

Further research is necessary to investigate cost-effectiveness.

*Impactfactor: 3.666*

### **Geer S van der**

#### **One-stop-shop treatment for basal cell carcinoma, part of a new disease management strategy**

Geer S van der\*, Frunt M, Romero HL, Dellaert NP, Jansen-Vullers MH, Demeyere TB\*, Neumann HA, Krekels GA\*

J Eur Acad Dermatol Venereol. 2012 Sep;26(9):1154-7. Epub 2011 Jul 19

BACKGROUND: The number of skin cancer patients, especially patients with basal cell carcinoma (BCC), is rapidly increasing. Resources available at dermatology units have not increased proportionally, which affects the throughput time of patients.

OBJECTIVE: To assess the feasibility and safety of implementation of the one-stop-shop concept for the treatment of patients with BCC at a dermatology unit.

METHODS: A pilot study on a one-stop-shop concept for BCC was performed to investigate procedure safety and patient satisfaction. Fresh frozen sections were used to diagnose the tumours, and subsequently treatment with photodynamic therapy or excision was performed on the same day. Time spent in the hospital was measured and questionnaires were used to evaluate patient satisfaction.

RESULTS: Sixteen patients, who together had 19 tumours, were included. Diagnoses were made within a mean time of 100 min (range 27-160 min). The mean throughput time was 4 hours and 7 min (range 60-420 min). No complications were observed, and patient satisfaction was high.

CONCLUSION: The one-stop-shop concept for the treatment of skin cancer patients is feasible and efficient for both patients and dermatology units. Further research is necessary to investigate cost-effectiveness when larger patient groups are involved.

*Impactfactor: 2.980*

### **Kessels JP**

#### **The use of tumescent local anaesthesia in ablative laser treatments**

Kessels JP\*, Ostertag JU\*

J Eur Acad Dermatol Venereol. 2012 Nov;26(11):1456-7. Epub 2011 Nov 19

*Impactfactor: 2.980*

## **Krekels GA**

### **Imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for nodular basal cell carcinoma in the face, a prospective randomized controlled study imiquimod as pre-treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*, Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

## **Krekels GA**

### **Internet based computer tailored feedback on sunscreen use**

Vries H de, Logister M, Krekels G\*, Klaasse F, Servranckx V, Osch L van

J Med Internet Res. 2012 Apr 30;14(2):e48

**BACKGROUND:** Skin cancer incidence rates signify the need for effective programs for the prevention of skin cancer and for helping skin cancer patients. Internet and computer tailored (CT) technology fosters the development of highly individualized health communication messages. Yet, reactions to Internet CT programs may differ per level of involvement and education level and remain understudied. **OBJECTIVE:** First, we identified perceptions concerning sunscreen use in Dutch adults and assessed differences in differences between the general public and skin cancer patients, and between low and high educated respondents. Second, we assessed program evaluations of these groups about a new Dutch CT Internet-based program promoting sunscreen use, and potential differences between groups.

**METHODS:** A cross-sectional research design was used. In total, 387 respondents participated and filled out an online questionnaire based on the I-Change Model assessing socio-demographics, history of skin cancer, sunscreen use, and beliefs about sunscreen use. The responses were fed into a computer program that generated personal tailored feedback on screen; next we assessed their program evaluations.

**RESULTS:** Of the 132 patients, 92 were female (69.7%) and 40 were male (30.3%). In the general population (N = 225), 139 (54.5%) respondents were female and 116 (45.5%) were male. Men (50.9 years) were 8 years older than women (43.1 years). Most patients were diagnosed with basal cell carcinoma (N = 65; 49.2%), followed by melanoma (N = 28; 21.2%) and squamous cell carcinoma (N = 10; 7.6%); 22% (N = 29) did not remember their skin cancer type. Patients had higher knowledge levels, felt significantly more at risk, were more convinced of the pros of sunscreen, experienced more social support to use sunscreen, had higher self-efficacy, and made more plans to use sunscreen than respondents without skin cancer (N=255; all P's< .01). Low (N=196) educated respondents scored lower on knowledge (P<.003) but made more action plans (P<.03) than higher educated respondents (N=191). The CT feedback was evaluated positively by all respondents, and scored a 7.8 on a 10 point scale. Yet, patients evaluated the CT program slightly more (P<.05) positive (8.1) than non-patients. (7.6). Lower educated respondents were significantly (P<.05) more positive about the advantages of the program.

**CONCLUSIONS:** First, involvement with skin cancer was reflected in more positive beliefs toward sunscreen use in patients in comparison with non-patients. Second, the CT Internet program was well accepted by both patients and non-patients, and low and high educated respondents, perhaps because higher educated respondents were more knowledgeable

about sunscreen use and skin cancer. Third, a pro-active approach as conducted in our study is very well suited to reach various groups of people and is more likely to be successful than a reactive approach.

*Impactfactor: 4.409*

### **Krekels GA**

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Geer S van der\*, Frunt M, Romero HL, Dellaert NP, Jansen-Vullers MH, Demeyere TB\*, Neumann HA, Krekels GA\*

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*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 2.980*

### **Martens J**

#### **Imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for nodular basal cell carcinoma in the face, a prospective randomized controlled study imiquimod As pre-treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*, Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

### **Ostertag JU**

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Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

### **Ostertag JU**

#### **The use of tumescent local anaesthesia in ablative laser treatments**

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*Impactfactor: 2.980*

**Roij J van**

**Imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for nodular basal cell carcinoma in the face, a prospective randomized controlled study  
imiquimod As pre-treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*,  
Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

**Verhaegh ME**

**Imiquimod 5% cream as pre-treatment of Mohs micrographic surgery for nodular basal cell carcinoma in the face, a prospective randomized controlled study  
imiquimod As pre-treatment of Mohs**

Geer S van der\*, Martens J\*, Roij J van\*, Brand E\*, Ostertag JU\*, Verhaegh ME\*,  
Neumann HA, Krekels GA\*

Br J Dermatol. 2012 Jul;167(1):110-5. Epub 2012 May 21

*Voor abstract zie: Dermatologie - Geer S van der*

*Impactfactor: 3.666*

\* = *Werkzaam in het Catharina Ziekenhuis*

## **ECC / Bloedmanagement**

## **Feron JC**

### **Clinical evaluation of the Sorin Xtra(R) Autotransfusion System.**

**Overdevest EP\*, Lanen PW,\* Feron JC\*, Hees JW van\*, Tan ME\***

Perfusion. 2012 Jul;27(4):278-83. Epub 2012 Mar 29

*Voor abstract zie: ECC - Overdevest EP*

*Impactfactor: 0.918*

## **Hees JW van**

### **Clinical evaluation of the Sorin Xtra(R) Autotransfusion System**

**Overdevest EP\*, Lanen PW,\* Feron JC\*, Hees JW van\*, Tan ME\***

Perfusion. 2012 Jul;27(4):278-83. Epub 2012 Mar 29

*Voor abstract zie: ECC - Overdevest EP*

*Impactfactor: 0.918*

## **Lanen PW**

### **Clinical evaluation of the Sorin Xtra(R) Autotransfusion System**

**Overdevest EP\*, Lanen PW,\* Feron JC\*, Hees JW van\*, Tan ME\***

Perfusion. 2012 Jul;27(4):278-83. Epub 2012 Mar 29

*Voor abstract zie: ECC - Overdevest EP*

*Impactfactor: 0.918*

## **Overdevest EP**

### **Clinical evaluation of the Sorin Xtra(R) Autotransfusion System**

**Overdevest EP\*, Lanen PW,\* Feron JC\*, Hees JW van\*, Tan ME\***

Perfusion. 2012 Jul;27(4):278-83. Epub 2012 Mar 29

The performance of the Sorin Xtra® Autotransfusion System (ATS) was studied in 62 patients undergoing coronary artery bypass grafting. Blood was collected intraoperatively and washed using three different wash sets in 4 groups. Both collected and washed blood were analysed for haemoglobin levels and hematocrit, concentrations of proteins, albumin, heparin and plasma free hemoglobin (PFH) were determined, erythrocytes, platelets and leukocytes were counted. Hematocrit measurements of the Xtra® were compared with laboratory measurements to study the accuracy of the Xtra® hematocrit sensor. In addition, the red blood cell recovery rate and elimination rates were calculated to evaluate the clinical performance of the Xtra®. The Xtra® ATS produced a volume of concentrated red blood cells with an average hematocrit from 58% to 63%, depending on the size of the bowl and the chosen default program. In all bowl sizes and programs, the Xtra® Hct-out measurement underestimated the CELLDYN measurement by approximately 15%. The calculated recovery rates for red blood cells (RBC) in the 4 groups ranged from 86.7% to 91.6%. Elimination rates were calculated in each group for proteins (96.8-99.2%), albumin (96.4-98.7%), plasma free hemoglobin (83.6-91.2%), heparin (98.8-99.9%), platelets (82.4-94.3%) and white blood cells (28.6-42.3%). The Xtra® ATS can be appealing for its performance by producing high hematocrit levels in the washed RBC volume, while keeping RBC recovery rate at the same high level (H 90%) as in its predecessor, the Electa® Autotransfusion System.

*Impactfactor: 0.918*

\* = *Werkzaam in het Catharina Ziekenhuis*

## **Geestelijke Verzorging & Ethiek**

**Laar EF van de**

**Toekomst van de geestelijke verzorging**

Laar EF van de\*, Plum R

Tijdschrift voor Geestelijke Verzorging (TGV). 2012; 15 (68), 24-32

themanummer: Toekomstscenario's geestelijke verzorging

*Impactfactor: --*

**Schrijver LA**

**Geestelijke verzorging voor kinderen**

Schrijver LA\*, Smeets V

Tijdschrift voor Geestelijke Verzorging (TGV). 2012; 15 (68), 44-48

themanummer: Toekomstscenario's geestelijke verzorging

*Impactfactor: --*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Geriatric**

**Aa GC van der**

**Effectiveness of dementia follow-up care by memory clinics or general practitioners: randomised controlled trial**

Meeuwse EJ, Melis RJ, Aa GC van der\*, Golüke-Willemse GA, Leest BJ de, Raak FH van, Schölzel-Dorenbos CJ, Verheijen DC, Verhey FR, Visser MC, Wolfs CA, Adang EM, Olde Rikkert MG

BMJ. 2012 May 15;344:e3086

OBJECTIVE: To examine the effectiveness of post-diagnosis dementia treatment and coordination of care by memory clinics compared with general practitioners.

DESIGN: Multicentre randomised controlled trial.

SETTING: Nine memory clinics and 159 general practitioners in the Netherlands.

PARTICIPANTS: 175 patients with a new diagnosis of mild to moderate dementia living in the community and their informal caregivers.

INTERVENTIONS: Usual care provided by memory clinic or general practitioner.

MAIN OUTCOME MEASURES: Caregiver rated quality of life of the patient measured with the quality of life in Alzheimer's disease instrument and self perceived burden of the informal caregiver measured with the sense of competence questionnaire (intention to treat analysis).

RESULTS: The quality of life of the patients in the memory clinic group was 0.5 (95% confidence interval -0.7 to 1.6) points higher than in the general practitioner group. Caregivers' burden was 2.4 (-5.8 to 1.0) points lower in the memory clinic group than in the general practitioner group.

CONCLUSION: No evidence was found that memory clinics were more effective than general practitioners with regard to post-diagnosis treatment and coordination care for patients with dementia. Without further evidence on the effectiveness of these modalities, other arguments, such as cost minimisation, patients' preferences, or regional health service planning, can determine which type of dementia care is offered.

*Impactfactor: 14.093*

**Linden CM van der**

**An electronic system to document reasons for medication discontinuation and to flag unwanted prescriptions in geriatric patients**

Linden CM van der\*, Jansen PA, Marum RJ van, Grouls RJ\*, Egberts TC, Korsten EH\*

Drugs Aging. 2012 Dec;29(12):957-62. Epub 2012 Nov 10

BACKGROUND: Earlier studies have shown poor documentation of the reasons for medication discontinuation during hospitalization. Communication of reasons for discontinuation, e.g. adverse drug reactions (ADRs), to general practitioners and pharmacists was also found to be insufficient, leading to a rate of prescription after an ADR of 27 % during the first 6 months after discharge.

OBJECTIVE: The aim of this study was to develop and implement a user-friendly electronic clinical decision support system to document reasons for medication discontinuation in hospitalized geriatric patients and to flag potentially undesirable prescriptions.

METHODS: The electronic clinical decision support module was developed using the Gaston framework. Pop-up windows force physicians to document reasons for medication discontinuation, and the system alerts physicians to the prescription of drugs withdrawn because of an ADR. We interviewed users regarding the acceptability of the system.

RESULTS: On a 20-bed geriatric ward, the electronic system documented 2,228 medication

discontinuations and the reasons for them over 11.4 months and alerted physicians to represcription of drugs associated with an ADR 20 times. The system was considered to be user-friendly.

**CONCLUSIONS:** This clinical decision support system fulfilled its aims of documenting the reasons for medication discontinuation and alerting physicians to potentially undesirable represcription of previously withdrawn drugs. It was found to be user-friendly.

*Impactfactor: 2.671*

*\* = Werkzaam in het Catharina Ziekenhuis*



## Gynaecologie

## **Dietz V**

### **Can preoperative urodynamic investigation be omitted in women with stress urinary incontinence? A non-inferiority randomized controlled trial**

Leijsen SA van, Kluivers KB, Mol BW, Broekhuis SR, Milani AL, Bongers MY, Aalders CI, Dietz V\*, Malmberg GG, Vierhout ME, Heesakkers JP

Neurourol Urodyn. 2012 Sep;31(7):1118-23 Epub 2012 Apr 6

**AIMS:** To assess in women with stress urinary incontinence (SUI) the value of urodynamics prior to treatment.

**METHODS:** We performed a multicenter non-inferiority randomized controlled trial. Women with SUI were randomly allocated to management based on a workup with or without urodynamics. The primary outcome was clinical reduction of complaints as measured with the Urogenital Distress Inventory urinary incontinence subscale (UDI-UI) at 12 months after the onset of treatment. A mean difference in improvement of less than 8 was considered non-inferior. The study was analyzed according to intention-to-treat.

**RESULTS:** The trial was stopped prematurely because of slow recruitment. We randomly allocated 59 women to a strategy with (N = 31) or without (N = 28) urodynamics. The mean difference in improvement on the UDI-UI was 14 in favor of the group without urodynamics (48 SD ± 22 vs. 34 SD ± 22, 95% CI: -28 to -0.26), confirming non-inferiority. Addition of urodynamics did not result in a lower occurrence of de novo overactive bladder complaints compared to a workup without urodynamics (6/31 vs. 1/28; RR 5.4, 95% CI: 0.70-42). In the group allocated to urodynamics, initial surgical management was more often abandoned compared to the group not allocated to urodynamics (5/31 vs. 1/28; RR 4.5, 95% CI: 0.56-36).

**CONCLUSIONS:** In this relatively small study, the omission of urodynamics was not inferior to the use of urodynamics in the preoperative workup of women with SUI. Women with SUI undergoing urodynamics had the risk of a choice for more prudent treatment, which seemed to result in a delay until effective treatment.

*Impactfactor: 2.958*

## **Dietz V**

### **Electrosurgical bipolar vessel sealing versus conventional clamping and suturing for vaginal hysterectomy: a randomised controlled trial**

Lakeman M, The S, Schellart R, Dietz V\*, Haar J ter, Thurkow A, Scholten P, Dijkgraaf M, Roovers J

BJOG. 2012 Nov;119(12):1473-1482. Epub 2012 Aug 24

**OBJECTIVE:** To compare the effects of electrical bipolar vessel sealing and conventional suturing on postoperative pain, recovery, costs and micturition symptoms in women undergoing vaginal hysterectomy.

**DESIGN:** Randomised controlled trial.

**SETTING:** Eight teaching hospitals in the Netherlands.

**POPULATION:** One hundred women scheduled to undergo vaginal hysterectomy for benign conditions excluding pelvic organ prolapse.

**METHODS:** Women were randomised to vessel sealing or conventional surgery. The quality of life related to pelvic floor function was assessed using validated questionnaires before surgery and 6 months after surgery. Pain scores and recovery were assessed using a diary, including daily visual analogue scale scores, starting from the day before surgery until 6 weeks after surgery.

MAIN OUTCOME MEASURES: Visual analogue scale pain scores, surgery time, blood loss, complications, quality of life related to pelvic floor function and costs.

RESULTS: The evening after surgery, women in the vessel-sealing group reported significantly less pain (5.7 versus 4.5 on a scale of 0-10,  $P = 0.03$ ), but after that pain scores were similar. Operation duration was shorter for vessel sealing (60 versus 71 minutes,  $P = 0.05$ ). Blood loss and hospital stay did not differ. We observed no major difference in costs between the two interventions (2903 versus 3102 €,  $P = 0.26$ ). Changes in micturition and defecation symptoms were not affected by the surgical technique used.

CONCLUSION: Using vessel sealing during vaginal hysterectomy resulted in less pain on the first postoperative day, shorter operating time, similar morbidity and similar pelvic floor function. No major differences in costs were found between the two interventions.

*Impactfactor: 3.407*

## **Haest K**

### **Stellate ganglion block for the management of hot flashes and sleep disturbances in breast cancer survivors: an uncontrolled experimental study with 24 weeks of follow-up**

Haest K\*, Kumar A, Calster B van, Leunen K, Smeets A, Amant F, Berteloot P, Wildiers H, Paridaens R, Limbergen E van, Weltens C, Janssen H, Peeters S, Menten J, Vergote I, Morlion B, Verhaegen J, Christiaens MR, Neven P

Ann Oncol. 2012 Jun;23(6):1449-54. Epub 2011 Oct 29

BACKGROUND: We studied the stellate ganglion block (SGB) recently suggested for the treatment of severe vasomotor symptoms and sleep disturbances in breast cancer survivors. Following an initial pilot study, which focused on the acceptability and safety of SGB for this important problem, we evaluated its short- and long-term efficacy. Materials and methods: Postmenopausal breast cancer survivors with severe vasomotor symptoms resistant to standard nonhormonal pharmacological intervention were eligible. Diaries were used to measure daily hot flash scores (frequency and intensity) and sleep quality (Pittsburgh Sleep Quality Index) during scheduled visits at baseline, 1, 4, 12 and 24 weeks following the SGB. Efficacy data were analyzed using longitudinal regression models.

RESULTS: Thirty-four patients participated and none refused the SGB procedure. Most patients received more than one SGB. The pilot study found SGB to be safe. In the main study, hot flash scores were reduced from baseline by 64% [95% confidence interval (CI) -74% to -49%] and 47% (95% CI -62% to -27%) at weeks 1 and 24, respectively. The odds ratio of better sleep quality relative to baseline was 3.4 at week 1 (95% CI 1.6-7.2) and 4.3 at week 24 (95% CI 1.9-9.8).

CONCLUSION: In the short term, SGB appears to be an effective treatment with acceptable morbidity for some breast cancer survivors with therapy-resistant vasomotor symptoms and/or sleep disturbances. Although sleep quality was maintained out to 24 weeks the efficacy of SGB for hot flashes was reduced over time. A randomized controlled trial is needed to confirm these findings.

*Impactfactor: 6.425*

**Hasaart TH**

**Anafylaxie na ijzerdextraan bij een zwangere vrouw. [Anaphylaxis after iron dextran administration in a pregnant woman]**

Kortenhorst MS\*, Harmsze AM\*, Hasaart TH\*

Ned Tijdschr Geneeskd. 2012;156(48):A5264

Voor abstract zie: *Gynaecologie - Kortenhorst MS*

*Impactfactor: --*

**Hasaart TH**

**Effect of 17-alpha hydroxyprogesterone caproate on cervical length in twin pregnancies**

Lim AC, Schuit E, Papatsonis D, Eyck J van, Porath MM, Oirschot CM van, Hummel P, Hasaart TH\*, Kleiverda G, Graaf IM de, Ginkel AA van, Mol BW, Bruinse HW

Ultrasound Obstet Gynecol. 2012 Oct;40(4):426-30

**OBJECTIVES:** Previous studies on singleton pregnancies have indicated that progestogens may reduce the rate of cervical shortening during pregnancy. The aim of this study was to investigate whether treatment with 17-alpha hydroxyprogesterone caproate (17-OHPC) has an effect on cervical shortening in twin pregnancies.

**METHODS:** This was a secondary analysis of patients who had participated in a multicenter randomized clinical trial on the effectiveness of 17-OHPC in preventing preterm birth in multiple pregnancies (the AMPHIA-trial). We included all trial participants with a twin gestation who had undergone repeat cervical length measurements during pregnancy. We performed a separate analysis of women with repeat measurements in centers where this was standard protocol for multiple pregnancies. The rate of cervical shortening for both the 17-OHPC group and the placebo group was analyzed using a linear mixed model.

**RESULTS:** Of the 671 patients who participated in the trial, 282 (42%) had a twin pregnancy and underwent two or more cervical length measurements. Of these women, 140 were monitored in centers where repeat measurements were standard protocol. We observed an overall reduction of cervical length from 44.3 mm at 14-18 weeks to 30.0 mm at 30-34 weeks' gestation. In the 17-OHPC group, cervical length decreased by 1.04 mm each gestational week, while this was 1.11 mm per week for the placebo group ( $P = 0.6$ ). For the overall group, each 10% decrease in cervical length led to an increase in the risk of preterm birth (hazard ratio, 1.14; 95% CI, 1.08-1.21).

**CONCLUSION:** In women with a twin pregnancy, there is progressive shortening of the cervix during pregnancy, regardless of 17-OHPC use.

*Impactfactor: 3.007*

**Havermans SY**

**Single versus multimodality training basic laparoscopic skills**

Brinkman WM\*, Havermans SY\*, Buzink SN, Botden SM, Jakimowicz JJ\*, Schoot BC\*

Surg Endosc. 2012 Aug;26(8):2172-8. Epub 2012 Feb 21

Voor abstract zie: *Urologie - Brinkman WM*

*Impactfactor: 4.013*

**Hermans RH**

**Laparoscopy to predict the result of primary cytoreductive surgery in advanced ovarian cancer patients (LapOvCa-trial): a multicentre randomized controlled study**

Rutten MJ, Gaarenstroom KN, Gorp T van, Meurs HS van, Arts HJ, Bossuyt PM, Brugge HG ter, Hermans RH\*, Opmeer BC, Pijnenborg JM, Schreuder HW, Schutter EM, Spijkerboer AM, Wensveen CW, Zusterzeel P, Mol BW, Kenter GG, Buist MR

BMC Cancer. 2012 Jan 20;12(1):31

**BACKGROUND:** Standard treatment of advanced ovarian cancer is surgery and chemotherapy. The goal of surgery is to remove all macroscopic tumour, as the amount of residual tumour is the most important prognostic factor for survival. When removal of all tumour is considered not feasible, neoadjuvant chemotherapy (NACT) in combination with interval debulking surgery (IDS) is performed. Current methods of staging are not always accurate in predicting surgical outcome, since approximately 40% of patients will have more than 1 cm residual tumour after primary debulking surgery (PDS). In this study we aim to assess whether adding laparoscopy to the diagnostic work-up of patients suspected of advanced ovarian carcinoma may prevent unsuccessful PDS for ovarian cancer.

**METHODS:** Multicentre randomized controlled trial, including all gynaecologic oncologic centres in the Netherlands and their affiliated hospitals. Patients are eligible when they are planned for PDS after conventional staging. Participants are randomized between direct PDS or additional diagnostic laparoscopy. Depending on the result of laparoscopy patients are treated by PDS within three weeks, followed by six courses of platinum based chemotherapy or with NACT and IDS 3-4 weeks after three courses of chemotherapy, followed by another three courses of chemotherapy. Primary outcome measure is the proportion of PDS's leaving more than one centimetre tumour residual in each arm. In total 200 patients will be randomized. Data will be analysed according to intention to treat.

**DISCUSSION:** Patients who have disease considered to be resectable to less than one centimetre should undergo PDS to improve prognosis. However, there is a need for better diagnostic procedures because the current number of debulking surgeries leaving more than one centimetre residual tumour is still high. Laparoscopy before starting treatment for ovarian cancer can be an additional diagnostic tool to predict the outcome of PDS. Despite the absence of strong evidence and despite the possible complications, laparoscopy is already implemented in many countries. We propose a randomized multicentre trial to provide evidence on the effectiveness of laparoscopy before primary surgery for advanced stage ovarian cancer patients.

*Impactfactor: 3.011*

**Hessel M**

**Face and Construct Validity of the SimSurgery SEP VR Simulator for Salpingectomy in Case of Ectopic Pregnancy**

Hessel M\*, Buzink SN\*, Schoot D\*, and Jakimowicz JJ\*

Journal of Gynecologic Surgery. December 2012, 28(6): 411-417

**Objective:** To secure patient safety, skills needed for laparoscopy are preferably obtained in a nonpatient setting. Therefore, we assessed face and construct validity of performance of a salpingectomy in case of ectopic pregnancy on the SimSurgery SEP VR simulator.

**Materials and Methods:** Fifteen experienced gynecologists (=ESGE level 2) and 17 novices (no laparoscopy experience) performed the Place Arrow (PA), Inspect Abdomen (IA), and Ectopic Pregnancy (EP) tasks and evaluated realism and didactic value of the simulator on 5-point scales. Their task performance was assessed according to the time needed to complete

the tasks, total instrument path length, and parameters that indicated quality of performance. Results: The experienced gynecologists performed the PA task significantly faster ( $p=0.003$ , Mann\_Whitney U-test) and with a shorter total instrument path length ( $p=0.001$ ) compared to novices. The experienced gynecologists performed the EP task significantly better on parameters that indicate quality of performance, such as amount of blood loss ( $p=0.019$ ), time to react to blood loss ( $p=0.020$ ), and time of suction in the air ( $p=0.007$ ) compared to novices. Between both groups, no significant differences were found at all for the IA task. Data from the questionnaire revealed that, in general, all participants had a favorable opinion toward the EP module on the SimSurgery SEP.

Conclusions: This study demonstrates that the SimSurgery SEP simulator offers a realistic representation of the salpingectomy procedural task according to both experienced gynecologists as well as novices (face validity), and that the simulator can discriminate between different levels of expertise (construct validity) for the PA and EP tasks. The simulator is also perceived as an important additional training tool for gynecological residents.

*Impactfactor: --*

### **Kortenhorst MS**

#### **Anafylaxie na ijzerdextraan bij een zwangere vrouw. [Anaphylaxis after iron dextran administration in a pregnant woman]**

Kortenhorst MS\*, Harmsze AM\*, Hasaart TH\*

Ned Tijdschr Geneeskd. 2012;156(48):A5264

BACKGROUND: Iron deficiency is a frequent cause of anaemia in pregnancy and often results in fatigue and malaise. To prevent complications during labour, timely iron supplementation is important.

CASE DESCRIPTION: A 30-year-old multiparous female presented at the outpatient clinic in her 38<sup>th</sup> week of this pregnancy because of fatigue and lightheadedness. She had been prescribed oral iron supplementation a month earlier but had not taken the tablets. Because her haemoglobin level had decreased to 6.3 mmol/l, it was decided to start her on intravenous iron dextran treatment. During administration of the test dose, the patient experienced acute dyspnoea and severe abdominal and back pain. Foetal bradycardia was observed and the patient underwent an emergency caesarean section. She delivered a healthy boy whose arterial pH was 7.05 (base excess: -7.6 mmol/l) and venous pH was 7.18 (base excess: -6.8 mmol/l).

CONCLUSION: This case demonstrates that dextran anaphylaxis can occur, with potentially lethal consequences, even when no known underlying risk factors are present.

*Impactfactor: --*

### **Kuppens SM**

#### **Induction of labor versus expectant management in women with preterm prelabor rupture of membranes between 34 and 37 weeks: a randomized controlled trial**

Ham DP van der, Vijgen SM, Nijhuis JG, Beek JJ van, Opmeer BC, Mulder AL, Moonen R, Groenewout M, Pampus MG van, Mantel GD, Bloemenkamp KW, Wijngaarden WJ van, Sikkema M, Haak MC, Pernet PJ, Porath M, Molkenboer JF, Kuppens SM\* Kwee A, Kars ME, Woiski M, Weinans MJ, Wildschut HI, Akerboom BM, Mol BW, Willekes C; PPRMEXIL trial group

PLoS Med. 2012;9(4):e1001208. Epub 2012 Apr 24

**BACKGROUND:** At present, there is insufficient evidence to guide appropriate management of women with preterm prelabor rupture of membranes (PPROM) near term.

**METHODS AND FINDINGS:** We conducted an open-label randomized controlled trial in 60 hospitals in The Netherlands, which included non-laboring women with >24 h of PPROM between 34(+0) and 37 (+0) wk of gestation. Participants were randomly allocated in a 1:1 ratio to induction of labor (IoL) or expectant management (EM) using block randomization. The main outcome was neonatal sepsis. Secondary outcomes included mode of delivery, respiratory distress syndrome (RDS), and chorioamnionitis. Patients and caregivers were not blinded to randomization status. We updated a prior meta-analysis on the effect of both interventions on neonatal sepsis, RDS, and cesarean section rate. From 1 January 2007 to 9 September 2009, 776 patients in 60 hospitals were eligible for the study, of which 536 patients were randomized. Four patients were excluded after randomization. We allocated 266 women (268 neonates) to IoL and 266 women (270 neonates) to EM. Neonatal sepsis occurred in seven (2.6%) newborns of women in the IoL group and in 11 (4.1%) neonates in the EM group (relative risk [RR] 0.64; 95% confidence interval [CI] 0.25 to 1.6). RDS was seen in 21 (7.8%, IoL) versus 17 neonates (6.3%, EM) (RR 1.3; 95% CI 0.67 to 2.3), and a cesarean section was performed in 36 (13%, IoL) versus 37 (14%, EM) women (RR 0.98; 95% CI 0.64 to 1.50). The risk for chorioamnionitis was reduced in the IoL group. No serious adverse events were reported. Updating an existing meta-analysis with our trial results (the only eligible trial for the update) indicated RRs of 1.06 (95% CI 0.64 to 1.76) for neonatal sepsis (eight trials, 1,230 neonates) and 1.27 (95% CI 0.98 to 1.65) for cesarean section (eight trials, 1,222 women) for IoL compared with EM.

**CONCLUSIONS:** In women whose pregnancy is complicated by late PPROM, neither our trial nor the updated meta-analysis indicates that IoL substantially improves pregnancy outcomes compared with EM.

*Impactfactor: 16.269*

### **Rumste MM van**

#### **Fatale afloop na ovarieel hyperstimulatiesyndroom bij in-vitrofertilisatie**

Sigterman TA, Monen L, Rumste MM van\*

NTOG: Nederlands tijdschrift voor Obstetrie & Gynaecologie; 125(8):393-6

Bij vrouwen die een ovariële stimulatietherapie ondergaan, dient men zich bewust te zijn van het verhoogde risico van ernstige trombo-embolische complicaties met mogelijk fatale afloop. De arteriële complicatie treedt vroeg op in vergelijking met de veneuze complicatie. Er is nog veel onduidelijk over de veranderingen in bloedstolling als gevolg van ovariële stimulatie. De kans op tromboembolische complicaties na OHSS blijft verhoogd gedurende het eerste trimester van de zwangerschap.

*Impactfactor: --*

### **Rumste MM van**

#### **Long-term outcome in couples with unexplained subfertility and an intermediate prognosis initially randomized between expectant management and immediate treatment**

Custers IM, Rumste MM van\*, Steeg JW van der, Wely M van, Hompes PG, Bossuyt P, Broekmans FJ, Renckens CN, Eijkemans MJ, Dessel TJ van, Veen F van der, Mol BW, Steures P; CECERM

Hum Reprod. 2012 Feb;27(2):444-50. Epub 2011 Nov 23

**BACKGROUND** We recently reported that treatment with intrauterine insemination and controlled ovarian stimulation (IUI-COS) did not increase ongoing pregnancy rates compared with expectant management (EM) in couples with unexplained subfertility and intermediate prognosis of natural conception. Long-term cost-effectiveness of a policy of initial EM is unknown. We investigated whether the recommendation not to treat during the first 6 months is valid, regarding the long-term effectiveness and cumulative costs.

**METHODS** Couples with unexplained subfertility and intermediate prognosis of natural conception (n=253, at 26 public clinics, the Netherlands) were randomly allocated to 6 months EM or immediate start with IUI-COS. The couples were then treated according to local protocol, usually IUI-COS followed by IVF. We followed couples until 3 years after randomization and registered pregnancies and resources used. Primary outcome was time to ongoing pregnancy. Secondary outcome was treatment costs. Analysis was by intention-to-treat. Economic evaluation was performed from the perspective of the health care institution.

**RESULTS** Time to ongoing pregnancy did not differ between groups (log-rank test P=0.98). Cumulative ongoing pregnancy rates were 72-73% for EM and IUI-COS groups, respectively [relative risk 0.99 (95% confidence interval (CI) 0.85-1.1)]. Estimated mean costs per couple were -3424 (95% CI -880--5968) in the EM group and -6040 (95% CI -4055--8125) in the IUI-COS group resulting in an estimated saving of -2616 per couple (95% CI -385--4847) in favour of EM.

**CONCLUSIONS** In couples with unexplained subfertility and an intermediate prognosis of natural conception, initial EM for 6 months results in a considerable cost-saving with no delay in achieving pregnancy or jeopardizing the chance of pregnancy. Further comparisons between aggressive and milder forms of ovarian stimulation should be performed.

*Impactfactor: 4.475*

## **Rumste MM van**

### **The value of chromosomal analysis in oligozoospermic men**

Stegen Ç, Rumste MM van\*, Mol BW, Koks CA

Fertil Steril. 2012 Dec;98(6):1438-42

**OBJECTIVE:** To determine the prevalence of chromosomal abnormalities in relation to sperm concentration in subfertile oligozoospermic men.

**DESIGN:** Retrospective cohort study. **SETTING:** Two teaching hospitals.

**PATIENT(S):** We retrospectively studied all men who received chromosomal analysis prior to intracytoplasmic sperm injection (ICSI) treatment from 2000 to 2010 in two teaching hospitals.

**INTERVENTION(S):** None.

**MAIN OUTCOME MEASURE(S):** The results of chromosomal analysis and semen analysis were recorded. The frequency of abnormal karyotypes was analyzed in relation to the sperm concentration, categorized as extreme oligozoospermia (>0 to d 1 million/mL), severe oligozoospermia (>1 to d 5 million/mL), moderate oligozoospermia (>5 to d 20 million/mL), or normospermia (>20 million/mL).

**RESULT(S):** Among 582 male ICSI candidates, the rates of abnormal karyotypes were 1.2% (2/162), 2.2% (5/227), and 1.5% (2/130) for men with extreme, severe, and moderate oligozoospermia, respectively. No abnormalities were present in normospermic men.

**CONCLUSION(S):** The risk of conceiving a viable child with unbalanced structural chromosomal abnormalities in men with oligozoospermia may not justify karyotyping.

*Impactfactor: 3.775*

**Schoot BC**

**Face and Construct Validity of the SimSurgery SEP VR Simulator for Salpingectomy in Case of Ectopic Pregnancy**

Hessel M\*, Buzink SN\*, Schoot D\*, and Jakimowicz JJ\*

Journal of Gynecologic Surgery. December 2012, 28(6): 411-417

*Voor abstract zie: Gynaecologie – Hessel M*

*Impactfactor: --*

**Schoot BC**

**Single versus multimodality training basic laparoscopic skills**

Brinkman WM\*, Havermans SY\*, Buzink SN, Botden SM, Jakimowicz JJ\*, Schoot BC\*

Surg Endosc. 2012 Aug;26(8):2172-8. Epub 2012 Feb 21

*Voor abstract zie: Urologie - Brinkman WM*

*Impactfactor: 4.013*

**Vliet HA van**

**Perioperative antibiotics to prevent infection after first-trimester abortion**

Low N, Mueller M, Vliet HA van\*, Kapp N

Cochrane Database Syst Rev. 2012 Mar 14;3:CD005217

**BACKGROUND:** There are two main strategies for the prevention of post-abortion upper genital tract infection: antibiotics given around the time of surgery for all women; and 'screen-and-treat', in which all women presenting for abortion are screened for genital infections and those with positive results are treated. **OBJECTIVES:** To determine: 1. the effectiveness of antibiotic prophylaxis in preventing post-abortion upper genital tract infection; 2. the most effective antibiotic regimen; 3. the most effective strategy. **SEARCH METHODS:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, POPLINE and LILACS. The search was updated in May 2011. **SELECTION CRITERIA:** Randomised controlled trials (RCTs) in any language including women undergoing induced first trimester surgical or medical abortion, comparing: 1) any antibiotic regimen to placebo, nothing, or another antibiotic; 2) screen-and-treat versus antibiotics. The primary outcome was the proportion of women diagnosed with post-abortion upper genital tract infection. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently selected references and extracted data. We calculated risk ratios (RR) with 95% confidence intervals (CI). We used meta-analysis where appropriate and examined between trial heterogeneity using the I(2) statistic. In the presence of between trial heterogeneity we also estimated the 95% prediction interval (PI). **MAIN RESULTS:** A total of 703 unique items was identified. We included 19 RCTs. There was evidence of small study biases (Egger test, P = 0.002). In 15 placebo-controlled RCTs there was an effect of antibiotic prophylaxis (pooled RR 0.59, 95% CI 0.46 to 0.75, 95% PI 0.30 to 1.14, I(2) = 39%). There were insufficient data (three trials) to determine whether one regimen was superior to another. In one trial, the incidence of post-abortion upper genital tract infection was higher in women allocated to the screen-and-treat strategy (RR 1.53, 95% CI 0.99 to 2.36). **AUTHORS' CONCLUSIONS:** Antibiotic prophylaxis at the time of first trimester surgical abortion is effective in preventing post-abortion upper genital tract infection. Evidence of between trial heterogeneity suggests that the effect might not apply to all settings, population groups or interventions. This review did not determine the most effective antibiotic prophylaxis regimen. Antibiotic choice should take into account the local epidemiology of genital tract infections, including sexually transmitted infections. Further RCTs comparing different antibiotics or combinations of antibiotics with each other would be useful. Such trials could be done in low and middle income countries

and where the prevalence of genital tract infections in women presenting for abortion is high.

*Impactfactor: --*

## **Vliet HA van**

### **Sex hormone-binding globulin as a marker for the thrombotic risk of hormonal contraceptives**

Raps M, Helmerhorst F, Fleischer K, Thomassen S, Rosendaal F, Rosing J, Ballieux B, Vliet H van\*

J Thromb Haemost. 2012 Jun;10(6):992-7

**BACKGROUND:** It takes many years to obtain reliable values for the risk of venous thrombosis of hormonal contraceptive users from clinical data. Measurement of activated protein C (APC) resistance via thrombin generation is a validated test for determining the thrombogenicity of hormonal contraceptives. Sex hormone-binding globulin (SHBG) might serve as a marker for the risk of venous thrombosis, and can be easily and rapidly measured in routine laboratories. **OBJECTIVE:** To determine whether SHBG is a useful marker for the thrombotic risk of hormonal contraceptive users by comparing plasma SHBG levels with normalized APC sensitivity ratio (nAPCsr) values and thrombosis risks reported in the recent literature. **METHODS:** We conducted an observational study in 262 users of different contraceptives, and measured nAPCsr and SHBG levels. **RESULTS:** Users of contraceptives with a higher risk of causing venous thrombosis, i.e. combined hormonal contraceptives containing desogestrel, cyproterone acetate or drospirenone, and the transdermal patch, had higher SHBG levels than users of combined hormonal contraceptives containing levonorgestrel, which carry a lower thrombosis risk. Users of the patch had the highest SHBG levels, with a mean difference of 246 nmol L(-1) (95% confidence interval 179-349) from that in users of levonorgestrel-containing combined hormonal contraceptives. SHBG levels were positively associated with both the nAPCsr and the risks of venous thrombosis reported in the recent literature. **CONCLUSION:** SHBG is a useful marker with which to estimate the thrombotic safety of a preparation.

*Impactfactor: 5.731*

\* = *Werkzaam in het Catharina Ziekenhuis*

∞ = *Ten tijde van publicatie werkzaam bij: Leiden University Medical Center, Department of Gynaecology, Division of Reproductive Medicine, Leiden, Netherlands*

## **Intensive Care**

## **Aarts RP**

### **Risk factors for osteoporosis in Caucasian patients with moderate chronic obstructive pulmonary disease: a case control study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA,

Donkers-van Rossum AB\*, Aarts RP\*, Wouters EF

Bone. 2012 Jun;50(6):1234-9. Epub 2012 Mar 9

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 4.023*

## **Bindels AJ**

### **Approach to hypophosphataemia in intensive care units - a nationwide survey**

Geerse DA\*, Bindels AJ\*, Kuiper MA, Roos AN\*, Spronk PE, Schultz MJ

Neth J Med. 2012 Nov;70(9):425-30

*Voor abstract zie: Intensive care - Geerse DA*

*Impactfactor: 2.072*

## **Bindels AJ**

### **Selective decontamination of the oral and digestive tract in surgical versus non-surgical patients in intensive care in a cluster-randomized trial**

Melsen WG, Smet AM de, Kluytmans JA, Bonten MJ; Dutch SOD-SDD Trialists' Group

Br J Surg. 2012 Feb;99(2):232-7. Epub 2011 Oct 24

**BACKGROUND:** Selective digestive decontamination (SDD) and selective oropharyngeal decontamination (SOD) are effective in improving survival in patients under intensive care. In this study possible differential effects in surgical and non-surgical patients were investigated.

**METHODS:** This was a post hoc subgroup analysis of data from a cluster-randomized multicentre trial comparing three groups (SDD, SOD or standard care) to quantify effects among surgical and non-surgical patients. The primary study outcome was 28-day mortality rate. Duration of mechanical ventilation, duration of intensive care unit (ICU) and hospital length of stay, and bacteraemia rates were secondary outcomes.

**RESULTS:** The subgroup analyses included a total of 2762 surgical and 3165 non-surgical patients. Compared with standard care, adjusted odds ratios (ORs) for mortality were comparable in SDD-treated surgical and non-surgical patients: 0.86 (95 per cent confidence interval 0.69 to 1.09;  $P = 0.220$ ) and 0.85 (0.70 to 1.03;  $P = 0.095$ ) respectively. However, duration of mechanical ventilation, ICU stay and hospital stay were significantly reduced in surgical patients who had SDD. SOD did not reduce mortality compared with standard treatment in surgical patients (adjusted OR 0.97, 0.77 to 1.22;  $P = 0.801$ ); in non-surgical patients it reduced mortality (adjusted OR 0.77, 0.63 to 0.94;  $P = 0.009$ ) by 16.6 per cent, representing an absolute mortality reduction of 5.5 per cent with number needed to treat of 18.

**CONCLUSION:** Subgroup analysis found similar effects of SDD in reducing mortality in surgical and non-surgical ICU patients, whereas SOD reduced mortality only in non-surgical patients. The hypothesis-generating findings mandate investigation into mechanisms between different ICU populations.

*Impactfactor: 4.606*

**Geerse DA**

**Approach to hypophosphataemia in intensive care units - a nationwide survey**

Geerse DA\*, Bindels AJ\*, Kuiper MA, Roos AN\*, Spronk PE, Schultz MJ

Neth J Med. 2012 Nov;70(9):425-30

Background: Evidence-based guidelines for monitoring of serum phosphate levels and for the treatment of hypophosphataemia in critically ill patients are lacking. The aim of this survey was to evaluate current practice with respect to diagnosis and treatment of hypophosphataemia in critically ill patients among intensive care unit (ICU) physicians in the Netherlands.

Methods: A survey was conducted among all hospitals with an ICU in the Netherlands. Paediatric ICUs were excluded from participation. A questionnaire was sent, with questions on practice regarding serum phosphate monitoring and treatment of hypophosphataemia. Respondents returned the questionnaire either by mail or through a web-based survey.

Results: A response was received from 67÷89 ICUs (75%). Respondents mentioned renal replacement therapy, sepsis and malnutrition, as well as surgery involving cardiopulmonary bypass as the most important causes of hypophosphataemia in intensive care unit patients. Of all respondents, 46% reported to measure serum phosphate levels on a daily basis, whereas in 12% serum phosphate levels were measured only on clinical indication. Less than half of the respondents had some sort of guideline for correction of hypophosphataemia. In a vast majority (79%), correction of hypophosphataemia was reported to start with serum phosphate levels.

*Impactfactor: 2.072*

**Roos AN**

**Approach to hypophosphataemia in intensive care units - a nationwide survey**

Geerse DA\*, Bindels AJ\*, Kuiper MA, Roos AN\*, Spronk PE, Schultz MJ

Neth J Med. 2012 Nov;70(9):425-30

*Voor abstract zie: Intensive care - Geerse DA*

*Impactfactor: 2.072*

\* = *Werkzaam in het Catharina Ziekenhuis*



## **Inwendige Geneeskunde**

## Beijers HJ

### **Clustering of metabolic syndrome traits is associated with maladaptive carotid remodeling and stiffening: a 6-year longitudinal study**

Ferreira I, Beijers HJ\*, Schouten F, Smulders YM, Twisk JW, Stehouwer CD

Hypertension. 2012 Aug;60(2):542-9

Maladaptive arterial remodeling may constitute a mechanism underlying the risk of stroke in individuals with metabolic syndrome (MetS), but evidence supporting this contention derives from cross-sectional studies only. We, therefore, investigated, in apparently healthy adults, whether changes in MetS status between the ages of 36 and 42 years (never [n=207, reference group], incident [n=31], recovery [n=23], and persistent [n=32]) were associated with changes in carotid interadventitial diameter, lumen diameter, intima-media thickness, circumferential wall tension and stress, and Young's elastic modulus.

All data analyses were adjusted for sex, height, and (changes in) age, lifestyle variables, low-density lipoprotein cholesterol, and use of antihypertensive medication. At baseline and as compared with the reference group, individuals with persistent MetS had significantly higher interadventitial diameter, circumferential wall tension, circumferential wall stress, and Young's elastic modulus but not intima-media thickness. In the course of follow-up, these individuals (versus reference group) displayed significantly steeper increases in intima-media thickness (0.011 versus 0.005 mm/y), which were accompanied by significantly steeper increases in interadventitial diameter (0.077 versus 0.032 mm/y) and lumen diameter (0.055 versus 0.023 mm/y) but not circumferential wall stress, which decreased (-0.34 versus 0.12 kPa/y). These findings suggest that increases in intima-media thickness in young adults with the MetS may primarily reflect an adaptive mechanism that attempts to restore local hemodynamic conditions to an equilibrium rather than atherosclerosis, per se. However, carotid adaptations did not restore circumferential wall stress to levels comparable with those of the reference group, and, therefore, outward remodeling was maladaptive. Importantly, individuals who recovered from the MetS restored carotid properties to levels comparable to the reference group, emphasizing the potential for reversibility.

*Impactfactor: 6.207*

## Beijers HJ

### **Impaired glucose metabolism and type 2 diabetes are associated with hypercoagulability: potential role of central adiposity**

Beijers HJ\*, Ferreira I, Spronk HM, Bravenboer B\*, Dekker JM, Nijpels G, Cate H ten, Stehouwer CD

Thromb Res. 2012 May;129(5):557-62. Epub 2011 Aug 17

**INTRODUCTION:** Type 2 diabetes (DM2) is associated with greater risk for cardiovascular disease (CVD), which may, at least partially, be explained by prothrombotic alterations. We therefore investigated; first, the extent to which individuals with impaired glucose metabolism (IGM) and/or DM2 had greater levels of thrombin generation than those with normal glucose metabolism (NGM); and second, whether any differences were independent of other cardiovascular risk factors, such as smoking, hypertension, dyslipidaemia, (micro)albuminuria, glycemic control and (central) adiposity, and/or were potentially 'mediated' by low-grade inflammation (high-sensitivity C-reactive protein (hsCRP)).

**MATERIALS AND METHODS:** We studied 744 individuals from the Hoorn Study (275 NGM, 176 IGM and 293 DM2, mean age 68.6±7.1years). Thrombin generation in platelet-poor plasma was measured using the Calibrated Automated Thrombogram and three parameters were derived: lag time, peak height and endogenous thrombin potential (ETP). Data were analyzed with multiple linear regression analyses.

RESULTS: After adjustment for age, sex, prior CVD and smoking status, individuals with IGM or DM2 had a longer lag time [ $\beta=0.14\text{min}$  (95% CI: 0.02; 0.26)], higher peak height [ $\beta=7.29\text{nM}$  (-1.33; 15.91)] and ETP [ $\beta=35.65\text{nM}\cdot\text{min}$  (0.97; 70.34)] than those with NGM. These differences were attenuated to  $\beta=0.06\text{min}$  (-0.07; 0.19), 3.82nM (-5.46; 13.10) and 16.34nM $\cdot\text{min}$  (-20.92; 53.59), respectively, when further adjusted for waist circumference and hsCRP.

CONCLUSION: Individuals with IGM or DM2 had up to 4% higher thrombin generation compared with NGM, which may be explained, to a great extent, by the greater levels of central adiposity and related low-grade inflammation characterizing these individuals.

*Impactfactor: 2.440*

### **Bravenboer B**

#### **Dose accuracy of new versus used Novopen 4 insulin pens**

Yucel H\*, Taks M\*, Menheere P, Grouls R\*, Bravenboer B\*

Diabetes Technol Ther. 2012 Sep;14(9):810-2. Epub 2012 Aug 6

*Voor abstract zie: Inwendige geneeskunde - Yucel H*

*Impactfactor: 1.931*

### **Bravenboer B**

#### **Hypogonadism in a patient with mild hereditary haemochromatosis**

Wlazlo N\*, Peters W\*, Bravenboer B\*

Neth J Med. 2012 Sep;70(7):318-20

*Voor abstract zie: Inwendige geneeskunde - Wlazlo N*

*Impactfactor: 2.072*

### **Bravenboer B**

#### **Impaired glucose metabolism and type 2 diabetes are associated with hypercoagulability: potential role of central adiposity**

Beijers HJ\*, Ferreira I, Spronk HM, Bravenboer B\*, Dekker JM, Nijpels G, Cate H ten, Stehouwer CD

Thromb Res. 2012 May;129(5):557-62. Epub 2011 Aug 17

*Voor abstract zie: Inwendige geneeskunde - Beijers HJ*

*Impactfactor: 2.440*

### **Bravenboer B**

#### **Improved resistance to ischemia and reperfusion, but impaired protection by ischemic preconditioning in patients with type 1 diabetes mellitus: a pilot study**

Engbersen R, Riksen NP, Mol MJ, Bravenboer B\*, Boerman OC, Meijer P, Oyen WJ, Tack C, Rongen GA, Smits P

Cardiovasc Diabetol. 2012 Oct 10;11(1):124

BACKGROUND: In patients with type 1 diabetes mellitus (T1DM), cardiovascular events are more common, and the outcome following a myocardial infarction is worse than in nondiabetic subjects. Ischemic or pharmacological preconditioning are powerful interventions to reduce ischemia reperfusion

(IR)-injury. However, animal studies have shown that the presence of T1DM can limit these protective effects. Therefore, we aimed to study the protective effect of ischemic preconditioning in patients with T1DM, and to explore the role of plasma insulin and glucose on this effect.

**METHODS:** 99mTechnetium-annexin A5 scintigraphy was used as a model of IR-injury. IR-injury was induced by unilateral forearm ischemic exercise. At reperfusion, Tc-annexin A5 was administered, and IR-injury was expressed as the percentage difference in radioactivity in the thenar muscle between the experimental and control arm 4 hours after reperfusion. 15 patients with T1DM were compared to 21 nondiabetic controls. The patients were studied twice, with or without ischemic preconditioning (10 minutes of forearm ischemia and reperfusion). Patients were studied in either normoglycemic hyperinsulinemic conditions (n = 8) or during hyperglycemic normoinsulinemia (n = 7). The controls were studied once either with (n = 8) or without (n = 13) ischemic preconditioning.

**RESULTS:** Patients with diabetes were less vulnerable to IR-injury than nondiabetic healthy controls (12.8 +/- 2.4 and 11.0 +/- 5.1% versus 27.5 +/- 4.5% in controls; p < 0.05). The efficacy of ischemic preconditioning to reduce IR-injury, however, was lower in the patients and was even completely abolished during hyperglycemia.

**CONCLUSIONS:** Patients with T1DM are more tolerant to forearm IR than healthy controls in our experimental model. The efficacy of ischemic preconditioning to limit IR-injury, however, is reduced by acute hyperglycemia. Trial.

*Impactfactor: 3.346*

## **Bravenboer B**

### **Low-grade inflammation and insulin resistance independently explain substantial parts of the association between body fat and serum C3: The CODAM study**

Wlazlo N\*, Greevenbroek MM van, Ferreira I, Jansen EJ, Feskens EJ, Kallen CJ van der, Schalkwijk CG, Bravenboer B\*, Stehouwer CD

Metabolism. 2012 Dec;61(12):1787-96. Epub 2012 Jul 2

*Voor abstract zie: Inwendige geneeskunde - Wlazlo N*

*Impactfactor: 2.664*

## **Bravenboer B**

### **Patients with chronic gastrointestinal ischemia have a higher cardiovascular disease risk and mortality**

Sana A, Noord D van, Mensink PB, Kooij S, Dijk K van, Bravenboer B\*, Lieveise AG, Sijbrands EJ, Langendonk JG, Kuipers EJ

Atherosclerosis. 2012 Sep;224(1):235-41

**OBJECTIVES:** We determined the prevalence of classical risk factors for atherosclerosis and mortality risk in patients with CGI.

**METHODS:** A case-control study was conducted. Patients referred with suspected CGI underwent a standard work-up including risk factors for atherosclerosis, radiological imaging of abdominal vessels and tonometry. Cases were patients with confirmed atherosclerotic CGI. Controls were healthy subjects previously not known with CGI. The mortality risk was calculated as standardized mortality ratio derived from observed mortality, and was estimated with ten-year risk of death using SCORE and PREDICT.

**RESULTS:** Between 2006 and 2009, 195 patients were evaluated for suspected CGI. After a median follow-up of 19 months, atherosclerotic CGI was diagnosed in 68 patients. Controls consisted of 132 subjects. Female gender, diabetes, hypercholesterolemia, a personal and family history of cardiovascular disease (CVD), and current smoking are highly associated with CGI. After adjustment, female gender (OR 2.14 95% CI 1.05-4.36), diabetes (OR 5.59, 95% CI 1.95-16.01), current smoking (OR 5.78, 95% CI 2.27-14.72), and history of CVD (OR 21.61, 95% CI 8.40-55.55) remained significant. CGI patients >55 years had a higher median ten-year risk of death (15% vs. 5%, P = 0.001) compared to controls. During follow-up of 116

person-years, standardized mortality rate was higher in CGI patients (3.55; 95% CI 1.70-6.52).

**CONCLUSIONS:** Patients with atherosclerotic CGI have an increased estimated CVD risk, and severe excess mortality. Secondary cardiovascular prevention therapy should be advocated in patients with CGI.

*Impactfactor: 3.794*

## **Bravenboer B**

### **The diagnosis of non-alcoholic fatty liver disease**

Wlazlo N\*, Greevenbroek MM van, Ferreira I, Bravenboer B\*, Stehouwer CD

*Aliment Pharmacol Ther.* 2012 Jan;35(1):204-5

*Voor abstract zie: Inwendige geneeskunde - Wlazlo N*

*Impactfactor: 3.769*

## **Creemers GJ**

### **Preoperative chemoradiotherapy for esophageal or junctional cancer**

Hagen P van, Hulshof MC, Lanschot JJ van, Steyerberg EW, Berge Henegouwen MI van, Wijnhoven BP, Richel DJ, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Kate FJ ten, Creemers GJ\*, Punt CJ, Plukker JT, Verheul HM, Spillenaar Bilgen EJ, Dekken H van, Sangen MJ van der\*, Rozema T, Biermann K, Beukema JC, Piet AH, Rij CM van, Reinders JG, Tilanus HW, Gaast A van der; CROSS Group

*N Engl J Med.* 2012 May 31;366(22):2074-84

*Voor abstract zie: Chirurgie - Nieuwenhuijzen GA*

*Impactfactor: 53.298*

## **Creemers GJ**

### **Randomised phase II/III study of docetaxel with or without risedronate in patients with metastatic Castration Resistant Prostate Cancer (CRPC), the Netherlands Prostate Study (NePro)**

Meulenbeld HJ, Werkhoven ED van, Coenen JL, Creemers GJ\*, Loosveld OJ, Jong PC de, Ten Tije AJ, Fosså SD, Polee M, Gerritsen W, Dalesio O, Wit R de

*Eur J Cancer.* 2012 Nov;48(16):2993-3000. Epub 2012 Jun 6

**BACKGROUND:** This multicentre, randomised, open label, phase II/III study aimed to investigate the potential benefit of adding risedronate (R) to docetaxel (D) in patients with metastatic Castration Resistant Prostate Cancer (CRPC).

**PATIENTS AND METHODS:** CRPC patients with bone metastasis were randomly assigned to receive D 75mg/m<sup>2</sup> every 3weeks and prednisone as first line chemotherapy, with or without R 30mg oral once daily. The primary end-point was time to progression (TTP). A composite end-point of objective progression by RECIST criteria, PSA progression, or pain progression, whichever occurred first, was applied. The study had 80% power to detect an improvement of 30% in median TTP in the DR group (two-sided =0.05).

**RESULTS:** Five hundred and ninety-two men (301 D versus 291 DR) were randomised. TTP was 7.4 [D] versus 6.5 [DR] months (p=0.75). PSA and pain response rates were similar, 66.3% [D] versus 65.9% [DR] and 27.9% [D] versus 31.2% [DR], respectively. Median overall survival (OS) was 18.4 [D] versus 19.2 [DR] months (p=0.33). There were no differences in toxicity.

CONCLUSION: The addition of the third generation bisphosphonate, risedronate, in the setting of effective first line docetaxel based chemotherapy did not increase efficacy, as indicated by the lack of improvement in TTP, OS, PSA- and pain response.

*Impactfactor: 5.536*

### **Creemers GJ**

#### **T3+ and T4 rectal cancer patients seem to benefit from the addition of oxaliplatin to the neoadjuvant chemoradiation regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

### **Creemers GJ**

#### **The effect of socioeconomic status on staging and treatment decisions in esophageal cancer**

Bus P, Aarts MJ, Lemmens VE, Oijen MG van, Creemers GJ\*, Nieuwenhuijzen GA\*, Baal JW van, Siersema PD

J Clin Gastroenterol. 2012 Nov;46(10):833-9

BACKGROUND: : Optimal treatment choice for patients with esophageal cancer (EC) is complex and largely determined by tumor characteristics, comorbidity, and age.

GOALS: : This study describes the role of patient characteristics, among which is socioeconomic status (SES), in EC treatment. STUDY: : Patients diagnosed with primary EC between 1990 and 2008 in the southern part of the Netherlands were identified using the Eindhoven Cancer Registry. Multivariable logistic and proportional hazard regression analyses were used to identify determinants of treatment and survival.

RESULTS: : We included 1914 patients, and 37% of them underwent intentionally curative treatment. Low-SES patients were diagnosed at older age (16% vs. 9%, age more than or equal to 80) and with more advanced tumor stages (13% vs. 10%, stage T4) than high-SES patients. Age less than 60 compared with 70 to 79 years [adjusted odds ratio, 4.51; 95% confidence interval (CI), 2.98-6.84] and high SES compared with low SES (adjusted odds ratio 1.59; 95% CI, 1.07-2.37) were independent predictors for curative treatment. Probability of death for high-SES patients undergoing palliative treatment was decreased compared with low-SES patients (hazard ratio, 0.84; 95% CI, 0.71-0.99).

CONCLUSIONS: : SES is an important factor in treatment choice of EC. As health care is equally accessible to the whole population in the Netherlands, this suggests that both patient-related and physician-related factors are involved in this phenomenon.

*Impactfactor: 3.159*

**Gilissen LP**

**Therapeutic drug monitoring of thiopurine metabolites in adult thiopurine tolerant IBD patients on maintenance therapy**

Gilissen LP\*, Wong DR, Engels LG, Bierau J, Bakker JA, Paulussen AD, Romberg-Camps MJ, Stronkhorst A\*, Bus P, Bos LP, Hooymans PM, Stockbrügger RW, Neef C, Masclee AA

J Crohns Colitis. 2012 Jul;6(6):698-707. Epub 2012 Jan 10

**BACKGROUND AND AIMS:** Therapeutic drug monitoring of active metabolites of thiopurines, azathioprine and 6-mercaptopurine, is relatively new. The proposed therapeutic threshold level of the active 6-thioguanine nucleotides (6-TGN) is  $\leq 235$  pmol/ $8 \times 10^8$  erythrocytes. The aim of this prospective cross-sectional study was to compare 6-TGN levels in adult thiopurine tolerant IBD patients with an exacerbation with those in remission, and to determine the therapeutic 6-TGN cut-off level.

**METHODS:** Hundred IBD patients were included. Outcome measures were thiopurine metabolite levels, calculated therapeutic 6-TGN cut-off level, CDAI/CAI scores, thiopurine dose and TPMT enzyme activity.

**RESULTS:** Forty-one patients had an exacerbation, 59 patients were in remission. In 17% of all patients 6-TGN levels were compatible with non-compliance. The median 6-TGN levels were not significantly different between the exacerbation and remission group (227 versus 263 pmol/ $8 \times 10^8$  erythrocytes,  $p=0.29$ ). The previous reported therapeutic 6-TGN cut-off level of 235 pmol/ $8 \times 10^8$  erythrocytes was confirmed in this study. Twenty-six of the 41 patients (63%) with active disease had 6-TGN levels below this threshold and 24 of 59 IBD patients (41%) in clinical remission ( $p=0.04$ ).

**CONCLUSIONS:** Thiopurine non-compliance occurs frequently both in active and quiescent disease. 6-TGN levels below or above the therapeutic threshold are associated with a significant higher chance of IBD exacerbation and remission, respectively. These data support the role of therapeutic drug monitoring in thiopurine maintenance therapy in IBD to reveal non-compliance or underdosing, and can be used as a practical tool to optimize thiopurine therapy, especially in case of thiopurine non-response.

*Impactfactor: 2.566*

**Konings CJ**

**Differences in quality of life of hemodialysis patients between dialysis centers**

Mazairac AH, Grooteman MP, Blankestijn PJ, Penne EL, Weerd NC van der, Hoedt CH den, Dorpel MA van den, Buskens E, Nubé MJ, Wee PM ter, Wit GA de, Bots ML; CONTRAST investigators. Konings CJ\*

Qual Life Res. 2012 Mar;21(2):299-307. Epub 2011 Jun 2

**PURPOSE:** Hemodialysis patients undergo frequent and long visits to the clinic to receive adequate dialysis treatment, medical guidance, and support. This may affect health-related quality of life (HRQOL). Although HRQOL is a very important management aspect in hemodialysis patients, there is a paucity of information on the differences in HRQOL between centers. We set out to assess the differences in HRQOL of hemodialysis patients between dialysis centers and explore which modifiable center characteristics could explain possible differences.

**METHODS:** This cross-sectional study evaluated 570 hemodialysis patients from 24 Dutch dialysis centers. HRQOL was measured with the Kidney Disease Quality Of Life-Short Form (KDQOL-SF).

RESULTS: After adjustment for differences in case-mix, three HRQOL domains differed between dialysis centers: the physical composite score (PCS,  $P = 0.01$ ), quality of social interaction ( $P = 0.04$ ), and dialysis staff encouragement ( $P = 0.001$ ). These center differences had a range of 11-21 points on a scale of 0-100, depending on the domain. Two center characteristics showed a clinically relevant relation with patients' HRQOL: dieticians' fulltime-equivalent and the type of dialysis center.

CONCLUSION: This study showed that clinically relevant differences exist between dialysis centers in multiple HRQOL domains. This is especially remarkable as hemodialysis is a highly standardized therapy.

*Impactfactor: 2.300*

### **Konings CJ**

#### **Effect of online hemodiafiltration on all-cause mortality and cardiovascular outcomes**

Grooteman MP, Dorpel MA van den, Bots ML, Penne EL, Weerd NC van der, Mazairac AH, Hoedt CH den, Tweel I van der, Lévesque R, Nubé MJ, Wee PM ter, Blankestijn PJ; CONTRAST Investigators. Konings CJ\*

J Am Soc Nephrol. 2012 Jun;23(6):1087-96. Epub 2012 Apr 26

In patients with ESRD, the effects of online hemodiafiltration on all-cause mortality and cardiovascular events are unclear. In this prospective study, we randomly assigned 714 chronic hemodialysis patients to online postdilution hemodiafiltration ( $n=358$ ) or to continue low-flux hemodialysis ( $n=356$ ). The primary outcome measure was all-cause mortality. The main secondary endpoint was a composite of major cardiovascular events, including death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, therapeutic coronary intervention, therapeutic carotid intervention, vascular intervention, or amputation. After a mean 3.0 years of follow-up (range, 0.4-6.6 years), we did not detect a significant difference between treatment groups with regard to all-cause mortality (121 versus 127 deaths per 1000 person-years in the online hemodiafiltration and low-flux hemodialysis groups, respectively; hazard ratio, 0.95; 95% confidence interval, 0.75-1.20). The incidences of cardiovascular events were 127 and 116 per 1000 person-years, respectively (hazard ratio, 1.07; 95% confidence interval, 0.83-1.39). Receiving high-volume hemodiafiltration during the trial associated with lower all-cause mortality, a finding that persisted after adjusting for potential confounders and dialysis facility. In conclusion, this trial did not detect a beneficial effect of hemodiafiltration on all-cause mortality and cardiovascular events compared with low-flux hemodialysis. On-treatment analysis suggests the possibility of a survival benefit among patients who receive high-volume hemodiafiltration, although this subgroup finding requires confirmation.

*Impactfactor: 9.663*

### **Konings CJ**

#### **Fluid state and blood pressure control: no differences between APD and CAPD**

Cnossen TT, Konings CJ\*, Fagel WJ, Sande FM van der, Geel K van, Leunissen KM, Kooman JP

ASAIO J. 2012 Mar-Apr;58(2):132-6

The aim of this study was to compare fluid state, ambulatory blood pressure, and sodium removal in automated peritoneal dialysis (APD) and continuous ambulatory peritoneal dialysis (CAPD). This observational, cross-sectional study comprised 20 APD and 24 CAPD

patients with a mean duration on peritoneal dialysis of  $30 \pm 26$  and  $21 \pm 23$  months, respectively. Sixty-four percent of the patients were treated with icodextrin.

The methods used were 24 hr dialysate and urine collections, standardized 3.86% glucose peritoneal equilibration test (PET), bioimpedance analysis, and 24 hr ambulatory blood pressure monitoring. Extracellular water (ECW) corrected for body weight was  $0.23 \pm 0.03$  L/kg both in APD and CAPD patients. The slope normovolemia value according to Chamney was  $0.06 \pm 0.02$  L/kg in APD patients and  $0.06 \pm 0.05$  L/kg in CAPD patients (not significant [NS]). Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were respectively,  $132 \pm 25$  and  $79 \pm 8$  mm Hg in APD and  $129 \pm 16$  and  $76 \pm 11$  mm Hg in CAPD patients (NS). Sodium concentration in dialysate was respectively,  $129.5 \pm 3.5$  mmol/L in APD and  $132.4 \pm 4.1$  mmol/L in CAPD ( $p = 0.017$ ). Dialysate sodium removal was  $80.6 \pm 78.4$  mmol/24 hr in APD and  $108.7 \pm 96.8$  mmol/24 hr in CAPD patients (NS).

Natriuresis was respectively, in APD  $76.6 \pm 65.5$  mmol/24 hr and in CAPD  $93.5 \pm 61.7$  mmol/24 hr (NS). Total sodium removal was  $149.5 \pm 76.6$  mmol/24 hr in APD and  $198.4 \pm 75.0$  mmol/24 hr in CAPD ( $p = .039$ ). Despite a higher daily sodium removal in CAPD patients, fluid state and blood pressure were not different between APD and CAPD.

In general, volume status and blood pressure appeared to be reasonably controlled in this unselected population.

*Impactfactor: 1.394*

### **Konings CJ**

#### **Moderate elevations of high-sensitivity cardiac troponin I and B-type natriuretic peptide in chronic hemodialysis patients are associated with mortality**

Geerse DA, Berkel M van\*, Vogels S, Kooman JP, Konings CJ\*, Scharnhorst V\*

Clin Chem Lab Med. 2012 Dec 10:1-8

*Voor abstract zie: Algemeen Klinisch Laboratorium - Berkel M van*

*Impactfactor: 2.150*

### **Konings CJ**

#### **Peritoneal dialysis in patients with heart failure**

Sande FM van der, Cnossen TT, Cornelis T, Konings CJ\*, Kooman JP, Leunissen KM

Minerva Urol Nefrol. 2012 Sep;64(3):163-72

Both in dialysis patients and non-uremic patients heart failure is associated with an adverse prognosis. In a state of abrupt worsening of cardiac function, acute cardiogenic shock or decompensated congestive heart failure, acute kidney injury may occur, whereas in a more chronic worsening of cardiac function chronic kidney injury may occur. Recently, the term cardiorenal syndrome was adopted and defined as "a pathophysiological disorder of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ".

Despite better treatment techniques and the continuous development of new medications volume overload in patients with cardiorenal syndrome is difficult to treat. Especially treatment of cardiorenal syndrome type I and II is notoriously difficult. Peritoneal dialysis might be, because of the gradual fluid removal, a therapeutic option in these patients. However, data on the effect of peritoneal dialysis in patients with heart failure with fluid overload and/or renal impairment are scarce. In this review, the role of peritoneal dialysis in the treatment cardiorenal syndrome type I, II and IV will be discussed.

*Impactfactor: --*

## **Konings CJ**

### **Poor compliance with guidelines on anemia treatment in a cohort of chronic hemodialysis patients**

Weerd NC van der, Grooteman MP, Blankestijn PJ, Mazairac AH, Dorpel MA van den, Hoedt CH den, Nubé MJ, Penne EL, Tweel I van der, Wee PM ter, Bots ML; CONTRAST investigators. Konings CJ\*

Blood Purif. 2012;34(1):19-27. Epub 2012 Aug 8

**BACKGROUND/AIMS:** Guidelines for the management of anemia and iron deficiency in chronic hemodialysis (HD) patients have been developed to standardize therapy and improve clinical outcome. The present study evaluated compliance with anemia guidelines and investigated whether differences between centers were present.

**METHODS:** Data on anemia management from patients in the baseline cohort of the CONTRAST study (NCT00205556) were analyzed. 598 chronic HD patients (62% male, age  $63.6 \pm 14.0$  years) from 26 Dutch dialysis centers were included.

**RESULTS:** Mean hemoglobin (Hb) level was  $11.9 \pm 1.3$  g/dl and Hb was  $\leq 11.0$  g/dl in 81% of the patients. Compliance with all anemia targets (Hb 11.0-12.0 g/dl, transferrin saturation ratio  $\geq 20\%$ , ferritin 100-500 ng/ml) was reached in 11.6% (95% CI 7.8-17.0) of the patients, with a wide range among centers (4-26%, adjusted for case mix, treatment-related factors and center-specific characteristics).

**CONCLUSION:** Compliance with anemia targets in stable HD patients was poor and showed a wide variation between treatment facilities.

*Impactfactor: 2.104*

## **Konings CJ**

### **Prospective study on clinical effects of renal replacement therapy in treatment-resistant congestive heart failure**

Cnossen TT, Kooman JP, Krepel HP, Konings CJ\*, Uszko-Lencer NH, Leunissen KM, Sande FM van der

Nephrol Dial Transplant. 2012 Jul;27(7):2794-9. Epub 2012 Apr 6

**BACKGROUND/AIMS:** Clinical outcome in cardiorenal syndrome (CRS) Type 2 and treatment with dialysis.

**METHODS:** Prospective observational non-randomized study.

**RESULTS:** Twenty-three patients were included, mean age  $66 \pm 21$  years. Twelve (52%) patients were treated with peritoneal dialysis (PD) and 11 (48%) with intermittent haemodialysis (IHD). Median survival time after start of dialysis was 16 months. Hospitalizations for cardiovascular causes were reduced ( $1.4 \pm 0.6$  pre-dialysis versus  $0.4 \pm 0.6$  days/patient/month post-dialysis,  $P=0.000$ ), without significant changes in hospitalization for all causes ( $1.8 \pm 1.6$  versus  $2.1 \pm 2.9$  days/patient/month). New York Heart Association (NYHA) class ( $3.8 \pm 0.4$  at start versus  $2.4 \pm 0.7$  after 4 months,  $P=0.000$ , versus  $2.7 \pm 0.9$  after 8 months,  $P=0.001$ ) and quality of life tended to improve ( $63 \pm 21$  at start, versus  $41 \pm 20$  after 4 months, versus  $51 \pm 25$  after 8 months;  $P=0.056$ ). Left ventricular ejection fraction did not change. The number of technical complications associated with dialysis therapy was relatively high in this population.

**CONCLUSIONS:** After starting dialysis for CRS, hospitalizations for cardiovascular causes were reduced, but not hospitalizations for all causes. Functional NYHA class improved and quality of life tended to improve, without evidence for a change in cardiac function. In this small study, no differences between IHD and PD were observed.

*Impactfactor: 3.396*

## **Konings CJ**

### **Steroid use is associated with clinically irrelevant biopsies in patients with suspected giant cell arteritis**

Thomassen I\*, Brok AN den, Konings CJ\*, Nienhuijs SW\*, Poll MC van de\*

Am Surg. 2012 Dec;78(12):1362-8

Voor abstract zie: *Chirurgie - Thomassen I*

Impactfactor: 1.285

## **Link LH**

### **Molecular detection of Plasmodium knowlesi in a Dutch traveler by real-time PCR**

Link L\*, Bart A, Verhaar N, Gool T van, Pronk M, Scharnhorst V\*

J Clin Microbiol. 2012 Jul;50(7):2523-4. Epub 2012 May 9

Plasmodium knowlesi infection with low parasitemia presents a diagnostic challenge, as rapid diagnostic tests are often negative and identification to the species level by microscopy is difficult. P. knowlesi malaria in a traveler is described, and real-time PCR is demonstrated to support fast and reliable diagnosis and identification to the species level.

Impactfactor: 4.153

## **Peters WG**

### **Chronic Lymphocytic Leukaemia in the Netherlands: Trends in incidence, treatment and survival, 1989-2008**

Broek EC van den, Kater AP, Schans SA van de, Karim-Kos HE, Janssen-Heijnen ML, Peters WG\*, Nooijen PT, Coebergh JW, Posthuma EF

Eur J Cancer. 2012 Apr;48(6):889-95. Epub 2011 Jul 25

We present trends in incidence, early treatment and survival of Chronic Lymphocytic Leukaemia (CLL) between 1989 and 2008, based on population-based data from the Netherlands Cancer Registry.

Incidence rates were stable at 5.1 per 100,000 person-years for males, but increased from 2.3 to 2.5 for females, especially for females aged 50-64years (from 3.6 to 4.3). Patients were less likely to receive chemotherapy within six months, i.e. from 29% to 24% among males and from 25% to 21% among females. Five-year relative survival increased from 61% in 1989-1993 to 70% 2004-2008 for males, and from 71% to 76% for females. The relative excess risk of dying decreased in time to 0.7 (males) and 0.9 (females) in 2004-2008, reference 1989-1993, and increased with age to 2.9 (males) and 1.8 (females) in patients aged 75-94years, reference 30-64years. The increasing incidence among females aged 50-64 coincided with the introduction of mass screening for breast cancer, which resulted in a large group of women under increased surveillance and possibly led to increased detection of CLL. The increase in survival might be underestimated due to possible decreased or delayed registration of indolent cases and the retroactive effect of the introduction of new therapies.

Impactfactor: 5.536

## **Peters WG**

### **Hypogonadism in a patient with mild hereditary haemochromatosis**

Wlazlo N\*, Peters W\*, Bravenboer B\*

Neth J Med. 2012 Sep;70(7):318-20

Voor abstract zie: *Inwendige geneeskunde - Wlazlo N*

Impactfactor: 2.072

**Pronk MJ**

**Aetiology of acute gastroenteritis in adults requiring hospitalization in The Netherlands**

Friesema IH, Boer RF de, Duizer E, Kortbeek LM, Notermans DW, Smeulders A, Bogerman J, Pronk MJ\*, Uil JJ, Brinkman K, Koopmans MP, Kooistra-Smid AM, Duynhoven YT van

Epidemiol Infect. 2012 Oct;140(10):1780-6. Epub 2011 Dec 8

SUMMARY Infectious gastroenteritis causes a considerable burden of disease worldwide. Effective control should be targeted at diseases with the highest burden and costs. Therefore, an accurate understanding of the relative importance of the different microorganisms is needed. The objective of this study was to determine the incidence and aetiology of gastroenteritis in adults requiring hospital admission in The Netherlands.

Five hospitals enrolled patients admitted with gastroenteritis for about 1 year during the period May 2008 to November 2009. Participants completed questionnaires and provided a faecal sample. The hospital completed a clinical questionnaire. In total, 44 adults hospitalized for gastroenteritis were included in the study. The cases had serious symptoms, with 31% subsequently developing kidney failure. One or more pathogens were found in 59% of cases. Overall, rotavirus (22%) was the most common infection. Co-infections were observed relatively often (22%).

This study emphasizes that rotavirus can also cause serious illness in adults.

*Impactfactor: 2.843*

**Pronk MJ**

**Costs of gastroenteritis in the Netherlands, with special attention for severe cases**

Friesema IH, Lugnér AK, Duynhoven YT van, Duizer E, Kortbeek LM, Notermans DW, Koopmans MP, Boer RF de, Kooistra-Smid AM, Norbruis OF, Bezemer DD, Smeulders A, Fraaij PL, Bogerman J, Heerbeek H van \*, Pronk MJ\*, Enk JG van, Uil JJ, Andel RN van, Brinkman K

Eur J Clin Microbiol Infect Dis. 2012 Aug;31(8):1895-900. Epub 2012 Jan 8

*Voor abstract zie: Kindergeneeskunde - Heerbeek H van*

*Impactfactor: 2.859*

**Pronk MJ**

**Microbiological challenges in the diagnosis of chronic Q fever**

Kampschreur LM, Oosterheert JJ, Koop AM, Wegdam-Blans MC\*, Delsing CE, Bleeker-Rovers CP, Jager-Leclercq MG de, Groot CA, Sprong T, Nabuurs-Franssen MH, Renders NH, Kasteren ME van, Soethoudt Y, Blank SN, Pronk MJ\*, Groenwold RH, Hoepelman AI, Wever PC

Clin Vaccine Immunol. 2012 May;19(5):787-90

*Voor abstract zie: PAMM- Wegdam-Blans MC*

*Impactfactor: 2.546*

## **Stronkhorst A**

### **Therapeutic drug monitoring of thiopurine metabolites in adult thiopurine tolerant IBD patients on maintenance therapy**

Gilissen LP\*, Wong DR, Engels LG, Bierau J, Bakker JA, Paulussen AD, Romberg-Camps MJ, Stronkhorst A\*, Bus P, Bos LP, Hooymans PM, Stockbrügger RW, Neef C, Masclee AA

J Crohns Colitis. 2012 Jul;6(6):698-707. Epub 2012 Jan 10

Voor abstract zie: *Inwendige geneeskunde - Gilissen LP*

*Impactfactor: 2.566*

## **Wlazlo N**

### **Hypogonadism in a patient with mild hereditary haemochromatosis**

Wlazlo N\*, Peters W\*, Bravenboer B\*

Neth J Med. 2012 Sep;70(7):318-20

Hypogonadism is a potential complication of haemochromatosis, usually seen in patients with severe iron overload and liver cirrhosis. We describe the diagnostic workup of a patient with an early stage of hereditary haemochromatosis, presenting with only mildly elevated liver enzymes and central hypogonadism in the absence of cirrhosis or diabetes, but with concurrent sarcoidosis.

*Impactfactor: 2.072*

## **Wlazlo N**

### **Lipid metabolism: a role for iron?**

Wlazlo N\*, Greevenbroek MM

Curr Opin Lipidol. 2012 Jun;23(3):258-9

*Impactfactor: 6.086*

## **Wlazlo N**

### **Low-grade inflammation and insulin resistance independently explain substantial parts of the association between body fat and serum C3: The CODAM study**

Wlazlo N\*, Greevenbroek MM van, Ferreira I, Jansen EJ, Feskens EJ, Kallen CJ van der, Schalkwijk CG, Bravenboer B\*, Stehouwer CD

Metabolism. 2012 Dec;61(12):1787-96. Epub 2012 Jul 2

**OBJECTIVE:** To investigate the role of low-grade inflammation and insulin resistance (HOMA2-IR) in adiposity-related increases in serum complement factor 3 (C3). Although C3 has been linked to type 2 diabetes and cardiovascular diseases, and C3 levels are closely related to body fat, the underlying mechanisms explaining this association are still unknown.

**METHODS:** Adiposity measures (including BMI, waist circumference (WC), sagittal diameter and several skinfolds), HOMA2-IR and markers of inflammation (hs-CRP, IL-6, SAA, haptoglobin, ceruloplasmin, sICAM-1) were determined in 532 individuals (62% men, mean age 59±6.9yrs) from the Cohort on Diabetes and Atherosclerosis Maastricht study. Markers of inflammation were standardized and compiled into an averaged inflammation score. Cross-sectional associations between adiposity measures and C3 and the mediating role of low-grade inflammation and/or HOMA2-IR herein were analysed with multiple linear regression models.

**RESULTS:** Adiposity measurements were significantly associated with C3 levels, with the strongest (adjusted) associations found for WC ( =0.383; 95%CI 0.302-0.464) and sagittal diameter ( =0.412; 95%CI 0.333-0.490). Further adjustment for inflammation and HOMA2-IR

attenuated these associations to  $\beta=0.115$  (95%CI 0.030-0.200) and  $\beta=0.163$  (95%CI 0.082-0.244) respectively. Multiple mediation analyses showed that inflammation [ $\beta=0.090$  (95%CI 0.060-0.126)] and HOMA2-IR [ $\beta=0.179$  (95%CI 0.128-0.236)] each explained, independently of one another, a significant portion of the association between WC and C3 (23% and 47%, respectively). Similar mediation by inflammation (19-27%) and HOMA2-IR (37-56%) was found for other adiposity measures.

**CONCLUSION:** Systemic low-grade inflammation and insulin resistance may represent two independent pathways by which body fat leads to elevated C3 levels.

*Impactfactor: 2.664*

## **Wlazlo N**

### **The diagnosis of non-alcoholic fatty liver disease**

Wlazlo N\*, Greevenbroek MM van, Ferreira I, Bravenboer B\*, Stehouwer CD  
Aliment Pharmacol Ther. 2012 Jan;35(1):204-5

Comment on:

Systematic review: the diagnosis and staging of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. [Aliment Pharmacol Ther. 2011]

*Impactfactor: 3.769*

## **Yucel H**

### **Dose accuracy of new versus used Novopen 4 insulin pens**

Yucel H\*, Taks M\*, Menheere P, Grouls R\*, Bravenboer B\*

Diabetes Technol Ther. 2012 Sep;14(9):810-2. Epub 2012 Aug 6

**OBJECTIVE:** To our knowledge, no studies have been performed testing dose accuracy in both new and used patient insulin injection pens. We hypothesized that the dose accuracy of used (>1 year) insulin pens to be less accurate than that of new insulin pens and investigated whether possible differences influence the treatment. This study compared the dosing accuracy of 11 new and 11 used (>1 year) Novopen(®) 4 pens (Novo Nordisk, Bagsvaerd, Denmark).

**MATERIALS AND METHODS:** Dosing accuracy differences between new and used pens were studied by weighing the volume of the dosage of 8 international units of insulin (IU) and 32 IU of 11 pens. Each measurement was repeated 15 times. Whether the pens complied with the International Organization for Standardization (ISO) limits of 10% for 8 IU and 5% for 32 IU was tested. The statistical analyses were performed using the Mann-Whitney rank sum test (within Sigmaplot version 12.0; Systat Software, Chicago, IL), and a P value of <0.05 was considered to be statistically significant.

**RESULTS:** For the 8 IU dose, the mean delivered dose was 8.04 IU in new pens and 7.91 IU in used insulin pens. For the 32 IU dose, the mean delivered dose was 31.90 in new pens and 31.68 IU in used insulin pens. The difference in the median values between the two groups was statistically significant ( $P<0.001$ ). Three individual doses in the 32 IU dose exceeded the ISO range in the lower range. The difference in mean variation coefficient between the two groups was also statistically significant ( $P<0.001$ ).

**CONCLUSIONS:** There was a significant difference between the accuracy of new versus used insulin pens. More studies with larger sample sizes are necessary to confirm our findings and further elucidate the relationship between age of insulin pens and dose accuracy.

*Impactfactor: 1.931*

\* = *Werkzaam in het Catharina Ziekenhuis*

# Kindergeneeskunde

**Heerbeek H van**

**Costs of gastroenteritis in the Netherlands, with special attention for severe cases**

Friesema IH, Lugnér AK, Duynhoven YT van, Duizer E, Kortbeek LM, Notermans DW, Koopmans MP, Boer RF de, Kooistra-Smid AM, Norbruis OF, Bezemer DD, Smeulders A, Fraaij PL, Bogerman J, Heerbeek H van\*, Pronk MJ\*, Enk JG van, Uil JJ, Andel RN van, Brinkman K

Eur J Clin Microbiol Infect Dis. 2012 Aug;31(8):1895-900. Epub 2012 Jan 8

In 1999, the costs of gastroenteritis in the Netherlands were estimated using data on hospitalizations from national registries, together with data on etiology and self-reported data on health care resource use in a community-based study. Now, more information on hospitalizations is available and these data were used to update the total costs of gastroenteritis in the Netherlands.

The costs of severe gastroenteritis in the Netherlands were estimated in more depth using a hospital-based study, with patient questionnaires including a follow-up period of 6 months. The overall costs of gastroenteritis were calculated taking direct medical costs, direct non-medical costs, and indirect non-medical costs into account. The costs for severe gastroenteritis in 2009 were estimated at <euro>2,203 per hospitalized child and <euro>6,834 per hospitalized adult. The overall costs of gastroenteritis in 2009 were estimated at <euro>611-695 million, which is <euro>133-151 per gastroenteritis case or <euro>37-42 per inhabitant.

The total health care costs for gastroenteritis were about 50% higher in 2009 compared to 1999, which is mostly due to the rise in health care costs. The costs per gastroenteritis episode in adults are higher compared to children, mainly due to differences in the reasons for hospitalization and course of disease, and productivity losses.

*Impactfactor: 2.859*

**Heerbeek H van**

**Etiology of acute gastroenteritis in children requiring hospitalization in the Netherlands**

Friesema IH, Boer RF de, Duizer E, Kortbeek LM, Notermans DW, Norbruis OF, Bezemer DD, Heerbeek H van\*, Andel RN van, Enk JG van, Fraaij PL, Koopmans MP, Kooistra-Smid AM, Duynhoven YT van

Eur J Clin Microbiol Infect Dis. 2012 Apr;31(4):405-15. Epub 2011 Jul 3

Infectious gastroenteritis causes a considerable burden of disease worldwide. Costs due to gastroenteritis are dominated by the hospitalized cases. Effective control of gastroenteritis should be targeted at the diseases with the highest burden and costs. For that, an accurate understanding of the relative importance of the different bacterial, viral, and parasitic pathogens is needed. The objective of the present study was to determine the incidence and etiology of gastroenteritis requiring hospital admission in the Netherlands. Six hospitals enrolled patients admitted with gastroenteritis for approximately one year over the period May 2008 to November 2009. Participants provided questionnaires and a fecal sample, and the hospital filled out a clinical questionnaire. In total, 143 children hospitalized for gastroenteritis and 64 matched controls were included in the study.

Overall incidence of gastroenteritis requiring hospitalization was estimated at 2.92 per 1,000 children aged 0-17 years per year, with the highest incidence in children under the age of 5 years. The full diagnostic panel of pathogens could be studied in fecal samples of 96 cases. One or more pathogens were found in 98% of these cases. Co-infections were observed relatively often (40%). Viruses were detected in 82% of the samples, with rotavirus being

most common (56%), bacteria in 32% and parasites in 10%. The present study emphasizes the importance of viral pathogens, especially rotavirus, in hospitalizations of children with gastroenteritis. Policies to reduce (costs of) hospitalizations due to gastroenteritis should therefore be first targeted at rotavirus.

*Impactfactor: 2.859*

## **Janssen RL**

### **Celiac disease is overrepresented in patients with constipation**

Pelleboer RA\*, Janssen RL\*, Deckers-Kocken JM, Wouters E, Nissen AC, Bolz WE, Ten WE, Feen C van der, Oosterhuis KJ, Rövekamp MH, Nikkels PG, Houwen RH

J Pediatr (Rio J). 2012 Mar;88(2):173-6. Epub 2012 Mar 20

*Voor abstract zie: Kindergeneeskunde - Pelleboer RA*

*Impactfactor: 1.013*

## **Odink RJ**

### **Adult height in short children born SGA treated with growth hormone and gonadotropin releasing hormone analog: results of a randomized, dose-response GH trial**

Lem AJ, Kaay DC van der, Ridder MA de, Bakker-van Waarde WM, Hulst FJ van der, Mulder JC, Noordam C, Odink RJ\*, Oostdijk W, Schroor EJ, Sulkers EJ, Westerlaken C, Hokken-Koelega AC

J Clin Endocrinol Metab. 2012 Nov;97(11):4096-105. Epub 2012 Aug 17

Context: GH treatment is effective in improving height in short children born small for gestational age (SGA). GH is thought to have limited effect when started during adolescence. Objective: The aim of this study was to investigate GH treatment efficacy in short SGA children when treatment was started during adolescence; to assess whether GH 2 mg/m(2) · d during puberty improves adult height (AH) compared with 1 mg/m(2) · d; and to assess whether an additional 2-yr postponement of puberty by GnRH analog (GnRHa) improves AH in children who are short at the start of puberty (<140 cm), with a poor AH expectation. Patients and Design: In this longitudinal, randomized, dose-response GH trial, we included 121 short SGA children (60 boys) at least 8 yr of age. We performed intention-to-treat analyses on all children and uncensored case analyses on 84 children who reached AH. Besides, we evaluated growth during 2 yr of combined GH/GnRHa and subsequent GH treatment until AH in a subgroup of 40 pubertal children with a height of less than 140 cm at the start. Results: Short SGA children started treatment at a median age of 11.2 yr, when 46% had already started puberty. Median height increased from -2.9 at start to -1.7 sd score (SDS) at AH (P < 0.001). Treatment with GH 2 vs. 1 mg/m(2) · d during puberty resulted in significantly better AH (P = 0.001), also after correction for gender, age at start, height SDS at start, treatment years before puberty, and target height SDS. AH was similar in children who started puberty at less than 140 cm and received GH/GnRHa, compared with children who started puberty greater than 140 cm and received GH only (P = 0.795). Conclusion: When started in adolescence, GH treatment significantly improves AH in short SGA children, particularly with GH 2 mg/m(2) · d during puberty. When SGA children are short at the start of puberty, they can benefit from combined GH/GnRHa treatment.

*Impactfactor: 5.967*

**Odink RJ**

**Beneficial effects of growth hormone treatment on cognition in children with Prader-Willi syndrome: a randomized controlled trial and longitudinal study**

Siemensma EP, Tummers-de Lind van Wijngaarden RF, Festen DA, Troeman ZC, Alfenvan der Velden AA van, Otten BJ, Rotteveel J, Odink RJ\*, Bindels-de Heus GC, Leeuwen M van, Haring DA, Oostdijk W, Bocca G, Mieke Houdijk EC, Trotsenburg AS van, Hoorweg-Nijman JJ, Wieringen H van, Vreuls RC, Jira PE, Schroor EJ, Pinxteren-Nagler E van, Willem Pilon J, Lunshof LB, Hokken-Koelega AC

J Clin Endocrinol Metab. 2012 Jul;97(7):2307-14. Epub 2012 Apr 16

BACKGROUND: Knowledge about the effects of GH treatment on cognitive functioning in children with Prader-Willi syndrome (PWS) is limited.

METHODS: Fifty prepubertal children aged 3.5 to 14 yr were studied in a randomized controlled GH trial during 2 yr, followed by a longitudinal study during 4 yr of GH treatment. Cognitive functioning was measured biennially by short forms of the WPPSI-R or WISC-R, depending on age. Total IQ (TIQ) score was estimated based on two subtest scores.

RESULTS: During the randomized controlled trial, mean sd scores of all subtests and mean TIQ score remained similar compared to baseline in GH-treated children with PWS, whereas in untreated controls mean subtest sd scores and mean TIQ score decreased and became lower compared to baseline. This decline was significant for the Similarities ( $P = 0.04$ ) and Vocabulary ( $P = 0.03$ ) subtests. After 4 yr of GH treatment, mean sd scores on the Similarities and Block design subtests were significantly higher than at baseline ( $P = 0.01$  and  $P = 0.03$ , respectively), and scores on Vocabulary and TIQ remained similar compared to baseline. At baseline, children with a maternal uniparental disomy had a significantly lower score on the Block design subtest ( $P = 0.01$ ) but a larger increment on this subtest during 4 yr of GH treatment than children with a deletion. Lower baseline scores correlated significantly with higher increases in Similarities ( $P = 0.04$ ) and Block design ( $P < 0.0001$ ) sd scores.

CONCLUSIONS: Our study shows that GH treatment prevents deterioration of certain cognitive skills in children with PWS on the short term and significantly improves abstract reasoning and visuospatial skills during 4 yr of GH treatment. Furthermore, children with a greater deficit had more benefit from GH treatment.

*Impactfactor: 5.967*

**Pelleboer RA**

**Celiac disease is overrepresented in patients with constipation**

Pelleboer RA\*, Janssen RL\*, Deckers-Kocken JM, Wouters E, Nissen AC, Bolz WE, Ten WE, Feen C van der, Oosterhuis KJ, Rövekamp MH, Nikkels PG, Houwen RH

J Pediatr (Rio J). 2012 Mar;88(2):173-6. Epub 2012 Mar 20

OBJECTIVE: It is suggested that patients with constipation should be screened for celiac disease. Similarly, it is recommended to investigate these patients for hypothyroidism and hypercalcemia. However, no evidence for these recommendations is available so far. We therefore set out to determine the prevalence of celiac disease, hypothyroidism, and hypercalcemia in children with constipation.

METHODS: Prospective cohort study of 370 consecutive patients who met the Rome III criteria for constipation. These patients were referred by a general practitioner to a pediatrician because of failure of laxative treatment.

RESULTS: Seven of these patients had biopsy-proven celiac disease. This is significantly higher ( $p < 0.001$ ) than the 1:198 prevalence of celiac disease in the Netherlands. Two patients had auto-immune thyroiditis. No patient had hypercalcemia.

CONCLUSIONS: We conclude that celiac disease is significantly overrepresented in patients with constipation who are referred by a general practitioner to a pediatrician because of failure of laxative treatment. All such patients should, therefore, be screened for celiac disease.

*Impactfactor: 1.013*

*\* = Werkzaam in het Catharina Ziekenhuis*



## Klinische Fysica

## **Hurkmans CW**

### **Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience**

Hurkmans CW\*, Dijckmans I\*, Reijnen M\*, Leer J van der \*, Vliet-Vroegindewij C van, Sangen M van der\*

Radiother Oncol. 2012 May;103(2):183-7. Epub 2012 Jan 24

**PURPOSE:** It has been shown that seroma volumes decrease during breast conserving radiotherapy in a significant percentage of patients. We report on our experience with an adaptive radiation therapy (ART) strategy involving rescanning and replanning patients to take this reduction into account during a course of intensity-modulated radiation therapy with simultaneously integrated boost (IMRT-SIB).

**MATERIALS:** From April 2007 till December 2009, 1274 patients eligible for SIB treatment were enrolled into this protocol. Patients for which the time between the initial planning CT (CT(1)) and lumpectomy was less than 30days and who had an initial seroma volume >30cm(3) were rescanned at day 10 of treatment (CT(2)) and replanned when significant changes were observed by the radiation oncologist. Patients received 28 fractions of 1.81Gy to the breast and 2.30Gy to the boost volume.

**RESULTS:** Nine percent (n=113) of the 1274 patients enrolled met the criteria and were rescanned. Of this group, 77% (n=87) of treatment plans were adapted. Time between surgery and CT(1) (20days versus 20days for adapted and non-adapted plans, p=0.89) and time between CT(1) and CT(2) (21days versus 22days for adapted and non-adapted plans, p=0.43) revealed no procedural differences which might have biased our results. In the adapted plans, seroma decreased significantly from 60 to 27cm(3) (p<0.001), TBV from 70 to 45cm(3) (p<0.001) and PTV(boost) from 277 to 220cm(3) (p<0.001). The volume receiving more than 95% of the boost dose (V(95%(total-dose))) could be reduced by 19% (linear fit, R(2)=0.73) from on average 360 to 292cm(3) (p<0.001). Delay in treatment and the use of a prolonged treatment schedule with different fractionation for patients with seroma could thus be prevented.

**CONCLUSION:** The adaptive radiation therapy IMRT-SIB procedure has proven to be efficient and effective, leading to a clinically significant reduction of the high dose volume. Seroma present in a subgroup of patients referred for breast radiation therapy does not hamper the introduction of highly conformal IMRT-SIB techniques.

*Impactfactor: 5.580*

## **Hurkmans CW**

### **Development of clinical trial protocols involving advanced radiation therapy techniques: the European Organisation for Research and Treatment of Cancer Radiation Oncology Group approach**

Fairchild A, Bar-Deroma R, Collette L, Haustermans K, Hurkmans C\*, Lacombe D, Maingon P, Poortmans P, Tomsej M, Weber DC, Gregoire V

Eur J Cancer. 2012 May;48(7):1048-54. Epub 2012 Mar 1

The European Organisation for Research and Treatment of Cancer (EORTC) Master Protocol for phase III radiation therapy (RT) studies was published in 1995 to define in a consistent sequence the parameters which must be addressed when designing a phase III trial 'from the rationale to the references'. This was originally implemented to assist study investigators and writing committees, and to increase homogeneity within Radiation Oncology Group (ROG) study protocols. However, RT planning, delivery, treatment verification and quality assurance (QA) have evolved significantly over the last 15 years and clinical trial protocols

must reflect these developments. The goal of this update is to describe the incorporation of these developments into the EORTC-ROG protocol template. Implementation of QA procedures for advanced RT trials is also briefly described as these essential elements must also be clearly articulated. This guide may assist both investigators participating in current ROG trials and others involved in writing an advanced RT trial protocol.

*Impactfactor: 1.171*

## **Hurkmans CW**

### **Do results of the EORTC dummy run predict quality of radiotherapy delivered within multicentre clinical trials?**

Fairchild A, Collette L, Hurkmans CW\*, Baumert B, Weber DC, Gulyban A, Poortmans P. *Eur J Cancer*. 2012 Nov;48(17):3232-9

**OBJECTIVE:** The European Organisation for the Research and Treatment of Cancer (EORTC) Radiation Oncology Group (ROG) has performed radiotherapy quality assurance (QA) in clinical trials, including dummy runs (DR) and individual case reviews (ICR), since 1991. We investigated the influence of DR results on subsequent QA and patient outcomes.

**METHODS:** EORTC ROG studies were reviewed for DR inclusion, QA and mature clinical outcomes. A DR was classified as a failure if corrections necessitated re-submission. ICR were graded as acceptable, minor or major deviation overall. Fisher's exact test characterised potential correlations and the Mantel-Haenszel statistic quantified pooled odds ratios (OR).

**RESULTS:** DR and ICR data were available from 12 and 3 protocols, respectively. The proportion of institutions successful at first DR attempt varied per trial from 5.6% to 68.8%. Participants were 3.2 times more likely to pass at first attempt after previous DR participation ( $p=0.0002$ ). Pooled OR for an acceptable ICR was 1.69 ( $p=0.06$ ) for institutions successful at DR first attempt. The effect of DR participation was not significantly correlated with patient outcome in the trial available for analysis.

**CONCLUSIONS:** Implementing QA measures in ROG clinical trials should ensure optimal radiotherapy delivery. Centres which previously participated in a DR were significantly more likely to be successful at subsequent QA procedures.

*Impactfactor: 5.536*

## **Hurkmans CW**

### **EORTC Radiation Oncology Group quality assurance platform: Establishment of a digital central review facility**

Fairchild A, Aird E, Fenton PA, Gregoire V, Gulyban A, Lacombe D, Matzinger O, Poortmans P, Ruyskart P, Weber DC, Hurkmans CW\*

*Radiother Oncol*. 2012 Jun;103(3):279-86. Epub 2012 May 23

**OBJECTIVE:** Quality assurance (QA) in clinical trials is essential to ensure treatment is safely and effectively delivered. As QA requirements have increased in complexity in parallel with evolution of radiation therapy (RT) delivery, a need to facilitate digital data exchange emerged. Our objective is to present the platform developed for the integration and standardization of QART activities across all EORTC trials involving RT.

**METHODS:** The following essential requirements were identified: secure and easy access without onsite software installation; integration within the existing EORTC clinical remote data capture system; and the ability to both customize the platform to specific studies and adapt to future needs. After retrospective testing within several clinical trials, the platform was introduced in phases to participating sites and QART study reviewers.

**RESULTS:** The resulting QA platform, integrating RT analysis software installed at EORTC Headquarters, permits timely, secure, and fully digital central DICOM-RT based data review.

Participating sites submit data through a standard secure upload webpage. Supplemental information is submitted in parallel through web-based forms. An internal quality check by the QART office verifies data consistency, formatting, and anonymization. QART reviewers have remote access through a terminal server. Reviewers evaluate submissions for protocol compliance through an online evaluation matrix. Comments are collected by the coordinating centre and institutions are informed of the results.

**CONCLUSIONS:** This web-based central review platform facilitates rapid, extensive, and prospective QART review. This reduces the risk that trial outcomes are compromised through inadequate radiotherapy and facilitates correlation of results with clinical outcomes.

*Impactfactor: 5.580*

## **Hurkmans CW**

### **EORTC Radiation Oncology Group: 50 years of continuous Accomplishments**

Vincent Gregoire, Harry Bartelink, Jacques Bernier, Michel Bolla, Jean-Francois Bosset, Laurence Colette, Karin Haustermans, Jean-Claude Horiot, Coen W. Hurkmans\*, Rene Mirimanoff, Philip Poortmans, Damien C. Weber, Philippe Maingon

EJC Supplements 10 (1), 150-159

After the foundation of the EORTC in 1962, the Radio-Chemotherapy Group within this organization split in 1973 into two groups. One of these groups, concentrating on Hodgkin's and Non-Hodgkin's Lymphoma, later became the Lymphoma Group while the other became the Radiotherapy Group.

During the 1990's the latter changed its name to the Radiation Oncology Group (ROG), underscoring its position within the field of multidisciplinary oncology research. By 2011 the ROG had initiated or participated in 83 clinical studies, of which more than 73% were randomized phase III trials. It has concentrated on almost every disease site from brain to gynecological tumors with emphasis on brain, head and neck, breast, prostate, and lower gastro-intestinal tumours. The ROG has published several hundreds peer-reviewed articles, including publications in prestigious journals such as the New England Journal of Medicine or Lancet Oncology. Since its foundation, the ROG has understood the importance of conducting a proper Radiotherapy Quality Assurance (RT-QA) program for every clinical trial aiming at guaranteeing the quality of radiotherapy, i.e. minimizing any uncertainties in the conduction of trials.

As radiotherapy evolved from two-dimensional to Intensity Modulated Radio Therapy, this program has progressively matured with time to be part of a worldwide RT-QA consortium in 2012.

*Impactfactor: --*

## **Hurkmans CW**

### **hypofractionering bij primair operabel mammacarcinoom**

Westenberg AH, Sangen MJ van der \*, Bijker N, Stenfert Kroese MC, Stewart FA, Rodenhuis CC, Hurkmans CW\*

Gamma professional, oktober 2012

*Impactfactor: --*

## **Hurkmans CW**

### **In reply to Zagar and Marks**

Kong FM, Ritter T, Quint D, Marsh L, Senan S, Gaspar L, Komaki R, Hurkmans C\*, Timmerman R, Choy H, Bezjak A, Bradley J, Mosvas B, Okunieff P, Curran W

Int J Radiat Oncol Biol Phys. 2012 Oct 1;84(2):305-6

Comment on: Esophageal delineation: in regard to Kong et al "Consideration of dose limits for organs at risk of thoracic radiotherapy: Atlas for lung, proximal bronchial tree, esophagus, spinal cord, ribs, and brachial plexus" (Int J Radiat Oncol Biol Phys 2011;81:1442-1457). [Int J Radiat Oncol Biol Phys. 2012]

*Impactfactor: 4.105*

## **Hurkmans CW**

### **Management of radiation oncology patients with a pacemaker or ICD: A new comprehensive practical guideline in The Netherlands**

Hurkmans CW\*, Kneijens JL, Oei BS, Maas AJ, Uiterwaal GJ, Borden AJ, Ploegmakers MM, Erven L

Radiat Oncol. 2012 Nov 24;7(1):198

ABSTRACT: Current clinical guidelines for the management of radiotherapy patients having either a pacemaker or implantable cardioverter defibrillator (both CIEDs: Cardiac Implantable Electronic Devices) do not cover modern radiotherapy techniques and do not take the patient's perspective into account. Available data on the frequency and cause of CIED failure during radiation therapy are limited and do not converge.

The Dutch Society of Radiotherapy and Oncology (NYRO) initiated a multidisciplinary task group consisting of clinical physicists, cardiologists, radiation oncologists, pacemaker and ICD technologists to develop evidence based consensus guidelines for the management of CIED patients. CIED patients receiving radiotherapy should be categorised based on the chance of device failure and the clinical consequences in case of failure. Although there is no clear cut-off point nor a clear linear relationship, in general, chances of device failure increase with increasing doses. Clinical consequences of device failures like loss of pacing, carry the most risks in pacing dependent patients. Cumulative dose and pacing dependency have been combined to categorise patients into low, medium and high risk groups. Patients receiving a dose of less than 2 Gy to their CIED are categorised as low risk, unless pacing dependent since then they are medium risk. Between 2 and 10 Gy, all patients are categorised as medium risk, while above 10 Gy every patient is categorised as high risk. Measures to secure patient safety are described for each category. This guideline for the management of CIED patients receiving radiotherapy takes into account modern radiotherapy techniques, CIED technology, the patients' perspective and the practical aspects necessary for the safe management of these patients. The guideline is implemented in The Netherlands in 2012 and is expected to find clinical acceptance outside The Netherlands as well.

*Impactfactor: 2.321*

## **Hurkmans CW**

### **QA makes a clinical trial stronger: Evidence-based medicine in radiation therapy**

Weber DC, Tomsej M, Melidis C, Hurkmans CW\*

Radiat Oncol. 2012 Oct;105(1):4-8. Epub 2012 Sep 14

Quality assurance (QA) for radiation therapy (RT) in clinical trials is necessary to ensure treatment is safely and effectively administered. QA assurance requires however substantial human and financial resources, as it has become more comprehensive and labor intensive in

recent RT trials. It is presumed that RT deviations decrease therapeutic effectiveness of the studied regimen. This study assesses the impact of RT protocol-deviations on patient's outcome in prospective phase II-III RT trials. PubMed, Medline and Embase identified nine prospective RT trials detailing QA RT violation and patient's outcome. Planned QA analysis was performed retrospectively and prospectively in eight and one studies, respectively. Non-adherence to protocol-specified RT requirements in prospective trials is frequent: the observed major deviation rates range from 11.8% to 48.0% (mean, 28.1 ± 17.9%). QA RT deviations had a significant impact on the primary study end-point in a majority (62.5%) of studies. The number of patients accrued per center was a significant predictive factor for RT deviations in the largest series. These QA data stemming from prospective clinical trials show undisputedly that non adherence to protocol-specified RT requirements is associated with reduced survival, local control and potentially increased toxicity.

*Impactfactor: 5.580*

### **Hurkmans CW**

#### **Redesigning radiotherapy quality assurance: opportunities to develop an efficient, evidence-based system to support clinical trials--report of the National Cancer Institute Work Group on Radiotherapy Quality Assurance**

Bekelman JE, Deye JA, Vikram B, Bentzen SM, Bruner D, Curran WJ Jr, Dignam J, Efstathiou JA, FitzGerald TJ, Hurkmans C\*, Ibbott GS, Lee JJ, Merchant TE, Michalski J, Palta JR, Simon R, Haken RK ten, Timmerman R, Tunis S, Coleman CN, Purdy J  
Int J Radiat Oncol Biol Phys. 2012 Jul 1;83(3):782-90

*Impactfactor: 4.105*

### **Hurkmans CW**

#### **Reducing interobserver variation of boost-CTV delineation in breast conserving radiation therapy using a pre-operative CT and delineation guidelines**

Boersma LJ, Janssen T, Elkhuizen PH, Poortmans P, Sangen M van der\*, Scholten AN, Hanbeukers B, Duppen JC, Hurkmans C\*, Vliet C van  
Radiother Oncol. 2012 May;103(2):178-82. Epub 2012 Jan 20

*Voor abstract zie: Radiotherapie - Sangen, M van der*

*Impactfactor: 5.580*

### **Hurkmans CW**

#### **Standardizing Naming Conventions in Radiation Oncology**

Santanam L, Hurkmans C\*, Mutic S, Vliet-Vroegindewei C van, Brame S, Straube W, Galvin J, Tripuraneni P, Michalski J, Bosch W

Int J Radiat Oncol Biol Phys. 2012 Jul 15;83(4):1344-9. Epub 2012 Jan 13

**PURPOSE:** The aim of this study was to report on the development of a standardized target and organ-at-risk naming convention for use in radiation therapy and to present the nomenclature for structure naming for interinstitutional data sharing, clinical trial repositories, integrated multi-institutional collaborative databases, and quality control centers. This taxonomy should also enable improved plan benchmarking between clinical institutions and vendors and facilitation of automated treatment plan quality control.

**MATERIALS AND METHODS:** The Advanced Technology Consortium, Washington University in St Louis, Radiation Therapy Oncology Group, Dutch Radiation Oncology Society, and the Clinical Trials RT QA Harmonization Group collaborated in creating this new naming convention. The International Commission on Radiation Units and Measurements guidelines

have been used to create standardized nomenclature for target volumes (clinical target volume, internal target volume, planning target volume, etc.), organs at risk, and planning organ-at-risk volumes in radiation therapy. The nomenclature also includes rules for specifying laterality and margins for various structures. The naming rules distinguish tumor and nodal planning target volumes, with correspondence to their respective tumor/nodal clinical target volumes. It also provides rules for basic structure naming, as well as an option for more detailed names. Names of nonstandard structures used mainly for plan optimization or evaluation (rings, islands of dose avoidance, islands where additional dose is needed [dose painting]) are identified separately.

**RESULTS:** In addition to its use in 16 ongoing Radiation Therapy Oncology Group advanced technology clinical trial protocols and several new European Organization for Research and Treatment of Cancer protocols, a pilot version of this naming convention has been evaluated using patient data sets with varying treatment sites. All structures in these data sets were satisfactorily identified using this nomenclature.

**CONCLUSIONS:** Use of standardized naming conventions is important to facilitate comparison of dosimetry across patient datasets. The guidelines presented here will facilitate international acceptance across a wide range of efforts, including groups organizing clinical trials, Radiation Oncology Institute, Dutch Radiation Oncology Society, Integrating the Healthcare Enterprise, Radiation Oncology domain (IHE-RO), and Digital Imaging and Communication in Medicine (DICOM).

*Impactfactor: 4.105*

## **Lagerburg V**

### **A comparison of different energy window subtraction methods to correct for scatter and downscatter in I-123 SPECT imaging**

Lagerburg V\*, Nijs R de, Holm S, Svarer C

Nucl Med Commun. 2012 Jul;33(7):708-18

**OBJECTIVE:** One of the main problems in quantification of single photon emission computer tomography imaging is scatter. In iodine-123 (I-123) imaging, both the primary 159 keV photons and photons of higher energies are scattered. In this experimental study, different scatter correction methods, based on energy window subtraction, have been compared with each other.

**METHODS AND MATERIALS:** Iodine-123 single photon emission computed tomography images of a phantom with a known intensity ratio between background and hollow spheres were acquired for three different collimators (low energy high resolution, low energy general purpose, and medium energy general purpose). The hollow spheres were filled with a higher activity concentration than the uniform background activity concentration, resulting in hot spots. Counts were collected in different energy windows, and scatter correction was performed by applying different methods such as effective scatter source estimation, triple and dual energy window (TEW and DEW), double peak window (DPW) and downscatter correction. The intensity ratio between the spheres and the background was used to compare the performance of the different methods.

**RESULTS:** The results revealed that the efficiency of the scatter correction techniques vary depending on the collimator used. For the low energy high resolution collimator, all correction methods except the effective scatter source estimation and the DPW perform well. For the medium energy general purpose collimator, even without scatter correction, the calculated ratio is close to the real ratio. The DEW and DPW methods tend to overestimate the ratio. For the low energy general purpose collimator, only the DEW and the combined DEW and downscatter correction methods perform well.

CONCLUSION: The only correction method that provides a ratio that differs by less than 5% from the real ratio for all the collimators is the combined DEW and downscatter correction method.

*Impactfactor: 1.404*

### **Schuring D**

**High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers**

Meijer GJ\*, Toorn PP van der, Bal M\*, Schuring D\*, Weterings J\*, Wildt M de\*

Radiother Oncol. 2012 Sep 27. pii: S0167-8140(12)00362-3

*Voor abstract zie: Radiotherapie - Meijer GJ*

*Impactfactor: 5.580*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Longgeneeskunde**

**Balkom, RH van**

**Hemoptoë en respiratoire insufficiëntie**

Verhaert L\*, Balkom RHH van \*, Smeenk FW\*

NTvAA: Nederlands Tijdschrift voor Allergie en Astma 2012;12:25-31

*Voor abstract zie: Longgeneeskunde - Verhaert L*

*Impactfactor: --*

**Borne BE van den**

**A pulmonary shadow after lobectomy: an unexpected diagnosis**

Crijns K\*, Jansen FH\*, Straten AH van\*, Borne BE van den\*

Neth J Med. 2012 Jun;70(5):232, 235

*Impactfactor: 2.072*

**Borne BE van den**

**Cardiac herniation after operative management of lung cancer: a rare and dangerous complication**

Ponten JE\*, Elenbaas TW\*, Woorst JF ter\*, Korsten EH\*, Borne BE van den\*, Straten AH van\*

Gen Thorac Cardiovasc Surg. 2012 Oct;60(10):668-72. Epub 2012 May 25

*Voor abstract zie: Cardiothoracale chirurgie - Ponten JE*

*Impactfactor: --*

**Borne BE van den**

**Progression of osteoporosis in patients with COPD: A 3-year follow up study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Jansen FH\*, Enschoot JW van\*, Wouters EF

Respir Med. 2012 Jun;106(6):861-70. Epub 2012 Feb 26,

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 2.475*

**Borne BE van den**

**Risk factors for osteoporosis in Caucasian patients with moderate chronic obstructive pulmonary disease: a case control study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA,

Donkers-van Rossum AB\*, Aarts RP\*, Wouters EF

Bone. 2012 Jun;50(6):1234-9. Epub 2012 Mar 9

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 4.023*

**Creemers JP**

**Prediction and course of symptoms and lung function around an exacerbation in chronic obstructive pulmonary disease**

Berge M van den , Hop WC, Molen T van der, Noord JA van, Creemers JP\*, Schreurs AJ, Wouters EF, Postma DS; the COSMIC (COPD and Seretide: a Multi-Center Intervention and Characterization) study group

Respir Res. 2012 Jun 6;13(1):44

BACKGROUND: Frequent exacerbations induce a high burden to Chronic Obstructive Pulmonary Disease (COPD). We investigated the course of exacerbations in the published COSMIC study that investigated the effects of 1-year withdrawal of fluticasone after a 3-month run-in treatment period with salmeterol/fluticasone in patients with COPD.

METHODS: In 373 patients, we evaluated diary cards for symptoms, Peak Expiratory Flow (PEF), and salbutamol use and assessed their course during exacerbations.

RESULTS: There were 492 exacerbations in 224 patients. The level of symptoms of cough, sputum, dyspnea and nocturnal awakening steadily increased from 2 weeks prior to exacerbation, with a sharp rise during the last week. Symptoms of cough, sputum, and dyspnea reverted to baseline values at different rates (after 4, 4, and 7 weeks respectively), whereas symptoms of nocturnal awakening were still increased after eight weeks. The course of symptoms was similar around a first and second exacerbation. Increases in symptoms and salbutamol use and decreases in PEF were associated with a higher risk to develop an exacerbation, but with moderate predictive values, the areas under the receiver operating curves ranging from 0.63 to 0.70.

CONCLUSIONS: Exacerbations of COPD are associated with increased symptoms that persist for weeks and the course is very similar between a first and second exacerbation. COPD exacerbations are preceded by increased symptoms and salbutamol use and lower PEF, yet predictive values are too low to warrant daily use in clinical practice.

*Impactfactor: --*

**Crijns C**

**A pulmonary shadow after lobectomy: an unexpected diagnosis**

Crijns K\*, Jansen FH\*, Straten AH van\*, Borne BE van den\*

Neth J Med. 2012 Jun;70(5):232, 235

*Impactfactor: 2.072*

**Enschot JW van**

**Progression of osteoporosis in patients with COPD: A 3-year follow up study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Jansen FH\*, Enschoot JW van\*, Wouters EF

Respir Med. 2012 Jun;106(6):861-70. Epub 2012 Feb 26

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 2.475*

## **Graat-Verboom L**

### **Progression of osteoporosis in patients with COPD: A 3-year follow up study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Jansen FH\*, Enschoot JW van\*, Wouters EF

Respir Med. 2012 Jun;106(6):861-70

Currently, our knowledge on the progression of osteoporosis and its determinants is limited in patients with chronic obstructive pulmonary disease (COPD). Bone mineral density generally remains stable in patients with COPD over a period of 3 years. Nevertheless, the progression of vertebral fractures was not assessed, while an increase of vertebral fractures over time may be reasonable. Aims of the current study were to determine the percentage of newly diagnosed osteoporotic patients after a follow up of 3 years and to identify baseline risk factors for the progression of osteoporosis in COPD. Clinically stable COPD outpatients were included. Lung function parameters, body composition measures, six minute walk distance, DXA-scan and X-spine were assessed at baseline and repeated after 3 years.

Prevalence of osteoporosis in COPD patients increased from 47% to 61% in 3 years mostly due to an increase of vertebral fractures. Lower baseline T-score at the trochanter independently increased the risk for the development of osteoporosis. Additionally, baseline vitamin D deficiency increased this risk 7.5-fold.

In conclusion, the prevalence of osteoporosis increased over a 3-year period in patients with COPD. Baseline risk factors for the development of osteoporosis are osteopenia at the trochanter and vitamin D deficiency.

*Impactfactor: 2.475*

## **Graat-Verboom L**

### **Risk factors for osteoporosis in Caucasian patients with moderate chronic obstructive pulmonary disease: a case control study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Donkers-van Rossum AB\*, Aarts RP\*, Wouters EF

Bone. 2012 Jun;50(6):1234-9. Epub 2012 Mar 9

The prevalence of osteoporosis is high in chronic obstructive pulmonary disease (COPD) patients. The gold standard for the diagnosis of osteoporosis is bone mineral density (BMD) measurements as assessed by dual energy absorptiometry (DXA) scanning as well as vertebral fractures as assessed by instant vertebral assessment (IVA). The aim of this study was to compare COPD GOLD II patients (that is, patients with moderate COPD, stage II, according to the GOLD classification) with osteoporosis (cases) to COPD GOLD II patients without osteoporosis (controls) to identify risk factors for osteoporosis. The diagnosis of osteoporosis was based on BMD and vertebral fractures. Cases (n=49) were matched for gender, age and forced expiratory volume in the first second to controls (n=49). We assessed pulmonary function, body composition, vitamin D, emphysema score (by high-resolution computer tomography), medical history and medication use in all patients. Variables that were significantly different between the cases and controls were included in a logistic regression analysis.

COPD patients with osteoporosis had a significantly lower body mass index (BMI) and higher residual volume as the percentage of total lung capacity (RV%TLC) compared to COPD patients without osteoporosis. Decreasing BMI and increasing RV%TLC increased the odds ratio for osteoporosis. Overweight and obese BMI values were protective for osteoporosis. Screening for osteoporosis should be performed even in moderate COPD patients, especially in those with a low BMI and/or a high RV% TLC.

*Impactfactor: 4.023*

**Romme EA**

**Bone attenuation on routine chest CT correlates with bone mineral density on DXA in patients with COPD**

Romme EA\*, Murchison JT, Phang KF, Jansen FH\*, Rutten EP, Wouters EF, Smeenk FW\*, Beek EJ van, Macnee W

J Bone Miner Res. 2012 Nov;27(11):2338-2343. Epub 2012 Jun 12

COPD, although primarily a disease of the lungs, is associated with extra pulmonary effects such as muscle weakness and osteoporosis. Fractures due to osteoporosis cause significant morbidity and mortality, particularly in patients with COPD. To prevent osteoporotic fractures, it is important to diagnose osteoporosis in an early stage and to start anti-osteoporotic therapy in at risk patients.

Because routine chest Computed Tomography (CT) is increasingly used to assess the extent of emphysema and airways disease in patients with COPD, we investigated whether simple attenuation measurement of the thoracic spine on routine chest CT may provide useful information on bone health in patients with COPD. Fifty-eight patients with moderate to very severe COPD were included in our study. The average attenuation of thoracic vertebrae 4, 7 and 10 on chest CT was correlated with the lowest bone mineral density (BMD) of the hip and lumbar spine (L1 to L4) on dual-energy X-ray absorptiometry (DXA) in patients with COPD. The inter and intra-observer variabilities of the attenuation measurements were low as shown by Bland Altman plots. Pearson's correlation coefficient between the average attenuation of the three thoracic vertebrae and the lowest BMD of the hip and lumbar spine was high ( $r=0.827$ ,  $p<0.001$ ). A receiver-operating characteristic (ROC) analysis of the area under the curve for osteoporosis was 0.969 ( $p<0.001$ ), corresponding to an attenuation threshold of 147 Hounsfield Units (HU).

In conclusion, our data demonstrated that bone attenuation measured on routine chest CT correlated strongly with BMD assessed on DXA in patients with COPD. Routine chest CT may provide useful information on bone health in patients with COPD.

*Impactfactor: 6.373*

**Smeenk FW**

**Bone attenuation on routine chest CT correlates with bone mineral density on DXA in patients with COPD**

Romme EA\*, Murchison JT, Phang KF, Jansen FH\*, Rutten EP, Wouters EF, Smeenk FW\*, Beek EJ van, Macnee W

J Bone Miner Res. 2012 Nov;27(11):2338-2343. Epub 2012 Jun 12

*Voor abstract zie: Longgeneeskunde - Romme EA*

*Impactfactor: 6.373*

**Smeenk FW**

**Care delivery pathways for Chronic Obstructive Pulmonary Disease in England and the Netherlands: a comparative study**

Utens CM\*, Maarse JA, Schayck OC van, Maesen BL, Rutten MP, Smeenk FW\*

Int J Integr Care. 2012 Apr-Jun;12:e40. Epub 2012 May 18

*Voor abstract zie: Longgeneeskunde - Utens CM*

*Impactfactor: --*

**Smeenk FW**

### **Churg-strauss-syndroom als oorzaak van instabiel astma**

Verheijen NM, Smeenk FW\*

Ned Tijdschr Allergie & Astma 2012;12:57-62

De differentiaaldiagnostische overwegingen bij een patiënt met instabiel astma zijn groot. Hierbij moet onderscheid gemaakt worden tussen enerzijds factoren die een bestaand asthma bronchiale instabiel kunnen maken en anderzijds ziektebeelden die wat betreft hun presentatie lijken op asthma bronchiale. Wij presenteren een patiënte met het klinisch beeld van instabiel asthma bronchiale, sinusklachten en eosinofilie in het perifere bloed.

Na uitgebreide analyse blijkt er sprake te zijn van het churg-strauss-syndroom.

*Impactfactor: --*

**Smeenk FW**

### **Diagnostic accuracy of primary care asthma/COPD working hypotheses, a real life study**

Lucas AE, Smeenk FJ\*, Smeele IJ, van Schayck OP

Respir Med. 2012 Aug;106(8):1158-63

Misdiagnoses are inevitable when working hypotheses of asthma/COPD of General Practitioners (GPs) are not checked by spirometry. To reduce misdiagnoses, Asthma/COPD-support services (AC-services) offer support by performing spirometry assessed together with written medical history by consulting pulmonologists.

RESEARCH QUESTIONS: Which criteria do GPs use to justify their asthma/COPD working hypotheses? How do diagnostic assessments by an AC-service change GPs' working hypotheses? Do GPs' justifications for their working hypotheses influence the extent to which working hypotheses correspond with diagnoses given by an AC-service?

METHOD: We investigated the working hypotheses of 17 GPs for 284 patients with respiratory problems and their justifications: "clinical symptoms", "office spirometry", or "specialist's correspondence". Working hypotheses were compared with diagnoses given by an AC-service, and the influence of the different justifications categories on diagnostic accuracy of the working hypotheses was described.

RESULTS: 49% of the working hypothesis were only based on clinical information, 21% were also based on office spirometry. For 30% additional specialist information was available. 50% of the working hypotheses were confirmed by the AC-service. The working hypothesis asthma was confirmed more frequently (62%) than the working hypothesis COPD (40%). The justifications for the working hypotheses given by GPs did not influence these results.

CONCLUSION: Diagnostic assessments of the AC-service differed significantly from the working hypotheses of GPs, even when these were based on previous specialists' correspondence or on office spirometry. To optimize the diagnoses in primary care, diagnostic support of an AC-service is recommended for all primary care patients with respiratory problems.

*Impactfactor: 2.475*

**Smeenk FW****Early assisted discharge with generic community nursing for chronic obstructive pulmonary disease exacerbations: results of a randomised controlled trial**

Utens CM\*, Goossens LM, Smeenk FW\*, Rutten-van Mólken MP, Vliet M van, Braken MW, Eijdsden LM van, Schayck OC van

BMJ Open. 2012 Oct 16;2(5). pii: e001684

Voor abstract zie: Longgeneeskunde - Utens CM

Impactfactor: --

**Smeenk FW****Hemoptoë en respiratoire insufficiëntie**

Verhaert L\*, Balkom RH van \*, Smeenk FW\*

Ned Tijdschr Allergie & Astma 2012;12:25-31

Impactfactor: --

**Smeenk FW****Fenotypegedirigeerde behandeling voor astma een stap dichterbij?**

Smeenk FW\*

Ned Tijdschr Allergie & Astma 2012;12:71

Impactfactor: --

**Smeenk FW****Progression of osteoporosis in patients with COPD: A 3-year follow up study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Jansen FH\*, Enschoot JW van\*, Wouters EF

Respir Med. 2012 Jun;106(6):861-70. Epub 2012 Feb 26

Voor abstract zie: Longgeneeskunde - Graat-Verboom L

Impactfactor: 2.475

**Smeenk FW****Risk factors for osteoporosis in Caucasian patients with moderate chronic obstructive pulmonary disease: a case control study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Donkers-van Rossum AB\*, Aarts RP\*, Wouters EF

Bone. 2012 Jun;50(6):1234-9. Epub 2012 Mar 9

Impactfactor: 4.023

**Utens CM****Care delivery pathways for Chronic Obstructive Pulmonary Disease in England and the Netherlands: a comparative study**

Utens CM\*, Maarse JA, Schayck OC van, Maesen BL, Rutten MP, Smeenk FW\*

Int J Integr Care. 2012 Apr-Jun;12:e40. Epub 2012 May 18

INTRODUCTION: A remarkable difference in care delivery pathways for Chronic Obstructive Pulmonary Disease (COPD) is the presence of hospital-at-home for COPD exacerbations in England and its absence in the Netherlands. The objective of this paper is to explain this difference.

**METHODS:** Descriptive COPD statistics and care delivery pathways on all care levels within the institutional context, followed by a comparison of care delivery pathways and an explanation of the difference with regard to hospital-at-home.

**RESULTS:** The Netherlands and England show broad similarities in their care delivery pathways for COPD patients. A major difference is the presence of hospital-at-home for COPD exacerbations in England and its absence in the Netherlands. Three possible explanations for this difference are presented: differences in the urgency for alternatives (higher urgency for alternative treatment models in England), the differences in funding (funding in England facilitated the development of hospital-at-home) and the differences in the substitution of tasks to nurses (substitution to nurses has taken place to a larger extent in England).

**DISCUSSION AND CONCLUSION:** The difference between the Netherlands and England regarding hospital-at-home for COPD exacerbations can be explained in three ways. Hospital-at-home has proved to be a safe alternative for hospital care for selected patients, and should be considered as a treatment option for COPD exacerbations in the Netherlands.

*Impactfactor: --*

## **Utens CM**

### **Early assisted discharge with generic community nursing for chronic obstructive pulmonary disease exacerbations: results of a randomised controlled trial**

Utens CM\*, Goossens LM, Smeenk FW\*, Rutten-van Mólken MP, Vliet M van,

Braken MW, Eijdsen LM van, Schayck OC van

BMJ Open. 2012 Oct 16;2(5). pii: e001684

**OBJECTIVES:** To determine the effectiveness of early assisted discharge for chronic obstructive pulmonary disease (COPD) exacerbations, with home care provided by generic community nurses, compared with usual hospital care. **DESIGN:** Prospective, randomised controlled and multicentre trial with 3-month follow-up. **SETTING:** Five hospitals and three home care organisations in the Netherlands. **PARTICIPANTS:** Patients admitted to the hospital with an exacerbation of COPD. Patients with no or limited improvement of respiratory symptoms and patients with severe unstable comorbidities, social problems or those unable to visit the toilet independently were excluded.

**INTERVENTION:** Early discharge from hospital after 3 days inpatient treatment. Home visits by generic community nurses. Primary outcome measure was change in health status measured by the Clinical COPD Questionnaire (CCQ). Treatment failures, readmissions, mortality and change in generic healthrelated quality of life (HRQL) were secondary outcome measures.

**RESULTS:** 139 patients were randomised. No difference between groups was found in change in CCQ score at day 7 (difference in mean change 0.29 (95% CI -0.03 to 0.61)) or at 3 months (difference in mean change 0.04 (95% CI -0.40 to 0.49)). No difference was found in secondary outcomes. At day 7 there was a significant difference in change in generic HRQL, favouring usual hospital care.

**CONCLUSIONS:** While patients' disease-specific health status after 7-day treatment tended to be somewhat better in the usual hospital care group, the difference was small and not clinically relevant or statistically significant. After 3 months, the difference had disappeared. A significant difference in generic HRQL at the end of the treatment had disappeared after 3 months and there was no difference in treatment failures, readmissions or mortality. Early assisted discharge with community nursing is feasible and an alternative to usual hospital care for selected patients with an acute COPD exacerbation.

*Impactfactor: --*

**Verhaert, L**

### **Hemoptoë en respiratoire insufficiëntie**

Verhaert L\*, Balkom RH van \*, Smeenk FW\*

NTvAA: Nederlands Tijdschrift voor Allergie en Astma 2012;12:25-31

Een 53-jarige vrouw presenteerde zich op de spoedeisende hulp met koorts, kortademigheid en hemoptoë, aanvankelijk mild, nadien fulminant. Aanvullend onderzoek liet infiltratieve afwijkingen zien op de X-thorax, verhoogde inflammatoire parameters en hematurie.

Differentiaaldiagnostisch werd gedacht aan infectieuze oorzaken en een systeemvasculitis.

Hogeresolutiecomputertomografie van de thorax liet diffuse alveolaire consolidaties zien.

Laboratoriumonderzoek toonde een positieve c-ANC A met een titer van >1:512 welke anti-PR 3-positief was. Dit bevestigde het klinische vermoeden van de ziekte van Wegener.

De hemoptoë nam in enkele dagen snel toe. Vanwege een respiratoire insufficiëntie diende patiënt één dag na opname geïntubeerd te worden.

Na het bekend worden van de ANC Aserologie werd direct gestart met cyclofosfamide, een hoge dosis corticosteroiden en plasmaferese (acht maal) waardoor de hemoptoë uiteindelijk ophield. De mortaliteit van een fulminante hemoptoë op basis van pulmonale vasculitis waarvoor intensivecareopname noodzakelijk is, is 25 tot 50%. Snelle diagnose en agressieve behandeling zijn essentieel om de uitkomst te optimaliseren. De combinatie van een hoge dosis corticosteroiden en cyclofosfamide vormt de hoeksteen van de behandeling. Hiermee kan in 90% van de gevallen remissie worden bereikt.

*Impactfactor: --*

**Wielders PL**

### **Effects of an oral MMP-9 and -12 inhibitor, AZD1236, on biomarkers in moderate/severe COPD: a randomised controlled trial**

Dahl R, Titlestad I, Lindqvist A, Wielders P\*, Wray H, Wang M, Samuelsson V, Mo J, Holt A

Pulm Pharmacol Ther. 2012 Apr;25(2):169-77. Epub 2012 Feb 1

**BACKGROUND:** There is a pressing need for new forms of treatment for COPD. Based on the known pathophysiology of COPD, inhibition of matrix metalloproteinases is a theoretically promising approach. This Phase IIa study evaluated the effects of AZD1236, a selective MMP-9 and MMP-12 inhibitor, on the biomarkers of inflammation and emphysematous lung tissue degradation in patients with moderate-to-severe COPD.

**METHODS:** This was a multinational, randomized, double-blind, placebo-controlled signal-searching study conducted in men and women aged  $\geq$  40 years with stable moderate-to-severe COPD. After a 2-6-week period to eliminate any remaining effects of previous medication, 55 patients received oral AZD1236 75 mg or matching placebo twice daily for 6 weeks. Differential cell count and TNF- levels in induced sputum and 24-h urinary desmosine excretion were the main study variables, but a range of exploratory biomarkers was also assessed in induced sputum, blood and urine. Secondary variables included lung function and patient-recorded Clinical COPD Questionnaire (CCQ) responses and diary records of symptoms, adverse events, use of rescue medication and AZD1236 plasma concentrations.

**RESULTS:** The majority of variables showed little change compared to placebo although there was a possible, but not statistically significant reduction in urinary desmosine excretion and reductions in the number and percentage of lymphocytes in sputum and blood with AZD1236. No effect was seen on clinical parameters after 6 weeks of treatment. The proportion of patients experiencing adverse events was similar in both treatment groups.

**CONCLUSIONS:** AZD1236 dosed orally at 75 mg twice daily was generally well tolerated over 6 weeks in patients with moderate-to-severe COPD. No clinical efficacy of AZD1236 was

demonstrated in this short-term signal-searching study, although possible evidence of an impact on desmosine may suggest the potential value of selective inhibitors of MMPs in the treatment of COPD in longer term trials.

*Impactfactor: 2.800*

**Wielders PL**

**Inability to ventilate after tube exchange postoperative to pneumonectomy**

Verstraeten SE\*, Straten AH van\*, Korsten HH\*, Weber EW\*, Wielders PL\*, Berreklouw E\*

Case Rep Anesthesiol. 2012;2012:801093. Epub 2012 Apr 5

*Voor abstract zie: Cardiothoracale chirurgie - Verstraeten SE*

*Impactfactor: --*

\* = *Werkzaam in het Catharina Ziekenhuis*

## **Maag-darm-leverziekten**

## **Gilissen LP**

### **Uncommon complications of biliary stones**

Janssen S\*, Mierlo I van\*, Gilissen LP\*, Nienhuijs SW\*, Heemskerk J

Open Journal of Internal Medicine, 2012, 2, 19-26

*Voor abstract zie: Maag-darm-leverziekten - Janssen SJ*

*Impactfactor: --*

## **Janssen SJ**

### **Uncommon complications of biliary stones**

Janssen S\*, Mierlo I van\*, Gilissen LP\*, Nienhuijs SW\*, Heemskerk J

Open Journal of Internal Medicine, 2012, 2, 19-26

Gallstone disease has a high incidence, and most common presentations are well known and recognized. Particularly in the elderly population though, uncommon presentations of gallstone disease are more frequent, and can easily be missed or misinterpreted.

In this article we present 5 such patients with an atypical presentation of gallstone disease.

We will then discuss atypical gallstone disease in more detail.

*Impactfactor: --*

## **Mierlo I van**

### **Uncommon complications of biliary stones**

Janssen S\*, Mierlo I van\*, Gilissen LP\*, Nienhuijs SW\*, Heemskerk J

Open Journal of Internal Medicine, 2012, 2, 19-26

*Voor abstract zie: Maag-darm-leverziekten - Janssen SJ*

*Impactfactor: --*

## **Schoon EJ**

### **Circumferential balloon-based radiofrequency ablation of Barrett's esophagus with dysplasia can be simplified, yet efficacy maintained, by omitting the cleaning phase**

Vilsteren FG van, Phoa KN, Herrero LA, Pouw RE, Sondermeijer CM, Lijnschoten I van\*, Seldenrijk CA, Visser M, Meijer SL, Berge Henegouwen MI van, Weusten BL, Schoon EJ\*, Bergman JJ

Clin Gastroenterol Hepatol. 2012 Dec 22. pii: S1542-3565(12)01505-4

**BACKGROUND & AIMS:** The current procedure for circumferential balloon-based radiofrequency ablation (c-RFA) for the removal of dysplastic Barrett's esophagus (BE) is labor-intensive, comprising 2 ablation passes with a cleaning step to remove debris from the ablation zone and electrode. We compared the safety and efficacy of 3 different c-RFA ablation regimens.

**METHODS:** We performed a prospective trial of consecutive patients with flat-type BE with high-grade dysplasia. Fifty-seven patients (45 men, 64±15 y old, 28 with prior endoscopic resection) were randomly assigned to groups that underwent c-RFA with a double application of RFA (12 J/cm<sup>2</sup>). The standard group received c-RFA, with device removal and cleaning, followed by c-RFA; the simple-with-cleaning group underwent c-RFA, with device cleaning without removal, followed by c-RFA; and the simple-nocleaning group received 2 applications of c-RFA, and the device was not removed or cleaned. The primary outcome was surface regression of BE 3 months later, graded by 2 blinded, expert endoscopists. Calculated sample size was 57 patients, based on a non-inferiority design.

RESULTS: Median BE surface regression at 3 months was 83% in the standard group, 78% in the simple-with-cleaning group, and 88% in the simple-no-cleaning group (P =.14). RF ablation time was 20 min (inter-quartile range [IQR], 18-25 min) for the standard group, 13 min (IQR, 11-15 min) for the simple-with-cleaning group, and 5 min (IQR, 5-9 min) for the simple-no-cleaning group (P <.01). The median number of introductions (RFA devices/endoscope) for the standard group was 7, vs 4 for the simple groups (P <.01). CONCLUSIONS: This randomized, prospective study suggests that c-RFA is easier and faster, but equally safe and effective, when the cleaning phase between ablations is omitted or simplified.

*Impactfactor: 5.627*

## **Schoon EJ**

### **Competence measurement during colonoscopy training: the use of self-assessment of performance measures**

Koch AD, Haringsma J, Schoon EJ\*, Man RA de, Kuipers EJ

Am J Gastroenterol. 2012 Jul;107(7):971-5

OBJECTIVES: We evaluated a new assessment technique for colonoscopy training.

METHODS: We prospectively evaluated colonoscopy skills during training using the Rotterdam Assessment Form for colonoscopy. The questionnaire covers cecal intubation, procedural time, and subjective grading of performance. Individual learning curves are compared with a group reference.

RESULTS: Nineteen trainees self-assessed 2,887 colonoscopies. The cecal intubation rate improved from 65% at baseline to 78% and 85% after 100 and 200 colonoscopies, respectively. In our training program the 90% threshold was reached after 280 colonoscopies on average. Cecal intubation time improved from 13:10 minutes at baseline to 9:30 and 8:30 after 100 and 200 colonoscopies, respectively.

CONCLUSIONS: This novel self-assessment form allows individual learning curves to be compared with a group reference, provides data on the development of dexterity skills and individual training targets, and stimulates trainees to identify steps for self-improvement.

*Impactfactor: 7.282*

## **Schoon EJ**

### **Learning to perform endoscopic resection of esophageal neoplasia is associated with significant complications even within a structured training program**

Vilsteren FG van, Pouw RE, Herrero LA, Peters FP, Bisschops R, Houben M, Peters FT, Schenk BE, Weusten BL, Visser M, Kate FJ ten, Fockens P, Schoon EJ\*, Bergman JJ

Endoscopy. 2012 Jan;44(1):4-14. Epub 2011 Nov 22

Background and study aims: Endoscopic resection is the cornerstone of endoscopic treatment of esophageal high grade dysplasia or early cancer. Endoscopic resection is, however, a technically demanding procedure, which requires training and expertise. The aim of the current study was to prospectively evaluate efficacy and safety of the first 120 endoscopic resection procedures of early esophageal neoplasia performed by six endoscopists (20 endoscopic resections each) who were participating in an endoscopic resection training program. Patients and methods: The program consisted of four tri-monthly 1-day courses with lectures, live-demonstrations, hands-on training on anesthetized pigs, and one-on-one hands-on training days. Gastroenterologists from centers with multidisciplinary expertise in upper gastrointestinal oncology participated, together with an endoscopy nurse and a pathologist. Outcome measures were complete endoscopic removal of the target area and acute complications. Results: A total of 120 consecutive esophageal

endoscopic resection procedures (85 ERcap, 35 multiband mucosectomy [MBM]) were performed by six endoscopists: 109 in Barrett's esophagus, 11 for squamous neoplasia; 85 piecemeal endoscopic resections (median 3 specimens, interquartile range 2 (92.5 covered stent), and one patient underwent esophagectomy. There were 11 acute mild bleedings (9.2 %), which were managed endoscopically. Perforations occurred in ER-cap procedures performed by four participants (7.1 resections and 8.3 Conclusion: In this intense, structured training program, the first 120 esophageal endoscopic resections performed by six participants were associated with a 5.0 adequately managed, performing 20 endoscopic resections may not be sufficient to reach the peak of the learning curve in endoscopic resection.

*Impactfactor: 5.210*

## **Schoon EJ**

### **Radiofrequency ablation and endoscopic resection in a single session for Barrett's esophagus containing early neoplasia: a feasibility study**

Vilsteren FG van, Alvarez Herrero L, Pouw RE, Visser M, Kate FJ ten, Berge Henegouwen MI van, Schoon EJ\*, Weusten BL, Bergman JJ

Endoscopy 2012; 44(12): 1096-1104

Background and study aim: Endoscopic resection with radiofrequency ablation (RFA) 6 weeks later safely and effectively eradicates Barrett's esophagus with high grade dysplasia (HGD) and early cancer.

After widespread endoscopic resection, related scarring may hamper balloon-based circumferential RFA (c-RFA). However c-RFA immediately followed by endoscopic resection in the same session might avoid the impact of scarring and reduce laceration and stenosis risk. We aimed to assess the feasibility of such an approach.

Patients and methods: Patients with Barrett's esophagus  $\geq 3$  cm and  $\geq 1$  visible lesion (HGD/early cancer) were included. Visible lesions were marked with cautery, and c-RFA (12 J/cm<sup>2</sup>) was delivered using two applications and a cleaning step, followed by resection of the delineated area. Outcome measures were surface regression of Barrett's esophagus at 3 months, need for subsequent c-RFA, complications, and quality of resection specimens.

Results: 24 patients (20 men, 4 women; mean age 68 years, standard deviation [SD] 12; Barrett's esophagus median length 6.8 cm) underwent single-session c-RFA + endoscopic resection, providing a median of 4 (interquartile range [IQR] 2 - 6) resection specimens (early cancer 18 patients; HGD 6).

Complications included 1 perforation, 4 bleedings, and 5 stenoses; all were managed endoscopically. Specimens allowed assessment of neoplasia depth, differentiation, and lymphatic/vascular invasion. Median Barrett's esophagus surface regression at 3 months was 95 %. No patient required a second c-RFA procedure and 40 % required repeat endoscopic resection for visible lesions. Complete response for neoplasia was achieved in 100 % and complete response for intestinal metaplasia (CR-IM) in 95 %.

Conclusions: c-RFA followed by endoscopic resection in the same session is feasible, but technically demanding and associated with a substantial rate of complications and repeat endoscopic resection.

This approach should be reserved for selected cases in expert centers, with endoscopic resection and RFA 6 - 8 weeks later remaining the standard combined approach.

*Impactfactor: 5.210*

**Schoon EJ**

**Reply to mannath & ragunath**

Vilsteren FG van, Schoon EJ\*, Bergman JJ

Endoscopy. 2012 Jun;44(6):633. Epub 2012 May 25

*Impactfactor: 5.210*

\* = *Werkzaam in het Catharina Ziekenhuis*



# Mondziekten en Kaakchirurgie

**Pijpe J**

**Long term stability of mandibular advancement procedures: bilateral sagittal split osteotomy versus distraction osteogenesis**

Baas EM, Pijpe J\*, Lange J de

Int J Oral Maxillofac Surg. 2012 Feb;41(2):137-41

The aim of this study was to compare the postoperative stability of the mandible after a bilateral lengthening procedure, either by bilateral sagittal split osteotomy (BSSO) or distraction osteogenesis (DO). All patients who underwent mandibular advancement surgery between March 2001 and June 2004 were evaluated. There were 17 patients in the BSSO group and 18 patients in the DO group. The decision to use intra-oral distraction or BSSO for mandibular advancement primarily depended on the choice of the patient and their parents. In both groups, standardized cephalometric radiographs were taken preoperatively, postoperatively (BSSO group) or directly post-distraction (DO group) and during the last study measurement in May 2008. Cephalometric analysis was performed using the following measurements: sella/nasion-mandibular point B and sella/nasion-mandibular plane. Point B was used to estimate relapse.

This study showed no significant difference in relapse between the BSSO and the DO groups measured 46-95 months after advancement of the mandible ( $P > .05$ ). It can be concluded from this study that there is no postoperative difference in the stability between BSSO and DO after mandibular advancement after 4 years.

*Impactfactor: 1.506*

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**Neurologie**

## **Bouwman FH**

### **Serial CSF sampling in Alzheimer's disease: specific versus non-specific markers**

Kester MI, Scheffer PG, Koel-Simmelink MJ, Twaalfhoven H, Verwey NA, Veerhuis R, Twisk JW, Bouwman FH\*, Blankenstein MA, Scheltens P, Teunissen C, Flier WM van der Neurobiol Aging. 2012 Aug;33(8):1591-8. Epub 2011 Jul 7

In this longitudinal study we investigated change over time in cerebrospinal fluid (CSF) levels of amyloid-beta 40 and 42 (A 40 and A 42), total tau (tau), tau phosphorylated at threonine 181 (ptau -181), isoprostane, neurofilaments heavy (NfH) and light (NfL). Twenty-four nondemented subjects, 62 mild cognitive impairment (MCI) and 68 Alzheimer's disease (AD) patients underwent 2 lumbar punctures, with minimum interval of 6, and a mean  $\pm$  SD of 24  $\pm$  13 months. Linear mixed models were used to assess change over time. Amyloid-beta 42, tau, and tau phosphorylated at threonine 181, differentiated between diagnosis groups ( $p < 0.05$ ), whereas isoprostane, neurofilaments heavy, and NfL did not. In contrast, effects of follow-up time were only found for nonspecific CSF biomarkers: levels of NfL decreased, and levels of isoprostane, amyloid-beta 40, and tau increased over time ( $p < 0.05$ ).

Isoprostane showed the largest increase. In addition, increase in isoprostane was associated with progression of mild cognitive impairment to AD, and with cognitive decline as reflected by change in Mini Mental State Examination (MMSE). Contrary to AD-specific markers, nonspecific CSF biomarkers, most notably isoprostane, showed change over time. These markers could potentially be used to monitor disease progression in AD.

*Impactfactor: 6.189*

## **Gons RA**

### **Cerebral white matter lesions and lacunar infarcts contribute to the presence of mild parkinsonian signs**

Laat KF de, Norden AG van, Gons RA\*, Uden IW van, Zwiers MP, Bloem BR, Dijk EJ van, Leeuw FE

Stroke. 2012 Oct;43(10):2574-9. Epub 2012 Aug 2

**BACKGROUND AND PURPOSE:** Mild parkinsonian signs (MPS) are common in elderly people and may be an early stage of parkinson(ism). They might be related to cerebral small-vessel disease, although this association remains incompletely understood. To identify subjects at early stages of the disease, we investigated whether the presence of MPS was dependent on the severity and location of small-vessel disease, including white matter lesions and lacunar infarcts.

**METHODS:** Four hundred thirty individuals, with small-vessel disease, aged between 50 and 85 years, without dementia or parkinsonism, were included in this analysis and underwent MRI scanning. The number and location of lacunar infarcts were rated. White matter lesion volume was assessed by manual segmentation with automated delineating of different regions. Presence of MPS was based on the motor section of the Unified Parkinson's Disease Rating Scale. Associations were determined using logistic regression analysis adjusted for age, sex, and total brain volume.

**RESULTS:** Severe white matter lesions and the presence of lacunar infarcts were independently associated with the presence of MPS (OR, 2.6; 95% CI, 1.3-4.9 and OR, 1.8; 95% CI, 1.0-3.0). Frontal and parietal white matter lesions and, to a lesser extent, lacunar infarcts in the thalamus were associated with a higher risk of MPS. The presence of lacunar infarcts was independently related to the bradykinesia category of parkinsonian signs.

**CONCLUSIONS:** This study shows that severe small-vessel disease, especially at certain locations, is associated with MPS signs in older adults. Our findings suggest that small-vessel

disease interrupts basal ganglia-thalamocortical circuits involving both the frontal and parietal lobes and hence may result in MPS.

*Impactfactor: 5.729*

**Gons RA<sup>∞</sup>**

**Diffusion tensor imaging and cognition in cerebral small vessel disease: the RUN DMC study**

Norden AG van, Laat KF de, Dijk EJ van, Uden IW van, Oudheusden LJ van, Gons RA\*, Norris DG, Zwiers MP, Leeuw FE de

Biochim Biophys Acta. 2012 Mar;1822(3):401-7

**BACKGROUND:** Cerebral small vessel disease (SVD) is very common in elderly and related to cognition, although this relation is weak. This might be because the underlying pathology of white matter lesions (WML) is diverse and cannot be properly appreciated with conventional FLAIR MRI. In addition, conventional MRI is not sensitive to early loss of microstructural integrity of the normal appearing white matter (NAWM), which might be an important factor. Diffusion tensor imaging (DTI) provides alternative information on microstructural white matter integrity and we have used this to investigate the relation between white matter integrity, in both WML and NAWM, and cognition among elderly with cerebral SVD.

**METHODS:** The RUN DMC study is a prospective cohort study among 503 independently living, nondemented elderly with cerebral SVD aged between 50 and 85 years. All subjects underwent MRI and DTI scanning. WML were segmented manually. We measured mean diffusivity (MD) and fractional anisotropy (FA), as assessed by DTI in both WML and NAWM.

**RESULTS:** Inverse relations were found between MD in the WML and NAWM and global cognitive function ( =-.11, p<0.05; =-.18, p<0.001), psychomotor speed ( =-.15, p<0.01; =-.18, p<0.001), concept shifting ( =-.11, p<0.05; =-.10, p<0.05) and attention ( =-.12, p<0.05; =-.15, p<0.001). The relation between DTI parameters in both WML and NAWM and cognitive performance was most pronounced in subjects with severe WML.

**CONCLUSION:** DTI parameters in both WML and NAWM correlate with cognitive performance, independent of SVD. DTI may be a promising tool in exploring the mechanisms of cognitive decline and could function as a surrogate marker for disease progression in therapeutic trials. This article is part of a Special Issue entitled: Imaging Brain Aging and Neurodegenerative disease.

*Impactfactor: --*

**Gons RA<sup>∞</sup>**

**Diffusion tensor imaging of the hippocampus and verbal memory performance: the RUN DMC study**

Norden AG van, Laat KF de, Fick I, Uden IW van, Oudheusden LJ van, Gons RA\*

Norris DG, Zwiers MP, Kessels RP, Leeuw FE de

Hum Brain Mapp. 2012 Mar;33(3):542-51

**BACKGROUND:** Cerebral small vessel disease (SVD) and hippocampal atrophy are related to verbal memory failures and may ultimately result in Alzheimer's disease. However, verbal memory failures are often present before structural changes on conventional MRI appear. Changes in microstructural integrity of the hippocampus, which cannot be detected with conventional MRI, may be the underlying pathological substrate. With diffusion tensor imaging (DTI), we investigated the relation between the microstructural integrity of the hippocampus and verbal memory performance in 503 nondemented elderly with SVD.

**METHODS:** The Radboud University Nijmegen Diffusion tensor and Magnetic resonance imaging Cohort study is a prospective cohort study among 503 nondemented elderly with cerebral SVD aged between 50 and 85 years. All participants underwent T1 MPRAGE, fluid-attenuated inversion recovery, DTI scanning and the Rey Auditory Verbal Learning Test. After manual segmentation of the hippocampi, we calculated the mean diffusivity (MD) and fractional anisotropy in both hippocampi. The relation between memory performance and hippocampal DTI parameters was adjusted for age, sex, education, depressive symptoms, hippocampal, and white-matter lesions volume and lacunar infarcts.

**RESULTS:** We found inverse relations between hippocampal MD and verbal memory performance ( $= -0.22$ ;  $P < 0.001$ ), immediate recall ( $= -0.22$ ;  $P < 0.001$ ), delayed recall ( $= -0.20$ ;  $P < 0.001$ ), and forgetting rate ( $= -0.13$ ;  $P = 0.025$ ), most pronounced in participants with a normal hippocampal volume.

**CONCLUSION:** Microstructural integrity of the hippocampus assessed by DTI is related to verbal memory performance in elderly with SVD, also in participants with an intact appearing hippocampus. Changes in hippocampal microstructure may be an early marker of underlying neurodegenerative disease, before macrostructural (i.e., volumetric) changes occur.

*Impactfactor: 5.880*

## **Gons RA**

### **Hypertension is related to the microstructure of the corpus callosum: The RUN DMC Study**

Gons RA\*, Oudheusden LJ van, Laat KF de, Norden AG van, Uden IW van, Norris DG, Zwiers MP, Dijk E van, Leeuw FE de  
J Alzheimers Dis. 2012 Jan 1;32(3):623-31

Vascular factors play a role in the etiology of Alzheimer's disease (AD), presumably due to emergence of white matter lesions. However, important white matter structures involved in the etiology of AD,

including the corpus callosum (CC), remain invariably free from macroscopical white matter lesions, although loss of microstructural integrity assessed with diffusion tensor imaging (DTI) has been described in the CC. Vascular factors have been related to these microstructural white matter changes too, but little is known about their effect on the CC. In 499 subjects with cerebral small vessel disease, aged 50-85 years, we cross-sectionally investigated the relation between hypertension, hypertension treatment status, the microstructural integrity of the CC using DTI, and the attendant cognitive performance. Fractional anisotropy and mean diffusivity were calculated in four substructures of the CC (genu, anterior body, posterior body, and splenium). Differences between groups were calculated with analysis of variance, adjusted for age, gender, and cardiovascular risk factors. Compared with normotensive subjects, hypertensive subjects had a lower fractional anisotropy in the splenium and a significant higher mean diffusivity in both the anterior body and the splenium; this was most noticeable in treated uncontrolled hypertensive subjects. Furthermore we found that microstructural integrity of the CC was related to global cognition. Of this relation, 14 to 60% was explained by the mediating effect of small vessel disease elsewhere in the white matter. Our findings indicate that adequate blood pressure treatment might postpone these changes and the attendant cognitive dysfunction.

*Impactfactor: 3.745*

## **Gons RA**

### **Slechter cognitief presteren bij ouderen met kleine cerebrale bloedingen.**

#### **[Poorer cognitive performance in elderly suffering from cerebral microbleeds]**

Norden AG van, Berg HA van den, Laat KF de, Gons RA\*, Kessels RP, Dijk EJ van, Leeuw FE de

Ned Tijdschr Geneeskd. 2012;156(37):A4813

OBJECTIVE: Cerebral microbleeds, part of the spectrum of cerebral small vessel disease (CSVD), are possibly related to cognitive dysfunctioning. The goal of this study was to investigate the relationship between cerebral microbleeds and cognitive performance, adjusted for white matter lesions and lacunar infarcts.

DESIGN: Prospective cohort study.

METHODS: In 500 elderly without dementia suffering from CSVD, the presence, number and locations of microbleeds were rated on a gradient-echo T2\*-weighted MRI-scans. We assessed the cognitive performance with various tests. In the statistical analyses, we adjusted for age, sex, educational level, depressive symptoms, total brain volume, white matter lesion volume, and numbers of lacunar and territorial infarcts.

RESULTS: The mean age was 65.6 years (SD: 8.8) and 57% of the patients was male. A total of 52 patients (10.4%) had microbleeds. The patients with microbleeds were significantly older, had a higher white matter lesion volume and more lacunar infarcts (all  $p < 0.001$ ). The presence and number of microbleeds were related to poorer general cognitive functioning, lower psychomotor speed and decreased attention. Microbleeds in the frontal, temporal and deep-brain regions correlated strongest with cognitive dysfunctioning.

CONCLUSION: The presence of frontally-, temporally- and deeply-located microbleeds was related to poorer cognitive performance in elderly without dementia, independent of other CSVD-related lesions. The assessment of microbleeds should be included in the evaluation of vascular cognitive dysfunction.

*Impactfactor: --*

## **Hanse MC**

### **Acute neurological disorders following intraperitoneal administration of cisplatin**

Simkens GA\*, Hanse MC\*, Hingh IH de\*

*Impactfactor: 2.045*

## **Hengstman GJ**

### **Cutaneous adverse events associated with disease-modifying treatment in multiple sclerosis: a systematic review**

Balak DM, Hengstman GJ\*, Cakmak A, Thio HB

Mult Scler. 2012 Dec;18(12):1705-17

Glatiramer acetate and interferon-beta are approved first-line disease-modifying treatments (DMTs) for multiple sclerosis (MS). DMTs can be associated with cutaneous adverse events, which may influence treatment adherence and patient quality of life. In this systematic review, we aimed to provide an overview of the clinical spectrum and the incidence of skin reactions associated with DMTs.

A systematic literature search was performed up to May 2011 in Medline, Embase, and Cochrane databases without applying restrictions in study design, language, or publishing date. Eligible for inclusion were articles describing any skin reaction related to DMTs in MS patients. Selection of articles and data extraction were performed by two authors independently. One hundred and six articles were included, of which 41 (39%) were

randomized controlled trials or cohort studies reporting incidences of mainly local injection-site reactions. A large number of patients had experienced some form of localized injection-site reaction: up to 90% for those using subcutaneous formulations and up to 33% for those using an intramuscular formulation.

Sixty-five case-reports involving 106 MS patients described a wide spectrum of cutaneous adverse events, the most frequently reported being lipoatrophy, cutaneous necrosis and ulcers, and various immune-mediated inflammatory skin diseases. DMTs for MS are frequently associated with local injection-site reactions and a wide spectrum of generalized cutaneous adverse events, in particular, the subcutaneous formulations. Although some of the skin reactions may be severe and persistent, most of them are mild and do not require cessation of DMT.

*Impactfactor: 4.255*

### **Hengstman GJ**

#### **Fingolimod bij multiple sclerose: een praktische richtlijn**

Hengstman GJ\*, Hupperts RM, Munster ET van, Siepman TA, Frequin ST, Jong B, Sanders EA

Tijdschr Neurol Neurochir 2012;113:82-9

Fingolimod is het eerste orale immuunmodulerende middel dat geregistreerd is voor de behandeling van

relapsing remitting multipale sclerose. Naast een duidelijk gunstig effect op het beloop van multipale sclerose heeft het middel ook enkele potentieel nadelige effecten waarmee men in de dagelijkse praktijk rekening moet houden. Zo dient er aandacht te zijn voor het optreden van bradycardieën en atrioventriculaire geleidingsstoornissen na de eerste gift, macula-oedeem, een verhoogde kans op met name herpesinfecties, huidmaligniteiten, gestoorde leverfuncties, hypertensie en een verminderde longfunctie. In een consensusbijeenkomst is door een groep van neurologen met bijzondere expertise op het gebied van multipale sclerose een praktische richtlijn opgesteld omtrent het veilig en verantwoord gebruik van dit middel. Deze richtlijn is voor zover mogelijk gebaseerd op gegevens verkregen uit diverse klinische studies.

*Impactfactor: --*

### **Nuenen BF van**

#### **Cerebral pathological and compensatory mechanisms in the premotor phase of leucine-rich repeat kinase 2 parkinsonism**

Nuenen BF van\*, Helmich RC, Ferraye M, Thaler A, Hendler T, Orr-Urtreger A, Mirelman A, Bressman S, Marder KS, Giladi N, Warrenburg BP van de, Bloem BR, Toni I; on behalf of the LRRK2 Ashkenazi Jewish Consortium

Brain. 2012 Dec;135(Pt 12):3687-3698

Compensatory cerebral mechanisms can delay motor symptom onset in Parkinson's disease.

We aim to characterize these compensatory mechanisms and early disease-related changes by quantifying movement-related cerebral function in subjects at significantly increased risk of developing Parkinson's disease, namely carriers of a leucine-rich repeat kinase 2-G2019S mutation associated with dominantly inherited parkinsonism. Functional magnetic resonance imaging was used to examine cerebral activity evoked during internal selection of motor representations, a core motor deficit in clinically overt Parkinson's disease. Thirty-nine healthy first-degree relatives of Ashkenazi Jewish patients with Parkinson's disease, who carry the leucine-rich repeat kinase 2-G2019S mutation, participated in this study.

Twenty-one carriers of the leucine-rich repeat kinase 2-G2019S mutation and 18 non-carriers of this mutation were engaged in a motor imagery task (laterality judgements of left or right hands) known to be sensitive to motor control parameters. Behavioural performance of both groups was matched.

Mutation carriers and non-carriers were equally sensitive to the extent and biomechanical constraints of the imagined movements in relation to the current posture of the participants' hands. Cerebral activity differed between groups, such that leucine-rich repeat kinase 2-G2019S carriers had reduced imagery-related activity in the right caudate nucleus and increased activity in the right dorsal premotor cortex.

More severe striatal impairment was associated with stronger effective connectivity between the right dorsal premotor cortex and the right extrastriate body area. These findings suggest that altered movement-related activity in the caudate nuclei of leucine-rich repeat kinase 2-G2019S carriers might remain behaviourally latent by virtue of cortical compensatory mechanisms involving long-range connectivity between the dorsal premotor cortex and posterior sensory regions. These functional cerebral changes open the possibility to use a prospective study to test their relevance as early markers of Parkinson's disease.

*Impactfactor: 9.457*

### **Nuenen BF van<sup>∞</sup>**

#### **Compensatory activity in the extrastriate body area of Parkinson's disease patients**

Nuenen BF van\*, Helmich RC, Buenen N\*, Warrenburg BP van de, Bloem BR, Toni I

J Neurosci. 2012 Jul 11;32(28):9546-53

Compensatory mechanisms are a crucial component of the cerebral changes triggered by neurodegenerative disorders. Identifying such compensatory mechanisms requires at least two complementary approaches: localizing candidate areas using functional imaging, and showing that interference with these areas has behavioral consequences.

Building on recent imaging evidence, we use this approach to test whether a visual region in the human occipito-temporal cortex-the extrastriate body area-compensates for altered dorsal premotor activity in Parkinson's disease (PD) during motor-related processes. We separately inhibited the extrastriate body area and dorsal premotor cortex in 11 PD patients and 12 healthy subjects, using continuous theta burst stimulation.

Our goal was to test whether these areas are involved in motor compensatory processes. We used motor imagery to isolate a fundamental element of motor planning, namely subjects' ability to incorporate the current state of their body into a motor plan (mental hand rotation). We quantified this ability through a posture congruency effect (i.e., the improvement in subjects' performance when their current body posture is congruent to the imagined movement). Following inhibition of the right extrastriate body area, the posture congruency effect was lost in PD patients, but not in healthy subjects. In contrast, inhibition of the left dorsal premotor cortex reduced the posture congruency effect in healthy subjects, but not in PD patients.

These findings suggest that the right extrastriate body area plays a compensatory role in PD by supporting a function that is no longer performed by the dorsal premotor cortex.

*Impactfactor: 7.115*

**Nuenen BF van**

**"On" state freezing of gait in Parkinson disease: a paradoxical levodopa-induced complication**

Espay AJ, Fasano A, Nuenen BF van\*, Payne MM, Snijders AH, Bloem BR

Neurology. 2012 Feb 14;78(7):454-7

OBJECTIVE: To describe the phenotype of levodopa-induced "on" freezing of gait (FOG) in Parkinson disease (PD)

METHODS: We present a diagnostic approach to separate "on" FOG (deterioration during the "on state") from other FOG forms. Four patients with PD with suspected "on" FOG were examined in the "off state" (>12 hours after last medication intake), "on state" (peak effect of usual medication), and "supra-on" state (after intake of at least twice the usual dose).

RESULTS: Patients showed clear "on" FOG, which worsened in a dose-dependent fashion from the "on" to the "supra-on" state. Two patients also demonstrated FOG during the "off state," of lesser magnitude than during "on." In addition, levodopa produced motor blocks in hand and feet movements, while other parkinsonian features improved. None of the patients had cognitive impairment or a preexisting "off" FOG.

CONCLUSIONS: True "on" FOG exists as a rare phenotype in PD, unassociated with cognitive impairment or a preexisting "off" FOG. Distinguishing the different FOG subtypes requires a comprehensive motor assessment in at least 3 medication states.

*Impactfactor: 8.312*

**Nuenen BF van**

**Weight-specific anticipatory coding of grip force in human dorsal premotor cortex**

Nuenen BF van\*, Kuhtz-Buschbeck J, Schulz C, Bloem BR, Siebner HR

J Neurosci. 2012 Apr 11;32(15):5272-83

Erratum in: J Neurosci. 2012 Jul 25;32(30):10448

The dorsal premotor cortex (PMd) uses prior sensory information for motor preparation. Here, we used a conditioning-and-map approach in 11 healthy male humans (mean age 27 years) to further clarify the role of PMd in anticipatory motor control. We transiently disrupted neuronal processing in PMd, using either continuous theta burst stimulation (cTBS) at 80% (inhibitory cTBS) or 30% (sham cTBS) of active motor threshold.

The conditioning effects of cTBS on preparatory brain activity were assessed with functional MRI, while participants lifted a light or heavy weight in response to a go-cue (S2). An additional pre-cue (S1) correctly predicted the weight in 75% of the trials.

Participants were asked to use this prior information to prepare for the lift. In the sham condition, grip force showed a consistent undershoot, if the S1 incorrectly prompted the preparation of a light lift. Likewise, an S1 that falsely announced a heavy weight produced a consistent overshoot in grip force. In trials with incorrect S1, preparatory activity in left PMd during the S1-S2 delay period predicted grip force undershoot but not overshoot. Real cTBS selectively abolished this undershoot in grip force.

Furthermore, preparatory S1-S2 activity in left PMd no longer predicted the individual undershoot after real cTBS. Our results provide converging evidence for a causal involvement of PMd in anticipatory downscaling but not upscaling of grip force, suggesting an inhibitory role of PMd in anticipatory grip force control during object lifting.

*Impactfactor: 7.115*

**Vermeij AJ**

**Deterioration of Parkinson's disease during hospitalization: survey of 684 patients**

Gerlach OH, Broen MP, Domburg PH van, Vermeij AJ\*, Weber WE

BMC Neurol. 2012 Mar 8;12:13

**BACKGROUND:** A substantial fraction of Parkinson's disease patients deteriorate during hospitalisation, but the precise proportion and the reasons why have not been studied systematically and the focus has been on surgical wards and on Accident & Emergency departments. We assessed the prevalence and risk factors of deterioration of Parkinson's disease symptoms during hospitalization, including all wards.

**METHODS:** We invited Parkinson's disease patients from three neurology departments in The Netherlands to answer a standardised questionnaire on general, disease and hospital related issues. Patients who had been hospitalized in the previous year were included and analysed. Possible risk factors for Parkinson's disease deterioration were identified. Proportions were analysed using the Chi-Square test and a logistic regression analysis was performed.

**RESULTS:** Eighteen percent of 684 Parkinson's disease patients had been hospitalized at least once in the last year. Twenty-one percent experienced deterioration of motor symptoms, 33% did have one or more complications and 26% had received incorrect anti-Parkinson's medication. There were no statistically significant differences for these variables between admissions on neurologic or nonneurologic wards and between having surgery or not. Incorrect medication during hospitalization was significantly associated with higher risk (OR 5.8, CI 2.5-13.7) of deterioration, as were having infections (OR 6.7 CI 1.8-24.7). A higher levodopa equivalent dose per day was a significant risk factor for deterioration. When adjusting for different variables, wrong medication distribution was the most important risk factor for deterioration.

**CONCLUSIONS:** Incorrect medication and infections are the important risk factors for deterioration of Parkinson's disease patients both for admissions with and without surgery and both for admissions on neurologic and non-neurologic wards. Measures should be taken to improve care and incorporated in guidelines.

*Impactfactor: 2.167*

\* = *Werkzaam in het Catharina Ziekenhuis*

∞ = *Ten tijde van publicatie werkzaam bij: Donders Institute for Brain, Cognition and Behaviour, Centre for Neuroscience, Department of Neurology, Radboud University Nijmegen Medical Centre.*



# Nucleaire Geneeskunde

**Pijpers H**

**Lymphatic mapping after previous breast surgery**

Maaskant-Braat AJ\*, Bruijn SZ de, Woensdregt K\*, Pijpers H\*, Voogd AC,  
Nieuwenhuijzen GA\*

Breast. 2012 Aug;21(4):444-8. Epub 2011 Nov 21

*Voor abstract zie: Chirurgie - Maaskant Braat AJ*

*Impactfactor: 2.491*

*\* = Werkzaam in het Catharina Ziekenhuis*

## Onderwijs en Onderzoek

## **Broek KC van den**

### **Posttraumatic stress 18 months following cardioverter defibrillator implantation: Shocks, anxiety, and personality**

Habibovic M\*, Broek KC van den\*, Alings M, Voort PH van der\*, Denollet J  
Health Psychol. 2012 Mar;31(2):186-93. Epub 2011 Aug 1

*Voor abstract zie: Cardiologie - Habibovic M*

*Impactfactor: 3.873*

## **Buzink SN**

### **Face and Construct Validity of the SimSurgery SEP VR Simulator for Salpingectomy in Case of Ectopic Pregnancy**

Hessel M\*, Buzink SN\*, Schoot D\*, and Jakimowicz JJ\*

Journal of Gynecologic Surgery. December 2012, 28(6): 411-417

*Voor abstract zie: Gynaecologie - Hessel M*

*Impactfactor: --*

## **Buzink SN**

### **Laparoscopic Surgical Skills programme: Setting the European standard**

Buzink SN\*, Schiappa JM, Bicha Castelo H, Fingerhut A, Hanna G, Jakimowicz JJ\*

Revista portuguesa de cirurgia 20: 33-40

*Impactfactor:--*

## **Houterman S ∞**

### **Agreement between different parameters of dialysis dose in achieving treatment targets: results from the NECOSAD study**

Moret KE, Grootendorst DC, Dekker FW, Boeschoten EW, Krediet RT, Houterman S∞, Beerenhout CH, Kooman JP; NECOSAD Study Group

Nephrol Dial Transplant. 2012 Mar;27(3):1145-52

**BACKGROUND:** The recommended parameter of dialysis dose differs between K-DOQI and the European Best Practice Guidelines. It is not well known to what extent an agreement exists between the different parameters, nor if target and delivered dialysis dose are prescribed according to the urea reduction rate (URR), single-pool Kt/V (spKt/V) or equilibrated double-pool Kt/V (eKt/V) and which parameter is most strongly related to mortality.

**METHODS:** In 830 haemodialysis patients from the NECOSAD cohort URR, spKt/V and eKt/V were calculated and compared according to a classification regarding the recommended treatment targets (70%, 1.4 and 1.2, respectively) as well as minimum delivered dialysis dose (65%, 1.2 and 1.05, respectively). Moreover, the relation between treatment dose and survival was assessed using Cox regression analysis.

**RESULTS:** A spKt/V of e 1.4 and URR e 70% corresponded with eKt/V e 1.20 (as reference method) in, respectively, 98.0 and 90.6% of patients. spKt/V of e 1.2 and URR e 65% corresponded with eKt/V e 1.05 in, respectively, 95.5 and 91.2% of patients. Deviations from the reference method were significantly related to differences in urea distribution volume (spKt/V), treatment time (URR) and ultrafiltration volume (URR). The adjusted HR (95% CI) was 0.98 (0.96, 0.99) for URR, 0.51 (0.31, 0.84) for spKt/V and 0.46 (0.30, 0.80) for the eKt/V.

**CONCLUSION:** The use of URR leads to larger disagreement with the reference method (eKt/V) treatment target as compared to spKt/V. Low urea distribution volume, short treatment time and low ultrafiltration volumes are predictive parameters for overestimation

of dialysis dose when utilizing the alternative methods spKt/V and URR instead of eKt/V. Delivered eKt/V, spKt/V and URR were all positively related to survival.

*Impactfactor: 3.396*

## **Houterman S ∞**

### **Effect of obstetric team training on team performance and medical technical skills: a randomised controlled trial**

Fransen AF, Ven J van de, Meri n AE, Wit-Zuurendonk LD de, Houterman S∞, Mol BW, Oei SG

BJOG. 2012 Oct;119(11):1387-93. Epub 2012 Aug 13

**OBJECTIVE:** To determine whether obstetric team training in a medical simulation centre improves the team performance and utilisation of appropriate medical technical skills of healthcare professionals.

**DESIGN:** Cluster randomised controlled trial.

**SETTING:** The Netherlands.

**SAMPLE:** The obstetric departments of 24 Dutch hospitals.

**METHODS:** The obstetric departments were randomly assigned to a 1-day session of multiprofessional team training in a medical simulation centre or to no such training. Team training was given with highfidelity mannequins by an obstetrician and a communication expert. More than 6 months following training, two unannounced simulated scenarios were carried out in the delivery rooms of all 24 obstetric departments. The scenarios, comprising a case of shoulder dystocia and a case of amniotic fluid embolism, were videotaped. The team performance and utilisation of appropriate medical skills were evaluated by two independent experts.

**MAIN OUTCOME MEASURES:** Team performance evaluated with the validated Clinical Teamwork Scale (CTS) and the employment of two specific obstetric procedures for the two clinical scenarios in the simulation (delivery of the baby with shoulder dystocia in the maternal all-fours position and conducting a perimortem caesarean section within 5 minutes for the scenario of amniotic fluid embolism).

**RESULTS:** Seventy-four obstetric teams from 12 hospitals in the intervention group underwent teamwork training between November 2009 and July 2010. The teamwork performance in the training group was significantly better in comparison to the nontraining group (median CTS score: 7.5 versus 6.0, respectively; P = 0.014). The use of the predefined obstetric procedures for the two clinical scenarios was also significantly more frequent in the training group compared with the nontraining group (83 versus 46%, respectively; P = 0.009).

**CONCLUSIONS:** Team performance and medical technical skills may be significantly improved after multiprofessional obstetric team training in a medical simulation centre.

*Impactfactor: 3.407*

## **Houterman S∞**

### **Gallbladder cancer, a vanishing disease?**

Alexander S, Lemmens VE, Houterman S∞, Nollen L\*, Roumen R, Slooter GD

Cancer Causes Control. 2012 Oct;23(10):1705-9. Epub 2012 Aug 28

**OBJECTIVE:** Gallbladder cancer (GBC) is a rare gastrointestinal malignancy. A retrospective population-based study was conducted to evaluate trends in incidence, treatment, and outcome of GBC in the latter three decades in the south of the Netherlands.

**METHODS:** All patients diagnosed with GBC diagnosed in the Dutch Eindhoven Cancer Registry area between 1975 and 2008 were included (n = 659). Trend analyses were conducted for treatment and survival.

RESULTS: During this time period, standardized incidence in females and males plummeted from 4.5 to 0.7 and from 2.0 to 0.4 per 100,000 inhabitants, respectively. Resection rates decreased from 74.3 to 53.4 %. Chemotherapy and radiotherapy rates did not change and were used sparingly. Five-year survival remained stable (10 %) over time.

CONCLUSION: The age-standardized incidence of GBC declined drastically over the last three decades. An increasing number of early cholecystectomies for gallstones may play a role. Parallel to the decreasing incidence of stomach cancer, the effective treatment of *Helicobacter pylori* may also have resulted in a lowered incidence of GBC.

*Impactfactor: 2.877*

## **Houterman S∞**

### **Leg alignment and tibial slope after minimal invasive total knee arthroplasty: a prospective, randomized radiological study of intramedullary versus extramedullary tibial instrumentation**

Kroon KE de , Houterman S∞, Janssen RP

Knee. 2012 Aug;19(4):270-4

The purpose of the study was analysis of leg alignment and tibial slope comparing intramedullary versus extramedullary tibial instrumentation in the Genesis II MIS-TKA (Smith & Nephew, Memphis, USA). A prospective randomized study was performed according to the CONSORT guidelines. All patients (56 patients) for MIS-TKA were included, if the pre-operative standing long leg X-ray demonstrated the tibia eligible for use of both intra- and extramedullary MIS tibial instrumentation. Randomization was performed by envelope selecting intra- or extramedullary tibia MIS instrumentation. All patients were operated by, or under supervision of, one experienced knee surgeon (RJ). Measurements of leg alignment and tibial slope were made on standardized long leg standing X-rays and lateral knee X-rays performed pre-operatively and 4-12 months post-surgery. Leg alignment was defined as being within or outside the range of 3° varus-valgus on the mechanical leg. The tibial slope was compared pre- and post-surgery. In the present study, there was no difference in leg alignment after MIS-TKA comparing intramedullary versus extramedullary tibial instrumentation. Restoration of tibial slope was significantly better with use of the extramedullary tibial instrumentation.

*Impactfactor: 1.736*

## **Houterman S∞**

### **Long-term outcome in pyridoxine-dependent epilepsy**

Bok LA, Halbertsma FJ, Houterman S∞, Wevers RA, Vreeswijk C, Jakobs C, Struys E, Hoeven JH van der, Sival DA, Willemsen MA

Dev Med Child Neurol. 2012 Sep;54(9):849-54

AIM: The long-term outcome of the Dutch pyridoxine-dependent epilepsy cohort and correlations between patient characteristics and follow-up data were retrospectively studied.

METHOD: Fourteen patients recruited from a national reference laboratory were included (four males, 10 females, from 11 families; median age at assessment 6y; range 2y 6mo-16y). The following data were retrieved: sex; age at seizure onset; age at the start of pyridoxine therapy; level of urinary alphaaminoadipic semialdehyde; antiquitin mutations; developmental milestones; evaluation of neurocognitive functioning and school career; magnetic resonance imaging (MRI) and electroencephalography (EEG) assessments.

RESULTS: Pyridoxine was started antenatally in two children, in the first week of life in five, in the first month of life in three, or after the first month of life (range 2.5-8mo) in four. No

child was physically disabled; however, only five walked at 2 years of age. Mental development was delayed in most: median IQ or developmental index was 72 (SD 19). Pyridoxine monotherapy controlled seizures in 10 of 14 children, whereas four needed additional antiepileptic drugs. Seizure persistence, antiepileptic drugs (other than pyridoxine), EEG background, and epileptiform activity were not associated with outcome. On neonatal MRI, structural and white matter abnormalities occurred in five of eight children; on followup, the number of abnormal MRIs was increased. Delayed initiation of pyridoxine medication and corpus callosum abnormalities were significantly associated with unfavourable neurodevelopmental outcome, but normal follow-up imaging did not predict a good outcome.

**INTERPRETATION:** Outcome of patients with pyridoxine-dependent epilepsy remains poor. Individual outcome cannot be predicted by the evaluated characteristics. We suggest that collaborated research in structured settings could help to improve treatment strategies and outcome for pyridoxine-dependent epilepsy

*Impactfactor: 2.918*

## **Houterman S∞**

### **Rehabilitation using high-intensity physical training and long-term return-to-work in cancer survivors**

Thijs KM, Boer AG de, Vreugdenhil G, Wouw AJ van de, Houterman S∞, Schep G

*J Occup Rehabil.* 2012 Jun;22(2):220-9

**INTRODUCTION:** Due to large and increasing numbers of cancer survivors, long-term cancer-related health issues have become a major focus of attention. This study examined the relation between a highintensity physical rehabilitation program and return-to-work in cancer survivors who had received chemotherapy.

**METHODS:** The intervention group, consisting of 72 cancer survivors from one hospital (8 men and 64 women, mean age 49 years), followed an 18-weeks rehabilitation program including strength and interval training, and home-based activities. An age-matched control group, consisting of 38 cancer survivors (9 men and 29 women), was recruited from two other hospitals. They received only standard medical care. All subjects were evaluated during a telephone interview on employment issues, conducted at  $\pm 3$  years after diagnosis. The main outcomes were change in working hours per week and time until return-to-work.

**RESULTS:** Patients in the intervention group showed significant less reduction in working hours per week [-5.0 h/week vs. -10.8 h/week ( $P = .03$ )]. Multivariate analyses showed that the training intervention, the age of patients, and the number of working hours pre-diagnosis could explain the improvement in long-term participation at work. Time until (partial) return-to-work was 11.5 weeks for the intervention group versus 13.2 weeks for the control group ( $P = .40$ ). On long-term follow-up, 78% of the participants from the intervention group versus 66% from the control group had returned to work on the pre-diagnosis level of working hours ( $P = .18$ ).

**CONCLUSION:** Rehabilitation using high-intensity physical training is useful for working patients to minimize the decreased ability to work resulting from cancer and its treatment.

*Impactfactor: --*

### **Houterman S∞**

The measurement of urinary  $\Delta^1$ -piperidine-6-carboxylate, the alter ego of  $\alpha$ -aminoadipic semialdehyde, in Antiquitin deficiency

Struys EA, Bok LA, Emal D, Houterman S∞, Willemsen MA, Jakobs C

J Inherit Metab Dis. 2012 Sep;35(5):909-16. Epub 2012 Jan 17

The assessment of urinary  $\alpha$ -aminoadipic semialdehyde (-AASA) has become the diagnostic laboratory test for pyridoxine dependent seizures (PDS). -AASA is in spontaneous equilibrium with its cyclic form (1)-piperidine-6-carboxylate (P6C); a molecule with a heterocyclic ring structure. Ongoing diagnostic screening and monitoring revealed that in some individuals with milder ALDH7A1 variants, and patients co-treated with a lysine restricted diet, -AASA was only modestly increased. This prompted us to investigate the diagnostic power and added value of the assessment of urinary P6C compared to -AASA. Urine samples were diluted to a creatinine content of 0.1 mmol/L, followed by the addition of 0.01 nmol [(2)H(9)]pipercolic acid as internal standard (IS) and 5 L was injected onto a Waters C(18) including 0.03 % formic acid by volume with a flow rate of 150 L/min and detection was accomplished in the multiple reaction monitoring mode: P6C m/z 128.1 > 82.1; [(2)H(9)]pipercolic acid m/z 139.1 > 93.1. Due to the dualistic nature of -AASA/P6C, and the lack of a proper internal standard, the method is semi quantitative. The intra-assay CVs (n = 10) for two urine samples of proven PDS patients with only modest P6C increases were 4.7% and 8.1%, whereas their inter-assay CVs (n = 10) were 16 and 18% respectively. In all 40 urine samples from 35 individuals with proven PDS, we detected increased levels of P6C. Therefore, we conclude that the diagnostic power of the assessments of urinary P6C and  $\alpha$  -AASA is comparable.

*Impactfactor: 3.577*

### **Jakimowicz JJ**

**Face and Construct Validity of the SimSurgery SEP VR Simulator for Salpingectomy in Case of Ectopic Pregnancy**

Hessel M\*, Buzink SN\*, Schoot D\*, and Jakimowicz JJ\*

Journal of Gynecologic Surgery. December 2012, 28(6): 411-417

*Voor abstract zie: Gynaecologie – Hessel M*

*Impactfactor: --*

### **Jakimowicz JJ**

**Laparoscopic Surgical Skills programme: Setting the European standard**

Buzink SN\*, Schiappa JM, Bicha Castelo H, Fingerhut A, Hanna G, Jakimowicz JJ\*

Revista portuguesa de cirurgia 20: 33-40

*Impactfactor:--*

\* = *Werkzaam in het Catharina Ziekenhuis*

∞ = *Ten tijde van publicatie werkzaam bij: Maxima Medisch Centrum Academie*

## **Operatie Kamers**

## **Stepaniak PS**

### **Bariatric surgery with operating room teams that stayed fixed during the day: a multicenter study analyzing the effects on patient outcomes, teamwork and safety climate, and procedure duration**

Stepaniak PS\*, Heij C, Buise MP\*, Mannaerts GH, Smulders F, Nienhuijs SW\*

Anesth Analg. 2012 Dec;115(6):1384-92. Epub 2012 Nov 9

**BACKGROUND:**Bariatric surgery durations vary considerably because of differences in surgical procedures and patient factors. We studied the effects on patient outcomes, teamwork and safety climate, and procedure durations resulting from working with operating room (OR) teams that remain fixed for the day instead of OR teams that vary during the day.

**METHODS:**Data were collected in 2 general teaching hospitals, consisting of patient-related demographic and intraoperative data and of staff-related survey data on team work and safety climate. The procedure durations of fixed and conventional OR teams were analyzed by comparison of means tests and by regression methods to control for the effects of surgeon, surgical experience, and procedure type.

**RESULTS:**For both hospitals, we obtained the following 4 results for working on bariatric procedures with OR teams that remained fixed for the day. First, patient outcomes did not worsen. Second, teamwork and safety climate (both measured on a 5-point scale) improved significantly, for teamwork + 0.86 (95% confidence interval [CI], 0.54 to 1.18) and for safety climate + 0.75 (95% CI, 0.40 to 1.11). Third, the procedures were performed significantly faster, as both the mean and the SD of procedure durations decreased. After correcting for learning effects, the average reduction of durations was 10.8% (99% CI, 5.0% to 15.3%, or 4 to 13 minutes). This gain was mainly realized for surgical time (12%; 99% CI, 5% to 18%, or 3 to 11 minutes). The effect on peripheral time, defined as procedure time minus surgical time, is not significant (3%; 99% CI, -6% to 12%, or -1 to 3 minutes). Fourth, additional gains were obtained by performing the same type of procedure multiple times within the same day (5% per every next procedure of the same type; 99% CI, 3% to 7%, or 3 to 6 minutes).

**CONCLUSION:**Working with fixed teams in bariatric surgery reduced procedure durations and improved teamwork and safety climate, without adverse effects on patient outcomes.

*Impactfactor: 3.286*

## **Stepaniak PS**

### **Fast-track practice in cardiac surgery: results and predictors of outcome**

Haanschoten MC\*, Straten AH van\*, Woorst JF ter\*, Stepaniak PS\*, Meer AD van der\*, Zundert AA van\*, Soliman Hamad MA\*

Interact Cardiovasc Thorac Surg. 2012 Dec;15(6):989-94. Epub 2012 Sep 5

*Voor abstract zie: Anesthesiologie - Haanschoten MC*

*Impactfactor: --*

## **Stepaniak PS**

### **Modeling and management of variation in the operating rooms helps to improve patient outcome**

Stepaniak PS\*

Pol Przegl Chir. 2012 Feb;84(2):63-9

*Impactfactor: --*

\* = *Werkzaam in het Catharina Ziekenhuis*

## Orthopedie

**Devilee RJ**

**Is the use of autologous platelet-rich plasma gels in gynecologic, cardiac, and general, reconstructive surgery beneficial?**

Everts PA, Hoogbergen MM\*, Weber TA, Devilee RJ\*, Montfort G van\*, Hingh IH de\*  
Curr Pharm Biotechnol. 2012 Jun;13(7):1163-72. Epub 2011 Jul 8

*Voor abstract zie: Plastische Chirurgie - Hoogbergen MM*

*Impactfactor: 2.805*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Pamm**

**Beek M van****Lower sensitivity of screening mammography after previous benign breast surgery**

Breest Smalenburg V van\*, Duijm LE\*, Voogd AC, Groenewoud JH, Jansen FH\*,  
Beek M van\*, Louwman MW

Int J Cancer. 2012 Jan 1;130(1):122-8. Epub 2011 May 9

*Voor abstract zie: Radiologie - Breest Smalenburg V van*

*Impactfactor: 5.444*

**Bergland JN****Comparative study using phenotypic, genotypic and proteomics methods for identification of coagulase-negative staphylococci**

Loonen AJ\*, Jansz AR\*, Bergland JN\*, Valkenburg M\*, Wolffs PF, Brule AJ van den\*

J Clin Microbiol. 2012 Apr;50(4):1437-9. Epub 2012 Jan 11

*Voor abstract zie: Pamm - Loonen AJ*

*Impactfactor: 4.153*

**Bovenkamp J van de****Genotypic diversity of Coxiella burnetii in the 2007-2010 Q fever outbreak episodes in The Netherlands**

Tilburg JJ, Rossen JW, Hannen EJ v, Melchers WJ, Hermans MH, Bovenkamp J van de\*,  
Roest HJ, Bruin A de, Nabuurs-Franssen MH, Horrevorts AM, Klaassen CH

J Clin Microbiol. 2012 Mar;50(3):1076-8. Epub 2011 Dec 21

The genotypic diversity of *C. burnetii* in clinical samples obtained from the Dutch Q fever outbreak episodes of 2007 - 2010 was determined by using a 6-locus MLVA panel. The results are consistent with the introduction of one founder genotype that is gradually diversifying over time whilst spreading over the country.

*Impactfactor: 4.153*

**Brule AJ van den****Comparative study using phenotypic, genotypic and proteomics methods for identification of coagulase-negative staphylococci**

Loonen AJ\*, Jansz AR\*, Bergland JN\*, Valkenburg M\*, Wolffs PF, Brule AJ van den\*

J Clin Microbiol. 2012 Apr;50(4):1437-9. Epub 2012 Jan 11

*Voor abstract zie: Pamm - Loonen AJ*

*Impactfactor: 4.153*

**Jansz AR****Comparative study using phenotypic, genotypic and proteomics methods for identification of coagulase-negative staphylococci**

Loonen AJ\*, Jansz AR\*, Bergland JN\*, Valkenburg M\*, Wolffs PF, Brule AJ van den\*

J Clin Microbiol. 2012 Apr;50(4):1437-9. Epub 2012 Jan 11

*Voor abstract zie: Pamm - Loonen AJ*

*Impactfactor: 4.153*

### **Klinkhamer PJ**

#### **Causes and relevance of unsatisfactory and satisfactory but limited smears of liquid-based compared with conventional cervical cytology**

Siebers AG, Klinkhamer PJ\*, Vedder JE, Arbyn M, Bulten J

Arch Pathol Lab Med. 2012 Jan;136(1):76-83

Context.-Recent randomized controlled trials have shown a significant decrease in unsatisfactory rates for liquid-based cytology (LBC) compared with conventional Papanicolaou test (CP). The underlying causes and relevance of unsatisfactory results for LBC and CP have never been compared within the setting of a randomized controlled trial. Objective.-To examine differences in causes and relevance of unsatisfactory and satisfactory but limited by (SBLB) results for LBC and CP. Design.-Data from the Netherlands ThinPrep Versus Conventional Cytology (NETHCON) trial were used, involving 89 women. Causes and relevance of unsatisfactory and SBLB results were analyzed. Results.-The primary cause for unsatisfactory results for CP and LBC was scant cellularity. Other causes for unsatisfactory CPs were virtually eliminated with LBC. The same was true for SBLB subcategories, with the exception of SBLB absence of transformation zone component and SBLB scant cellularity. The SBLB absence of transformation zone component showed a statistically significant 22% and SBLB scant cellularity a 12% nonsignificant increase with LBC. The detection rates of abnormalities found during 18 months of followup of unsatisfactory test results did not differ significantly between the 2 study arms, nor did they differ from the initial test positivity rates from the NETHCON trial. Conclusions.-Liquid-based cytology shows an almost complete elimination of most causes for unsatisfactory CP, with scant cellularity remaining as the sole cause for unsatisfactory LBC. On the other hand, with LBC a significant increase of smears without a transformation zone component was noted. Women with an unsatisfactory test result are not at increased risk for cervical abnormalities either with LBC or with CP.

*Impactfactor: 2.577*

### **Klinkhamer PJ**

#### **Een jongen met pijn rechts in de onderbuik . [13-Year old boy with abdominal pain]**

Thomassen I\*, Klinkhamer PJ\*, Poll MC van den\*

Ned Tijdschr Geneeskd. 2012;156(18):A3566

*Voor abstract zie: Chirurgie - Thomassen I*

*Impactfactor: --*

### **Klinkhamer PJ**

#### **Liquid-based cervical cytology using ThinPrep technology: weighing the pros and cons in a costeffectiveness analysis.**

Bekker-Grob EW de, Kok IM de, Bulten J, Rosmalen J van, Vedder JE, Arbyn M, Klinkhamer PJ\*, Siebers AG, Ballegooijen M van

Cancer Causes Control. 2012 Aug;23(8):1323-31

PURPOSE: Cervical cancer screening with liquid-based cytology (LBC) has been developed as an alternative to the conventional Papanicolaou (CP) smear. Cost-effectiveness is one of the issues when evaluating LBC. Based on the results of a Dutch randomised controlled trial, we conducted costeffectiveness threshold analyses to investigate under what circumstances manually screened ThinPrep LBC is cost-effective for screening.

METHODS: The MISCAN-Cervix microsimulation model and data from the Dutch NETHCON trial (including 89,784 women) were used to estimate the costs and (quality-adjusted) life years ((QA)LyS) gained for EU screening schedules, varying cost-effectiveness threshold

values. Screening strategies were primary cytological screening with LBC or CP, and triage with human papillomavirus (HPV) testing.

RESULTS: Threshold analyses showed that screening with LBC as a primary test can be cost-effective if LBC is less than <euro>3.2 more costly per test than CP, if the sensitivity of LBC is at least 3-5 % points higher than CP, if the quality of life for women in triage follow-up is only 0.39, or if the rate of inadequate CP smears is at least 16.2 %.

CONCLUSIONS: Regarding test characteristics and costs of LBC and CP, only under certain conditions will a change from CP to manually screened ThinPrep LBC be cost-effective. If none of these conditions are met, implementation of manually screened ThinPrep LBC seems warranted only if there are advantages other than cost-effectiveness. Further research is needed to establish whether other LBC systems will be more favorable with regard to cost-effectiveness.

*Impactfactor: 2.877*

### **Lijnschoten I van**

#### **Circumferential balloon-based radiofrequency ablation of Barrett's esophagus with dysplasia can be simplified, yet efficacy maintained, by omitting the cleaning phase**

Vilsteren FG van, Phoa KN, Herrero LA, Pouw RE, Sondermeijer CM, Lijnschoten I van\*, Seldenrijk CA, Visser M, Meijer SL, Berge Henegouwen MI van, Weusten BL, Schoon EJ\*, Bergman JJ

Clin Gastroenterol Hepatol. 2012 Dec 22. pii: S1542-3565(12)01505-4

*Voor abstract zie: Maag-darm-leverziekten - Schoon EJ*

*Impactfactor: 5.627*

### **Lijnschoten I van**

#### **Focus on extralevator perineal dissection in supine position for low rectal cancer has led to better quality of surgery and oncologic outcome**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D,\* Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

### **Loonen AJ**

#### **Comparative study using phenotypic, genotypic and proteomics methods for identification of coagulase-negative staphylococci**

Loonen AJ\*, Jansz AR\*, Bergland JN\*, Valkenburg M\*, Wolffs PF, Brule AJ van den\*

J Clin Microbiol. 2012 Apr;50(4):1437-9. Epub 2012 Jan 11

Five methods were compared to determine the most accurate identification of coagulase-negative staphylococci (CoNS) (n=142 strains). MALDI-TOF MS showed the best results for rapid and accurate CoNS differentiation (correct identity in 99.3%). An alternative to this approach could be Vitek2 combined with partial *tuf* gene sequencing (100% correct identity when both methods are performed simultaneously).

*Impactfactor: 4.153*

### **Merrienboer F van**

#### **A rare case of diffuse mitral valve fibroelastoma**

Jonge M de\*, Straten A van\*, Dantzig JM van\*, Merrienboer F van\*, Elenbaas T\*  
Ann Thorac Surg. 2012 Aug;94(2):e53

*Impactfactor: 3.741*

### **Nollen L**

#### **Gallbladder cancer, a vanishing disease?**

Alexander S, Lemmens VE, Houterman S\*, Nollen L\*, Roumen R, Slooter GD  
Cancer Causes Control. 2012 Oct;23(10):1705-9. Epub 2012 Aug 28

*Impactfactor: 2.877*

### **Somers KY**

#### **Pathogenesis of the epigastric hernia**

Ponten JE\*, Somers KY\*, Nienhuijs SW\*

Hernia. 2012 Dec;16(6):627-33. Epub 2012 Jul 24

*Voor abstract zie: Chirurgie - Ponten JE*

*Impactfactor: 1.843*

### **Valkenburg M**

#### **Comparative study using phenotypic, genotypic and proteomics methods for identification of coagulase negative staphylococci.**

Loonen AJ\*, Jansz AR\*, Bergland JN\*, Valkenburg M\*, Wolffs PF, Brule AJ van den\*  
J Clin Microbiol. 2012 Apr;50(4):1437-9. Epub 2012 Jan 11

*Voor abstract zie: Pamm - Loonen AJ*

*Impactfactor: 4.153*

### **Wegdam-Blans MC**

#### **Chronic Q fever: Review of the literature and a proposal of new diagnostic criteria**

Wegdam-Blans MC\*, Kampschreur LM, Delsing CE, Bleeker-Rovers CP, Sprong T, Kasteren ME van, Notermans DW, Renders NH, Bijlmer HA, Lestrade PJ, Koopmans MP, Nabuurs-Franssen MH, Oosterheert JJ; The Dutch Q fever Consensus Group  
J Infect. 2012 Mar;64(3):247-259. Epub 2011 Dec 23

A review was performed to determine clinical aspects and diagnostic tools for chronic Q fever. We present a Dutch guideline based on literature and clinical experience with chronic Q fever patients in The Netherlands so far. In this guideline diagnosis is categorized as proven, possible or probable chronic infection based on serology, PCR, clinical symptoms, risk factors and diagnostic imaging.

*Impactfactor: 4.126*

### **Wegdam-Blans MC**

#### **David procedure during a reoperation for ongoing chronic Q fever infection of an ascending aortic prosthesis**

Wegdam-Blans MC\*, Woorst JF ter\*, Klompenhouwer EG\*, Teijink JA\*

Eur J Cardiothorac Surg. 2012 Jul;42(1):e19-20. Epub 2012 May 24

Chronic Q fever infections, caused by *Coxiella burnetii*, are associated with cardiovascular

complications, mainly endocarditis and vascular (graft) infections. We report a case of a patient with a *C. burnetii* infected thoracic aorta graft treated initially in a conservative way. However, surgical excision of the infected graft was eventually necessary. This case report highlights the challenges regarding the treatment of patients with chronic vascular *C. burnetii* infections. In the absence of practical guidelines, treatment is tailored to the individual patient. Furthermore, we want to emphasize the need to include chronic Q fever in the differential diagnosis in patients with culture negative aortitis, especially in the regions with Q fever epidemics in the recent past.

*Impactfactor: 2.550*

### **Wegdam-Blans MC**

#### **Detection of phase I IgG antibodies to *Coxiella burnetii* with EIA as a screening test for blood donations**

Hoek W van der, Wielders CC, Schimmer B, Wegdam-Blans MC\*, Meekelenkamp J, Zaaier HL, Schneeberger PM

Eur J Clin Microbiol Infect Dis. 2012 Nov;31(11):3207-9

The presence of a high phase I IgG antibody titre may indicate chronic infection and a risk for the transmission of *Coxiella burnetii* through blood transfusion. The outbreak of Q fever in the Netherlands allowed for the comparison of an enzyme immunoassay (EIA) with the reference immunofluorescence assay (IFA) in a large group of individuals one year after acute Q fever. EIA is 100 % sensitive in detecting high (e 1:1,024) phase I IgG antibody titres. The cost of screening with EIA and confirming all EIA-positive results with IFA is much lower than screening all donations with IFA. This should be taken into account in cost-effectiveness analyses of screening programmes.

*Impactfactor: 2.859*

### **Wegdam-Blans MC**

#### **Evaluation of commonly used serological tests for detection of *Coxiella burnetii* antibodies in welldefined acute and follow-up sera**

Wegdam-Blans MC\*, Wielders CC, Meekelenkamp J, Korbeeck JM, Herremans T, Tjhie HT, Bijlmer HA, Koopmans MP, Schneeberger PM

Clin Vaccine Immunol. 2012 Jul;19(7):1110-5 Epub 2012 May 23

In this study, we compared *Coxiella burnetii* IgG phase I, IgG phase II, and IgM phase II detection among a commercially available enzyme-linked immunosorbent assay (ELISA) (Virion/Serion), an indirect fluorescent antibody test (IFAT) (Focus Diagnostics), and a complement fixation test (CFT) (Virion/Serion). For this, we used a unique collection of acute- and convalescent-phase sera from 126 patients with acute Q fever diagnosed by positive *Coxiella burnetii* PCR of blood. We were able to establish a reliable date of onset of disease, since DNA is detectable within 2 weeks after the start of symptoms. In acute samples, at  $t = 0$ , IFAT demonstrated IgM phase II antibodies in significantly more sera than did ELISA (31.8% versus 19.7%), although the portion of solitary IgM phase II was equal for IFAT and for ELISA (18.2% and 16.7%, respectively). Twelve months after the diagnosis of acute Q fever, 83.5% and 62.2% of the sera were still positive for IgM phase II with IFAT and ELISA, respectively. At 12 months IFAT IgG phase II showed the slowest decline. Therefore, definitive serological evidence of acute Q fever cannot be based on a single serum sample in areas of endemicity and should involve measurement of both IgM and IgG antibodies in paired serum. Based on IgG phase II antibody detection in paired samples (at 0 and 3 months) from 62 patients, IFAT confirmed more cases than ELISA and CFT, but the differences were not statically significant (100% for IFAT, 95.2% for ELISA, and 96.8% for

CFT). This study demonstrated that the three serological tests are equally effective in diagnosing acute Q fever within 3 months of start of symptoms. In follow-up sera, more IgG antibodies were detected by IFAT than by ELISA or CFT, making IFAT more suitable for prevaccination screening programs.

*Impactfactor:--*

### **Wegdam-Blans MC**

#### **Microbiological challenges in the diagnosis of chronic Q fever**

Kampschreur LM, Oosterheert JJ, Koop AM, Wegdam-Blans MC\*, Delsing CE, Bleeker-Rovers CP, Jager-Leclercq MG De, Groot CA, Sprong T, Nabuurs-Franssen MH, Renders NH, Kasteren ME van, Soethoudt Y, Blank SN, Pronk MJ\*, Groenwold RH, Hoepelman AI, Wever PC

*Clin Vaccine Immunol.* 2012 May;19(5):787-90

Diagnosis of chronic Q fever is difficult. PCR and culture lack sensitivity; hence, diagnosis relies mainly on serologic tests using an immunofluorescence assay (IFA). Optimal phase I IgG cutoff titers are debated but are estimated to be between 1:800 and 1:1,600. In patients with proven, probable, or possible chronic Q fever, we studied phase I IgG antibody titers at the time of positive blood PCR, at diagnosis, and at peak levels during chronic Q fever. We evaluated 200 patients, of whom 93 (46.5%) had proven, 51 (25.5%) had probable, and 56 (28.0%) had possible chronic Q fever. Sixty-five percent of proven cases had positive *Coxiella burnetii* PCR results for blood, which was associated with high phase I IgG. Median phase I IgG titers at diagnosis and peak titers in patients with proven chronic Q fever were significantly higher than those for patients with probable and possible chronic Q fever. The positive predictive values for proven chronic Q fever, compared to possible chronic Q fever, at titers 1:1,024, 1:2,048, 1:4,096, and e 1:8,192 were 62.2%, 66.7%, 76.5%, and e 86.2%, respectively. However, sensitivity dropped to <60% when cutoff titers of e 1:8,192 were used. Although our study demonstrated a strong association between high phase I IgG titers and proven chronic Q fever, increasing the current diagnostic phase I IgG cutoff to >1:1,024 is not recommended due to increased false-negative findings (sensitivity < 60%) and the high morbidity and mortality of untreated chronic Q fever. Our study emphasizes that serologic results are not diagnostic on their own but should always be interpreted in combination with clinical parameters.

*Impactfactor: 2.546*

### **Wegdam-Blans MC**

#### **Shifting priorities in the aftermath of a Q fever epidemic in 2007 to 2009 in The Netherlands: from acute to chronic infection**

Hoek W van der, Schneeberger PM, Oomen T, Wegdam-Blans MC\*, Dijkstra F, Notermans DW, Bijlmer HA, Groeneveld K, Wijkmans CJ, Rietveld A, Kampschreur LM, Duynhoven Y van

*Euro Surveill.* 2012 Jan 19;17(3):20059

From 2007 to 2009, the Netherlands faced large seasonal outbreaks of Q fever, in which infected dairy goat farms were identified as the primary sources. Veterinary measures including vaccination of goats and sheep and culling of pregnant animals on infected farms seem to have brought the Q fever problem under control. However, the epidemic is expected to result in more cases of chronic Q fever among risk groups in the coming years. In the most affected area, in the south of the country, more than 12% of the population now have antibodies against *Coxiella burnetii*. Questions remain about the follow-up of acute

Q fever patients, screening of groups at risk for chronic Q fever, screening of donors of blood and tissue, and human vaccination. There is a considerable ongoing research effort as well as enhanced veterinary and human surveillance.

*Impactfactor: 6.15*

### **Wegdam-Blans MC**

#### **Tropheryma whipplei aortic valve endocarditis, cured without surgical treatment**

Algin A\*, Wegdam-Blans M\*, Verduin K, Janssen H, Dantzig JM van\*

BMC Res Notes. 2012 Oct 30;5(1):600

*Voor abstract zie: Cardiologie - Algin A*

*Impactfactor:--*

\* = *Werkzaam in het Catharina Ziekenhuis*

# Plastische Chirurgie

## **Hoogbergen MM**

### **Is the use of autologous platelet-rich plasma gels in gynecologic, cardiac, and general, reconstructive surgery beneficial?**

Everts PA, Hoogbergen MM\*, Weber TA, Devilee RJ\*, Montfort G van\*, Hingh IH de\*  
Curr Pharm Biotechnol. 2012 Jun;13(7):1163-72. Epub 2011 Jul 8

Tissue repair at wound sites begins with clot formation, and subsequently platelet degranulation with the release of platelet growth factors, which are necessary and well-regulated processes to achieve wound healing. Platelet-derived growth factors are biologically active substances that enhance tissue repair mechanisms, such as chemotaxis, cell proliferation, angiogenesis, extracellular matrix deposition, and remodeling. This review describes the biological background and results on the topical use of autologous platelet-rich plasma and platelet gel in gynecologic, cardiac, and general surgical procedures, including chronic wound management and soft-tissue injuries.

*Impactfactor: 2.805*

## **Hoogbergen MM**

### **Videolaryngoscopy offers advantages over classic laryngoscopy in a patient with seriously limited lip opening**

Zundert AA van\*, Pieters B\*, Hoogbergen M\*  
J Anesth. 2012 Jun;26(3):468-9. Epub 2012 Jan 12

*Impactfactor: 0.831*

## **Rappard JH van**

### **Modified antia buch repair for full-thickness middle auricular defect**

Schipper HJ de\*, Rappard JH van\*, Dumont EA  
Dermatol Surg. 2012 Jan;38(1):124-7

*Impactfactor: 1.798*

## **Schipper HJ de**

### **Modified antia buch repair for full-thickness middle auricular defect**

Schipper HJ de\*, Rappard JH van\*, Dumont EA  
Dermatol Surg. 2012 Jan;38(1):124-7

*Impactfactor: 1.798*

## **Smit JM**

### **Multilayer reconstructions for defects overlying the Achilles tendon with the lateral-arm flap: long-term follow-up of 16 cases**

Smit JM\*, Darcy CM, Audolfsson T, Hartman EH, Acosta R  
Microsurgery. 2012 Sep;32(6):438-44 Epub 2012 Mar 31

Defects of the Achilles tendon and the overlying soft tissue are challenging to reconstruct. The lateralarm flap has our preference in this region as it provides thin pliable skin, in addition, the fascia and tendon can be included in the flap as well. The aim of this report is to share the experience the authors gained with this type of reconstruction. The authors report the largest series in the published reports today.

**PATIENTS AND METHODS:** A retrospective review was performed of all patients treated between January 2000 and January 2009 with a lateral-arm flap for a soft-tissue defect overlying the Achilles tendon.

RESULTS: In the reviewed period, 16 soft-tissue defects overlying the Achilles tendon were reconstructed, with a mean follow-up of 63 months. In three cases, tendon was included into the flap and in two, a sensory nerve was coapted. Fifteen cases (94%) were successful, one failed. In seven cases, a secondary procedure was necessary for thinning of the flap.

CONCLUSION: The lateral-arm flap is a good and safe option for the reconstruction of defects overlying the Achilles tendon.

*Impactfactor: 1.605*

### **Smit JM**

#### **Similar risk for hemangiomas after amniocentesis and transabdominal chorionic villus sampling**

Bauland CG, Smit JM\*, Scheffers SM, Bartels RH, Berg P van den, Zeebregts CJ, Spauwen PH

J Obstet Gynaecol Res. 2012 Feb;38(2):371-5. Epub 2012 Jan 10

AIM: In an earlier study we have shown that transcervical chorionic villus sampling in excess of 90 mg increases the risk for hemangiomas of infancy three- to four-fold compared to amniocentesis. In the present study we investigated whether transabdominal chorionic villus sampling (TA-CVS), in which the samples are smaller, carries the same risk.

MATERIAL AND METHODS: Retrospectively, data were analyzed from 200 consecutive TA-CVS procedures and 200 consecutive amniocentesis procedures. Forty-two TA-CVS procedures and 27 amniocentesis procedures were excluded on predefined criteria. Questionnaires were sent to the parents asking if there was any skin mark on the child: vascular, pigmented or otherwise. All hemangiomas were clinically confirmed.

RESULTS: In the TA-CVS group, 118/158 questionnaires (75%), and in the amniocentesis group 134/173 questionnaires (77%) were returned. Based on the results of the questionnaire (i.e. mentioning of any skin lesion), 24 children in the TA-CVS group and 42 children in the amniocentesis group qualified for a physical examination. In the TA-CVS group 11/118 children (9%) had one or more hemangiomas. In the amniocentesis group 6/134 children (4%) had one or more hemangiomas. There was no statistical difference between the two groups ( $P = 0.134$ ).

CONCLUSION: These results suggest that TA-CVS does not cause an increase in the prevalence of hemangioma compared to amniocentesis. A larger series is, however, necessary to confirm this.

*Impactfactor: 0.942*

### **Smit JM**

#### **Value of the implantable doppler system in free flap monitoring**

Smit JM\*, Klein S, Jong EH de, Zeebregts CJ, Bock GH de, Werker PM

J Plast Reconstr Aesthet Surg. 2012 Sep;65(9):1276-7

*Impactfactor: 1.494*

\* = *Werkzaam in het Catharina Ziekenhuis*



**Radiologie**

### **Breest Smalenburg V van**

#### **Lower sensitivity of screening mammography after previous benign breast surgery**

Breest Smalenburg V van\*, Duijm LE\*, Voogd AC, Groenewoud JH, Jansen FH\*,  
Beek M van\*, Louwman MW

Int J Cancer. 2012 Jan 1;130(1):122-8. Epub 2011 May 9

Few data are available on the effect of previous benign breast surgery on screening mammography accuracy. We determined whether sensitivity of screening mammography and tumor characteristics are different for women with and without previous benign breast surgery. We included a consecutive series of 317,398 screening mammograms of women screened between 1997 and 2008. During 2 year followup, clinical data, breast imaging-, biopsy- and surgery reports were collected of women with screendetected or interval breast cancers. Screening sensitivity, tumor biology and tumor stages were compared between 168 women with breast cancer and prior ipsilateral benign breast surgery and 2,039 women with breast cancer, but without previous ipsilateral, benign breast surgery. The sensitivity of screening mammography was significantly lower for women with prior surgery (64.3% (108/168) versus 73.4% (1,496/2,039),  $p=0.01$ ). The concomitant increased interval cancer risk remained significant after logistic regression adjustment for age and breast density (OR=1.5, 95%CI: 1.1-2.1). Comparing screendetected cancers in women with and without prior breast surgery, no significant differences in estrogenreceptor status ( $p=0.56$ ), mitotic activity ( $p=0.17$ ), proportions of large (T2+) tumors ( $p=0.6$ ) or lymph node positive tumors ( $p=0.4$ ) were found. Also for interval cancers no differences were found in estrogen-receptor status ( $p=0.41$ ), mitotic activity ( $p=0.39$ ), proportions of large tumors ( $p=0.9$ ) and lymph node positive tumors ( $p=0.5$ ) between women with and without prior breast surgery. We conclude that sensitivity of screening mammography is significantly lower in women with previous benign breast surgery than without, but tumor characteristics are comparable both for screen detected cancers and interval cancers.

*Impactfactor: 5.444*

### **Breest Smalenburg V van**

#### **Malpractice claims following screening mammography in the Netherlands**

Breest Smalenburg V van\*, Setz-Pels W\*, Groenewoud JH, Voogd AC, Jansen FH\*,  
Louwman MW, Tielbeek AV\*, Duijm LE\*

Int J Cancer. 2012 Sep 15;131(6):1360-6. Epub 2012 Jan 11

Although malpractice lawsuits are frequently related to a delayed breast cancer diagnosis in symptomatic patients, information on claims at European screening mammography programmes is lacking. We determined the type and frequency of malpractice claims at a Dutch breast cancer screening region. We included all 85,274 women (351,009 screens) who underwent biennial screening mammography at a southern breast screening region in the Netherlands between 1997-2009. Two screening radiologists reviewed the screening mammograms of all screen detected cancers and interval cancers and determined whether the cancer had been missed at the previous screen or at the latest screen, respectively. We analysed all correspondence between the screening organization, clinicians and screened women, and collected complaints and claims until September 2011. At review, 20.9% (308/1,475) of screen detected cancers and 24.3% (163/670) of interval cancers were considered to be missed at a previous screen. A total of 19 women (of which 2, 6 and 11 women had been screened between 1997-2001 (102,439 screens), 2001-2005 (114,740 screens) and 2005-2009 (133,830 screens), respectively) had contacted the screening organization for additional information about their screen detected cancer or interval cancer, but filed no claim. Three other women directly initiated an insurance claim for

financial compensation of their interval cancer without previously having contacted the screening organization. We conclude that screening related claims were rarely encountered, although many screen detected cancers and interval cancers had been missed at a previous screen. A small, but increasing proportion of women sought additional information about their breast cancer from the screening organization.

*Impactfactor: 5.444*

### **Breest Smallenburg V van**

#### **Mammographic changes resulting from benign breast surgery impair breast cancer detection at screening mammography**

Breest Smallenburg V van\*, Duijm LE\*, Voogd AC, Jansen FH, Louwman MW

Eur J Cancer. 2012 Sep;48(14):2097-103

**PURPOSE:** To study possible explanations for lower screening performance after previous benign breast surgery.

**PATIENTS AND METHODS:** We included a consecutive series of 351,009 screening examinations in 85,274 women, obtained between January 1, 1997 and January 1, 2009. The examinations of women with screen detected cancers (SDC) or interval cancers (IC), diagnosed after previous benign breast surgery, were reviewed by two screening radiologists. They determined the presence and degree of post surgical changes, classified breast density and determined whether mammographic interpretation was hampered by tissue characteristics. They also assessed whether the cancer had already been visible at a previous screen.

**RESULTS:** Screening sensitivity was lower in women with prior benign breast surgery than without (63.5% (115/181) versus 73.5% (1643/2236),  $p=0.004$ ). A total of 115 SDCs and 66 ICs were diagnosed in breasts after previous benign breast surgery. Post surgical mammographic alterations in the breast segment where cancer was diagnosed were more distinct in ICs than in SDCs ( $p=0.001$ ). Women with post surgical mammographic changes at the location of the breast cancer had an increased interval cancer risk (OR=2.12, 95% confidence interval (CI)=1.05-4.26). Limited mammographic interpretation due to tissue characteristics was mentioned, only in three SDCs and one IC. The proportions of SDCs and ICs that were already visible at a previous screen were comparable for women with and without prior surgery (SDC: 47.5% versus 43.8%,  $p=0.3$ , IC: 50.0% versus 48.4%,  $p=0.8$ ).

**CONCLUSION:** Previous benign breast surgery decreases screening sensitivity and this is likely due to postoperative mammographic changes.

*Impactfactor: 1.171*

### **Breest Smallenburg V van**

#### **Two-view versus single-view mammography at subsequent screening in a region of the Dutch breast screening programme**

Smallenburg VV\*, Duijm LE\*, Heeten GJ den, Groenewoud JH, Jansen FH\*, Fracheboud J, Plaisier ML, Doorne-Nagtegaal HJ van, Broeders MJ

Eur J Radiol. 2012 Sep;81(9):2189-94. Epub 2011 Sep 8

We retrospectively determined the effect of analogue two-view mammography versus single-view mammography at subsequent screens on breast cancer detection and determined financial consequences for a current digital mammography setting. Two screening radiologists reviewed the mammograms of 536 screen detected cancers (SDCs) and 171 interval cancers (ICs) with single-view mammography (medio-lateral-oblique view) at the last but one screen (SDCs) or latest screen (ICs). They determined whether two-view mammography at the last (but one) screen could have increased the cancer detection rate at

that screening round. For subsequent screens, the radiologists also assessed the percentage of SDCs and ICs that had been missed at previous two-view screening mammography (SDC) or latest two-view screening (IC), respectively. Additional personnel and digital storage costs for standard two-view mammography at subsequent screening were calculated for digital screening. Two-view mammography could have facilitated earlier cancer detection in 40.9% (219/536) of SDCs and 39.8% (68/171) of ICs. For two-view screens, 24.4% of SDCs (213/871) were missed at previous two-view screening and 29.3% of ICs (110/375) were missed at the latest screen. Overall costs increase – 1.03/screen after implementation of digital two-view mammography. Standard two-view mammography at subsequent screening may modestly increase cancer detection at an earlier stage, whereas additional screening costs are limited.

*Impactfactor: 2.606*

### **Dijkmans I**

#### **Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience**

Hurkmans CW\*, Dijkmans I\*, Reijnen M\*, Leer J van der\*, Vliet-Vroegindewij C van, Sangen M van der\*

Radiother Oncol. 2012 May;103(2):183-7. Epub 2012 Jan 24

*Voor abstract zie: Klinische fysica - Hurkmans CW*

*Impactfactor: 5.580*

### **Donkers-van Rossum AB**

#### **Impact of transition from analog screening mammography to digital screening mammography on screening outcome in The Netherlands: a population-based study**

Nederend J\*, Duijm LE\*, Louwman MW, Groenewoud JH, Donkers-van Rossum AB\*, Voogd AC

Ann Oncol. 2012 Dec;23(12):3098-103. Epub 2012 Jun 27

*Voor abstract zie: Radiologie - Nederend J*

*Impactfactor: 6.425*

### **Donkers-van Rossum AB**

#### **Risk factors for osteoporosis in Caucasian patients with moderate chronic obstructive pulmonary disease: a case control study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA,

Donkers-van Rossum AB\*, Aarts RP\*, Wouters EF

Bone. 2012 Jun;50(6):1234-9. Epub 2012 Mar 9

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 4.023*

### **Duijm LE**

#### **Characteristics and screening outcome of women referred twice at screening mammography**

Setz-Pels W\*, Duijm LE\*, Louwman MW, Roumen RM, Jansen FH\*, Voogd AC

Eur Radiol. 2012 Dec;22(12):2624-32. Epub 2012 Jun 13

*Voor abstract zie: Radiologie - Setz-Pels W*

*Impactfactor: 3.222*

**Duijm LE**

**Endovascular treatment of a hepatic artery pseudoaneurysm associated with gastrointestinal tract bleeding**

Vainas T\*, Klompenhouwer E\*, Duijm L\*, Tielbeek X\*, Teijink J\*

J Vasc Surg. 2012 Apr;55(4):1145-9. Epub 2012 Feb 25

*Voor abstract zie: Chirurgie - Vainas T*

*Impactfactor: 3.153*

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*Impactfactor: 6.425*

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*Voor abstract zie: Radiologie - Breest Smalenburg V van*

*Impactfactor: 5.444*

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Breast Cancer Res. 2012 Jan 9;14(1):R10

*Voor abstract zie: Radiologie - Nederend J*

*Impactfactor: 5.245*

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Smallegenburg VV\*, Duijm LE\*, Heeten GJ den, Groenewoud JH, Jansen FH\*, Fracheboud J, Plaisier ML, Doorne-Nagtegaal HJ van, Broeders MJ  
Eur J Radiol. 2012 Sep;81(9):2189-94. Epub 2011 Sep 8

*Voor abstract zie: Radiologie - Breest Smallegenburg V van*

*Impactfactor: 2.606*

### **Jansen FH**

#### **A pulmonary shadow after lobectomy: an unexpected diagnosis**

Crijns K\*, Jansen FH\*, Straten AH van\*, Borne BE van den\*

Neth J Med. 2012 Jun;70(5):232, 235

*Impactfactor: 2.072*

### **Jansen FH**

#### **Bone attenuation on routine chest CT correlates with bone mineral density on DXA in patients with COPD**

Romme EA\*, Murchison JT, Phang KF, Jansen FH\*, Rutten EP, Wouters EF, Smeenk FW\*, Beek EJ van, Macnee W

J Bone Miner Res. 2012 Nov;27(11):2338-2343. Epub 2012 Jun 12

*Voor abstract zie: Longgeneeskunde - Romme EA*

*Impactfactor: 6.373*

### **Jansen FH**

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*Impactfactor: 5.444*

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*Voor abstract zie: Radiologie - Breest Smallegenburg V van*

*Impactfactor: 5.444*

## Jansen FH

### **Progression of osteoporosis in patients with COPD: A 3-year follow up study**

Graat-Verboom L\*, Smeenk FW\*, Borne BE van den\*, Spruit MA, Jansen FH\*, Enschoot JW van\*, Wouters EF

Respir Med. 2012 Jun;106(6):861-70. Epub 2012 Feb 26

*Voor abstract zie: Longgeneeskunde - Graat-Verboom L*

*Impactfactor: 2.475*

## Jansen FH

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Nederend J\*, Duijm LE\*, Voogd AC, Groenewoud JH, Jansen FH\*, Louwman MW

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*Impactfactor: 5.245*

## Jansen FH

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Fracheboud J, Plaisier ML, Doorne-Nagtegaal HJ van, Broeders MJ

Eur J Radiol. 2012 Sep;81(9):2189-94. Epub 2011 Sep 8

*Voor abstract zie: Radiologie - Brest Smalenburg V van*

*Impactfactor: 2.606*

## Klompshouwer E

### **ARM: axillary reverse mapping - the need for selection of patients**

Gobardhan PD, Wijsman JH, Dalen T van, Klompshouwer EG\*, Schelling GP van der, Los J, Voogd AC, Luiten EJ

Eur J Surg Oncol. 2012 Aug;38(8):657-61

**BACKGROUND:** Axillary reverse mapping (ARM) is a technique that discerns axillary lymphatic drainage of the arm from the breast. This study was performed to evaluate both the feasibility of this technique and the proportion of metastatic involvement of ARM-nodes.

**PATIENTS AND METHODS:** Patients with invasive breast cancer and an indication for axillary lymph node dissection (ALND) were enrolled in the study: patients with a tumor-positive sentinel lymph node (SLN(+)-group) and patients who had axillary metastases proven by preoperative cytology (CP-N(+)-group) were distinguished. ARM was performed in all patients by injecting blue dye. During surgery ARM-nodes were identified and removed first, followed by ALND.

**RESULTS:** Between October 2009 and June 2011 93 patients underwent ARM. There were 43 patients in the SLN(+)-group and 50 patients in the CP-N(+)-group. No significant differences in visualization rate of ARM-nodes between the groups (86 vs 94% respectively,  $P = 0.196$ ) were identified. In the SLN(+)-group none of the ARM-nodes contained metastases versus 11 patients (22%) in the CP-N(+)-group ( $P = 0.001$ ). Patients receiving neoadjuvant systemic therapy had a significantly lower risk of additional axillary lymph node metastases (24.6 vs 44.4%,  $P = 0.046$ ).

**DISCUSSION:** The ARM procedure is technically feasible with a high visualization rate. The proportion of patients with metastases in the ARM-nodes was significantly higher in patients

with proven axillary metastases than in patients with a positive SLN. Patients with SLN metastases appear to be good candidates for the ARM technique and possibly also patients with proven axillary metastases receiving neoadjuvant chemotherapy.

*Impactfactor: 2.499*

### **Klompenuouwer E**

#### **David procedure during a reoperation for ongoing chronic Q fever infection of an ascending aortic prosthesis**

Wegdam-Blans MC\*, Woorst JF ter\*, Klompenuouwer EG\*, Teijink JA\*

Eur J Cardiothorac Surg. 2012 Jul;42(1):e19-20. Epub 2012 May 24

*Voor abstract zie: Pamm - Wegdam-Blans MC*

*Impactfactor: 2.550*

### **Klompenuouwer E**

#### **Endovascular treatment of a hepatic artery pseudoaneurysm associated with gastrointestinal tract bleeding**

Vainas T\*, Klompenuouwer E\*, Duijm L\*, Tielbeek X\*, Teijink J\*

J Vasc Surg. 2012 Apr;55(4):1145-9. Epub 2012 Feb 25

*Voor abstract zie: Chirurgie - Vainas T*

*Impactfactor: 3.153*

### **Leer J van der**

#### **Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience**

Hurkmans CW\*, Dijckmans I\*, Reijnen M\*, Leer J van der \*, Vliet-Vroegindeweyj C van, Sangen M van der\*

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*Impactfactor: 5.580*

### **Nederend J**

#### **Impact of transition from analog screening mammography to digital screening mammography on screening outcome in The Netherlands: a population-based study**

Nederend J\*, Duijm LE\*, Louwman MW, Groenewoud JH, Donkers-van Rossum AB\*, Voogd AC

Ann Oncol. 2012 Dec;23(12):3098-103. Epub 2012 Jun 27

**Background** Full-field digital mammography (FFDM) has replaced screen-film mammography (SFM) in most breast screening programs. We analyzed the impact of this replacement on the screening outcome. **Patients and methods** The study population consisted of a consecutive series of 60 770 analog and 63 182 digital screens. During a 1-year follow-up, we collected breast imaging reports, biopsy results and surgical reports of all the referred women. **Results** The referral rate and the cancer detection rate at FFDM were, respectively, 3.0% and 6.60, compared with 1.5% ( $P < 0.001$ ) and 4.90 ( $P < 0.001$ ) at SFM. Positive predictive values of referral and percutaneous biopsies were lower at FFDM, respectively, 21.9% versus 31.6% ( $P < 0.001$ ) and 42.9% versus 62.8% ( $P < 0.001$ ). Per 1000 screened women, there was a significant increase with FFDM versus SFM in the detection rate of low- and intermediate-grade ductal carcinoma in situ (DCIS) (+0.7), invasive T1a-c cancers (+0.9), invasive ductal cancers (+0.9), low-grade (+1.1), node-negative invasive cancers (+1.2),

estrogen-receptor or progesterone-receptor-positive invasive cancers (respectively, +0.9 and +1.1) and Her2/Neu-negative (+0.8) invasive cancers. Mastectomy rates were stable at 1.1 per 1,000 screens.

Conclusions: FFDM significantly increased the referral rate and cancer detection rate, at the expense of a lower positive predictive value of referral and biopsy. Extra tumors detected at FFDM were mostly low-intermediate grade DCIS and smaller invasive tumors, of more favorable tumor characteristics. Mastectomy rates were not increased in the FFDM population, while increased over-diagnosis cannot be excluded.

*Impactfactor: 6.425*

## **Nederend J**

### **Trends in incidence and detection of advanced breast cancer at biennial screening mammography in The Netherlands: a population based study**

Nederend J\*, Duijm LE\*, Voogd AC, Groenewoud JH, Jansen FH\*, Louwman MW

Breast Cancer Res. 2012 Jan 9;14(1):R10

**INTRODUCTION:** The aims of this study were to determine trends in the incidence of advanced breast cancer at screening mammography and the potential of screening to reduce it.

**METHODS:** We included a consecutive series of 351,009 screening mammograms of 85,274 women aged 50-75 years, who underwent biennial screening at a Dutch breast screening region in the period 1997-2008. Two screening radiologists reviewed the screening mammograms of all advanced screen detected and advanced interval cancers and determined whether the advanced cancer (tumor >20 mm and/or lymph node positive tumor) had been visible at a previous screen. Interval cancers were breast cancers diagnosed in women after a negative screening examination (defined as no recommendation for referral) and before any subsequent screen. Patient and tumor characteristics were compared between women with advanced cancer and women with non-advanced cancer, including ductal carcinoma in situ.

**RESULTS:** A total of 1,771 screen detected cancers and 669 interval cancers were diagnosed in 2,440 women. Rates of advanced cancer remained stable over the 12-year period; the incidence of advanced screen-detected cancers fluctuated between 1.5 - 1.9 per 1,000 screened women (mean 1.6 per 1,000) and of advanced interval cancers between 0.8 - 1.6 per 1,000 screened women (mean 1.2 per 1,000). Of the 570 advanced screen-detected cancers, 106 (18.6%) were detected at initial screening; 265 (46.5%) cancers detected at subsequent screening had been radiologically occult at the previous screening mammogram, 88 (15.4%) had shown a minimal sign, and 111 (19.5%) had been missed. Corresponding figures for advanced interval cancers were 50.9% (216/424), 24.3% (103/424) and 25.1% (105/424), respectively. At multivariate analysis, women with a >30 months interval between the latest two screens had an increased risk of screen-detected advanced breast cancer (OR 1.63, 95%CI: 1.07-2.48) and hormone replacement therapy increased the risk of advanced disease among interval cancers (OR 3.04, 95%CI: 1.22-7.53).

**CONCLUSION:** We observed no decline in the risk of advanced breast cancer during 12 years of biennial screening mammography. The majority of these cancers could not have been prevented through earlier detection at screening.

*Impactfactor: 5.245*

**Reijnen M**

**Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience**

Hurkmans CW\*, Dijckmans I\*, Reijnen M\*, Leer J van der \*, Vliet-Vroegindeweyj C van, Sangen M van der\*

Radiother Oncol. 2012 May;103(2):183-7. Epub 2012 Jan 24

*Voor abstract zie: Klinische fysica- Hurkmans CW*

*Impactfactor: 5.580*

**Setz-Pels W**

**Characteristics and screening outcome of women referred twice at screening mammography**

Setz-Pels W\*, Duijm LE\*, Louwman MW, Roumen RM, Jansen FH\*, Voogd AC

Eur Radiol. 2012 Dec;22(12):2624-32. Epub 2012 Jun 13

OBJECTIVES: To determine the characteristics and screening outcome of women referred twice at screening mammography.

METHODS: We included 424,703 consecutive screening mammograms and collected imaging, biopsy and surgery reports of women with screen-detected breast cancer. Review of screening mammograms was performed to determine whether or not an initial and second referral comprised the same lesion.

RESULTS: The overall positive predictive value of referral for cancer was 38.6% (95% CI 37.3-39.8%). Of 147 (2.6%) women referred twice, 86 had been referred for a different lesion at second referral and 32 of these proved malignant (37.2%, 95% CI 27.0-47.4%). Sixty-one women had been referred twice for the same lesion, of which 22 proved malignant (36.1%, 95% CI 24.1-48.0%). Characteristics of these women were comparable to women with cancer diagnosed after first referral. Compared with women without cancer at second referral for the same lesion, women with cancer more frequently showed suspicious densities at screening mammography (86.4% vs 53.8%, P referral had less frequently included biopsy (22.7% vs 61.5%, P

CONCLUSIONS: Cancer risk in women referred twice for the same lesion is similar to that observed in women referred once, or referred for a second time but for a different lesion.

KEY POINTS : " Cancer risk was 36% for lesions referred twice at screening mammography " The cancer risk was similar for lesions referred only once at screening " Densities at first referral were associated with increased cancer risk at second referral " No biopsy at first referral was associated with increased cancer risk at second referral " Patient and tumour characteristics were similar for women with and without diagnostic delay.

*Impactfactor: 3.222*

**Setz-Pels W**

**Malpractice claims following screening mammography in the Netherlands**

Breest Smalenburg V van\*, Setz-Pels W\*, Groenewoud JH, Voogd AC, Jansen FH\*, Louwman MW, Tielbeek AV\*, Duijm LE\*

Int J Cancer. 2012 Sep 15;131(6):1360-6. Epub 2012 Jan 11

*Voor abstract zie: Radiologie - Breest Smalenburg V van*

*Impactfactor: 5.444*

**Tielbeek AV**

**Endovascular treatment of a hepatic artery pseudoaneurysm associated with gastrointestinal tract bleeding**

Vainas T\*, Klompenhouwer E\*, Duijm L\*, Tielbeek X\*, Teijink J\*

J Vasc Surg. 2012 Apr;55(4):1145-9. Epub 2012 Feb 25

*Voor abstract zie: Chirurgie - Vainas T*

*Impactfactor: 3.153*

**Tielbeek AV**

**Malpractice claims following screening mammography in the Netherlands**

Breest Smalenburg V van\*, Setz-Pels W\*, Groenewoud JH, Voogd AC, Jansen FH\*, Louwman MW, Tielbeek AV\*, Duijm LE\*

Int J Cancer. 2012 Sep 15;131(6):1360-6. Epub 2012 Jan 11

*Voor abstract zie: Radiologie - Breest Smalenburg V van*

*Impactfactor: 5.444*

\* = *Werkzaam in het Catharina Ziekenhuis*



# Radiotherapie

## **Berg HA van den**

### **Health related quality of life and symptoms after pelvic lymphadenectomy or radiotherapy vs. no adjuvant regional treatment in early-stage endometrial carcinoma: A large population-based study**

Poll-Franse LV van de, Pijnenborg JM, Boll D, Vos MC, Berg H van den\*, Lybeert ML\*, Winter K de, Kruitwagen RF

Gynecol Oncol. 2012 Oct;127(1):153-60. Epub 2012 Jun 13

**OBJECTIVES:** Routine lymphadenectomy (LA) in early stage endometrial cancer does not improve survival. However, in the absence of lymph node metastasis, radiotherapy (RT) could be withheld and hence could result in less morbidity. Our aim was to evaluate health related quality of life (HRQL) in endometrial cancer survivors that received routine pelvic LA without RT compared to no LA, but RT in the presence of risk factors.

**METHODS:** Stage I-II endometrial cancer survivors diagnosed between 1999 and 2007 were selected from the Eindhoven Cancer Registry. Survivors completed the SF-36 and the EORTC-QLQ-EN24. ANCOVA and multiple linear regression analyses were applied.

**RESULTS:** 742 (77%) of the endometrial cancer survivors returned a completed questionnaire. 377 (51%) had received no LA nor RT (LA-RT-), 198 (27%) had received LA+RT-, 153 (21%) LA-RT+ and 14 patients (2%) had received both. LA+ women reported as higher lymphedema symptom scores (25 vs. 20,  $p=0.04$ ). Women who were treated with RT reported higher gastrointestinal symptom scores vs. those who did not (23 vs. 16,  $p=0.04$ ). HRQL scales were comparable between all four treatment groups.

**CONCLUSION:** Despite distinct symptom patterns among women who received LA or RT, no clinically relevant differences in HRQL were observed when compared to women not receiving adjuvant therapy. Using LA to tailor adjuvant pelvic radiotherapy and prevent overtreatment in low-risk patients cannot be recommended.

*Impactfactor: 3.888*

## **Lybeert ML**

### **Brachytherapy after external beam radiotherapy and limited surgery preserves bladders for patients with solitary pT1-pT3 bladder tumors**

Koning CC, Blank LE, Koedooder C, van Os RM, van de Kar M, Jansen E, Battermann JJ, Beijert M, Gernaat C, Herpen KA van, Hoekstra C, Horenblas S, Jobsen JJ, Krol AD, Lybeert ML\*, Onna IE van, Pelger RC, Poortmans P, Pos FJ, Steen-Banasik E van der, Slot A, Visser A, Pieters BR

Ann Oncol. 2012 Nov;23(11):2948-53. Epub 2012 Jun 19

**Background:** Several French, Belgian and Dutch radiation oncologists have reported good results with the combination of limited surgery after external beam radiotherapy (EBRT) followed by brachytherapy in early-stage muscle-invasive bladder cancer. Patients and Methods Data from 12 of 13 departments which are using this approach have been collected retrospectively, in a multicenter database, resulting in 1040 patients: 811 males and 229 females with a median age of 66 years, range 28-92 years.

**Results:** were analyzed according to tumor stage and diameter, histology grade, age and brachytherapy technique, continuous low-dose rate (CLDR) and pulsed dose rate (PDR). Results At 1, 3 and 5 years, the local recurrence-free probability was 91%, 80% and 75%, metastasis-free probability was 91%, 80% and 74%, disease-free probability was 85%, 68% and 61% and overall survival probability was 91%, 74% and 62%, respectively. The differences in the outcome between the contributing departments were small. After multivariate analysis, the only factor influencing the local control rate was the brachytherapy

technique. Toxicity consisted mainly of 24 fistula, 144 ulcers/necroses and 93 other types.  
Conclusions: EBRT followed by brachytherapy, combined with limited surgery, offers excellent results in terms of bladder sparing for selected groups of patients suffering from bladder cancer.

*Impactfactor: 6.425*

### **Lybeert ML**

#### **Endometrial cancer survivors are unsatisfied with received information about diagnosis, treatment and follow-up: A study from the population-based PROFILES registry**

Nicolaije KA, Husson O, Ezendam NP, Vos MC, Kruitwagen RF, Lybeert ML\*,  
Poll-Franse LV van de

Patient Educ Couns. 2012 Sep;88(3):427-35. Epub 2012 Jun 1

**OBJECTIVE:** To evaluate perceived level of and satisfaction with information received by endometrial cancer survivors, and to identify associations with socio-demographic and clinical characteristics.

**METHODS:** All patients diagnosed with endometrial cancer between 1998 and 2007, registered in the Eindhoven Cancer Registry, received a questionnaire including EORTC-QLQ-INFO25.

**RESULTS:** Seventy-seven percent responded (n=742). Most patients indicated receiving quite a bit information about their disease and medical tests. However, most patients were not (54%) or a little (24%) informed about the cause of their disease, and possible side effects (36%; 27%). Especially information about additional help, rehabilitation, psychological assistance, and expected results on social and sexual life was lacking. Five percent was not or a little (36%) satisfied. Four percent found the information not or a little (35%) helpful. Fifteen percent preferred more information. Younger age, more recent diagnosis, radiotherapy, absence of comorbidities, having a partner, having received written information, and higher educational level were associated with higher perceived information receipt.

**CONCLUSION:** Many endometrial cancer survivors are unsatisfied with received information. Several areas of information provision are experienced as insufficient.

**PRACTICE IMPLICATIONS:** More patient-tailored information is probably needed to provide optimal information. Implementation of Survivorship Care Plans might be a way to achieve this.

*Impactfactor: 2.305*

### **Lybeert ML**

#### **Health related quality of life and symptoms after pelvic lymphadenectomy or radiotherapy vs. no adjuvant regional treatment in early-stage endometrial carcinoma: A large population-based study**

Poll-Franse LV van de, Pijnenborg JM, Boll D, Vos MC, Berg H van den\*, Lybeert ML\*,  
Winter K de, Kruitwagen RF

Gynecol Oncol. 2012 Oct;127(1):153-60. Epub 2012 Jun 13

*Voor abstract zie: Radiotherapie – Berg HA van den*

*Impactfactor: 3.888*

**Lybeert ML**

**Mapping use of radiotherapy for patients with non-small cell lung cancer in the Netherlands between 1997 and 2008**

Koning CC, Aarts MJ, Struikmans H, Poortmans PM, Lybeert ML\*, Jobsen JJ, Coebergh JW, Janssen-Heijnen ML, Visser O, Louwman WJ, Burgers JA

Clin Oncol (R Coll Radiol). 2012 Mar;24(2):e46-53. Epub 2011 Jul 22

AIM: After the publication of several reports that the utilisation rate of radiotherapy for patients with nonsmall cell lung cancer (NSCLC) varies for both medical and non-medical reasons, the utilisation of radiotherapy was studied in four regions in the Netherlands.

MATERIALS AND METHODS: Data from 1997-2008 were collected from the population-based cancer registries of four comprehensive cancer centres ('regions'), which represent about half of the Dutch population, resulting in 24 185 non-metastatic patients with NSCLC. Treatment had to be started or planned within 6 months of diagnosis. We evaluated the utilisation of radiotherapy according to age, gender and period for each region.

RESULTS: The utilisation of radiotherapy alone decreased over time (from 35 to 19%), whereas the utilisation of radiotherapy in combination with chemotherapy increased (from 5 to 19%). The total utilisation rate remained rather stable at about 40%. The differences between the four regions remained in general no more than 15%. Elderly patients with stage I and II disease had increased odds of receiving radiotherapy (e 75 versus <50 years: odds ratio 2.6, 95% confidence interval 2.0-3.3, whereas this was the opposite for patients with stage III disease: odds ratio 0.5, 95% confidence interval 0.4-0.6). For 17-24% of all patients, especially the elderly, best supportive care was applied.

CONCLUSIONS: In the Netherlands, with good accessibility to medical care and well-implemented national guidelines, variation between the four regions is limited for the treatment of non-metastatic NSCLC with radiotherapy.

*Impactfactor: 2.072*

**Lybeert ML**

**Use of primary radiotherapy for rectal cancer in the Netherlands between 1997 and 2008: A population-based study**

Jobsen JJ, Aarts MJ, Siesling S, Klaase J, Louwman WJ, Poortmans PM, Lybeert ML\*, Koning CC, Struikmans H, Coebergh JW

Clin Oncol (R Coll Radiol). 2012 Feb;24(1):e1-8. Epub 2011 Oct 2

AIMS: To describe variation in the utilisation rates of primary radiotherapy for patients with rectal cancer in the Netherlands, focusing on time trends and age effects.

MATERIALS AND METHODS: Data on primary non-metastatic rectal cancer were derived from the population-based cancer registries of four comprehensive cancer centres (regions) in the Netherlands (1997-2008, n=13,055).

RESULTS: An increase in the utilisation rate was noted for the four regions, from 37-46% in 1997 to 66-76% in 2008, for both genders. This increase was found predominately for preoperative radiotherapy (from 13-31% to 58-67%) and (unsurprisingly) was most pronounced for stage T2-3 patients (from 9-27% to 68-80%). The probability of receiving radiotherapy decreased with age: the odds of receiving preoperative radiotherapy was reduced in patients aged 65 years and older, as well as the odds of receiving postoperative radiotherapy in those aged 75 years and older, which remained significant after adjustment for stage, gender and region. Regional differences persisted in multivariable analyses, i.e. the odds of receiving preoperative radiotherapy was reduced in two regions: odds ratio: 0.4 (95% confidence interval: 0.4-0.5) and 0.7 (0.6-0.8). The odds of receiving postoperative

radiotherapy was significantly increased in these regions [odds ratio: 2.6 (2.2-3.2) and 1.6 (1.3-1.9), respectively] and reduced in another [odds ratio 0.8 (0.6-0.96)].

**CONCLUSIONS:** The utilisation rate of radiotherapy for rectal cancer increased significantly over time, particularly for preoperative radiotherapy and was most pronounced for T2-3 patients. Due to national multidisciplinary treatment guidelines, regional differences became limited in recent years after adjustment for age and stage of the disease. A low utilisation rate of radiotherapy was seen in women and elderly patients.

*Impactfactor: 2.072*

## **Martijn H**

### **Focus on extralevator perineal dissection in supine position for low Rectal Cancer Has Led to Better Quality of Surgery**

Martijnse IS\*, Dudink RL\*, West NP, Wasowicz D,\* Nieuwenhuijzen GA\*, Lijnschoten I van\*, Martijn H\*, Lemmens VE, Velde CJ van de, Nagtegaal ID, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Mar;19(3):786-93. Epub 2011 Aug 23

*Voor abstract zie: Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Martijn H**

### **Higher prevalence of sexual dysfunction in colon and rectal cancer survivors compared with the normative population: A population-based study**

Oudsten BL den, Traa MJ, Thong MS, Martijn H\*, Hingh IH de \*, Bosscha K, Poll-Franse LV van de

Eur J Cancer. 2012 Nov;48(17):3161-70. Epub 2012 May 17

**BACKGROUND:** To compare colorectal cancer survivors with a normative population regarding erectile dysfunction, ejaculation problems, dyspareunia, dry vagina, sexual functioning (SF) and enjoyment (SE). In addition, the sociodemographic, clinical and psychological correlates of (dys)function in survivors are examined.

**PATIENTS AND METHODS:** The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-CR38 sexuality subscales were completed by survivors (n=1371; response rate 82%), of which 1359 received surgical treatment and were included in the analysis. The normative population consisted of 400 participants (response rate 78%).

**RESULTS:** Erectile problems were more often present in rectal cancer (54%) than colon cancer survivors (25%) and the normative population (27%; p<.0001). They also had more ejaculation problems (68%) than colon cancer survivors (47%; p<.001). Dry vagina was common in colon (28%) and rectal cancer survivors (35%), while the normative population scored lower (5%; p=.003). In addition, colon (9%) and rectal cancer survivors (30%) experienced more pain during intercourse than the normative population (0%; p=.001). SE for men was similar across groups, while women with colorectal cancer reported lower scores than the normative population. Higher age, being a woman, not having a partner, a low educational level, rectal cancer, depressive symptoms and fatigue were associated with lower SF. Lower SE was associated with higher age and being a woman, depressive symptoms and cardiovascular disease.

**CONCLUSION:** SF was deteriorated in both sexes after cancer, which affected women's SE negatively. Attention towards sexual (dys)function in colorectal cancer survivors is needed.

*Impactfactor: 1.171*

## **Martijn H**

### **T3+ and T4 Rectal Cancer Patients Seem to Benefit From the Addition of Oxaliplatin to the Neoadjuvant Chemoradiation Regimen**

Martijnse IS\*, Dudink RL\*, Kusters M\*, Vermeer TA\*, West NP, Nieuwenhuijzen GA\*, Lijnschoten I van \*, Martijn H\*, Creemers GJ\*, Lemmens VE, Velde CJ van de, Sebag-Montefiore D, Glynne-Jones R, Quirke P, Rutten HJ\*

Ann Surg Oncol. 2012 Feb;19(2):392-401. Epub 2011 Jul 27

Voor abstract zie: *Chirurgie - Martijnse IS*

*Impactfactor: 4.166*

## **Meijer GJ**

### **High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers**

Meijer GJ\*, Toorn PP van der, Bal M\*, Schuring D\*, Weterings J\*, Wildt M de \*

Radiother Oncol. 2012 Sep 27. pii: S0167-8140(12)00362-3

**PURPOSE:** To increase local control and decrease side effects for urinary bladder cancer patients by integrating a library planning procedure with image guidance using lipiodol markers.

**METHODS AND MATERIALS:** Twenty patients with T2-T4N0M0 grade 2-3 invasive bladder carcinoma were treated according to an online adaptive protocol. Initially, the gross tumour volume (GTV) was demarcated during cystoscopy by injecting several drops of lipiodol in the submucosa around the tumour. Subsequently two CT scans were acquired with a full bladder and a voided bladder. On both scans, the boost volume (GTV) and the low-risk bladder volume were delineated. Using an interpolation tool, six concomitant boost IMRT plans with increasing bladder volumes were generated. For each fraction the procedure at the treatment unit was as follows: Firstly, a ConeBeam-CT was acquired and based on the amount of bladder filling the best fitting bladder contours and corresponding GTV and IMRT plans were selected. Secondly, the lipiodol markers were registered using the corresponding GTV contours and it was verified that the corresponding 95%-isodose surface covered the entire bladder. Finally, an online setup correction was applied based on this registration and the corresponding treatment plan was irradiated.

**RESULTS:** The lipiodol markers were very useful in outlining the GTV at the planning CT and for daily setup correction. While the patients strived for a full bladder filling at time of the treatment, this was seldom accomplished. Due to our protocol an appropriate plan with adequate coverage of the PTV and without excessive dose to healthy tissue was delivered every day. The treatment was very well tolerated by all patients. At the end of the treatment no grade 3 urinary or gastro-intestinal toxicity was observed. After a median follow-up of 28months two local relapses occurred.

**CONCLUSION:** Using the library planning approach combined with online image guidance using lipiodol markers, we were able to deliver a highly conformal dose distribution to all bladder cancer patients achieving promising clinical results.

*Impactfactor: 5.580*

**Sangen MJ van der**

**Adaptive radiation therapy for breast IMRT-simultaneously integrated boost: Three-year clinical experience**

Hurkmans CW\*, Dijckmans I\*, Reijnen M\*, Leer J van der \*, Vliet-Vroegindewei C van, Sangen M van der\*

Radiother Oncol. 2012 May;103(2):183-7. Epub 2012 Jan 24

*Voor abstract zie: Klinische fysica- Hurkmans CW*

*Impactfactor: 5.580*

**Sangen MJ van der**

**Histological type is not an independent prognostic factor for the risk pattern of breast cancer recurrences**

Kwast AB, Groothuis-Oudshoorn KC, Grandjean I, Ho VK, Voogd AC, Menke-Pluymers MB, Sangen MJ van der\*, Tjan-Heijnen VC, Kiemeney LA, Siesling S

Breast Cancer Res Treat. 2012 Aug;135(1):271-80

Invasive lobular breast cancer (ILC) is less common than invasive ductal breast cancer (IDC) and appears to have a distinct biology. Inconsistent findings regarding disease-free survival (DFS) are probably due to the fact that histologic type is related to hormone receptor status. This study aims to determine whether the type of the primary breast cancer histology is an independent prognostic factor for DFS, the risk pattern of loco-regional recurrences and distant metastases (DM), and whether it is a prognostic factor for the site of DM. All Dutch women diagnosed between 2003 and 2005 with ILC (n = 2,949) or IDC (n = 22,378) were selected from the Netherlands Cancer Registry. DFS was assessed using proportional hazard regression analysis. Compared to patients with IDC, those with ILC were significantly older and more likely to have more than three positive lymph nodes and have larger, better differentiated, more multifocal, and hormone receptor positive tumors (all P < 0.001). ILC was more likely to metastasize to the gastrointestinal organs and bones and less likely to the lung, central nervous system, and lymph nodes. Within the ER+PR+ and ER+PR- subgroups ILC was still more likely to metastasize to gastrointestinal organs and less likely to the lung. The timing of recurrence was correlated to hormone receptor status, independent of histological type. Highest risks were observed among ER-PR- patients within 2 years of surgery. Multivariable analysis showed that histological type is not an independent significant prognostic factor of DFS for the first 3 years post-surgery and thereafter (<3 years HR 0.91, 95 % CI 0.78-1.06, >3 years HR 1.07, 95 % CI 0.88-1.30). Histological type should not be considered an important prognostic factor for the risk and risk pattern of recurrences.

*Impactfactor: 5.245*

**Sangen MJ van der**

**Hormone Treatment without Surgery for Patients Aged 75 Years or Older with Operable Breast Cancer**

Wink CJ, Woensdregt K\*, Nieuwenhuijzen GA\*, Sangen MJ van der \*,

Hutschemaekers S, Roukema JA, Tjan-Heijnen VC, Voogd AC

Annals of Surgical Oncology 2012 Apr;19(4):1185-91. Epub 2011 Oct 27

*Voor abstract zie: Chirurgie - Woensdregt K*

*Impactfactor: 4.166*

### **Sangen MJ van der**

#### **Preoperative chemoradiotherapy for esophageal or junctional cancer**

Hagen P van, Hulshof MC, Lanschot JJ van, Steyerberg EW, Berge Henegouwen MI van, Wijnhoven BP, Richel DJ, Nieuwenhuijzen GA\*, Hospers GA, Bonenkamp JJ, Cuesta MA, Blaisse RJ, Busch OR, Kate FJ ten, Creemers GJ\*, Punt CJ, Plukker JT, Verheul HM, Spillenaar Bilgen EJ, Dekken H van, Sangen MJ van der \*, Rozema T, Biermann K, Beukema JC, Piet AH, Rij CM van, Reinders JG, Tilanus HW, Gaast A van der; CROSS Group

N Engl J Med. 2012 May 31;366(22):2074-84

Voor abstract zie: Chirurgie - Nieuwenhuijzen GA

Impactfactor: 53.298

### **Sangen MJ van der**

#### **Reducing interobserver variation of boost-CTV delineation in breast conserving radiation therapy using a pre-operative CT and delineation guidelines**

Boersma LJ, Janssen T, Elkhuzen PH, Poortmans P, Sangen M van der \*, Scholten AN, Hanbeukers B, Duppen JC, Hurkmans C\*, Vliet C van

Radiother Oncol. 2012 May;103(2):178-82. Epub 2012 Jan 20

AIMS: To investigate whether using a pre-operative CT scan (Preop-CT) (1) decreases interobserver variation of boost-CTV delineation in breast conserving therapy (BCT), and (2) influences the size of the delineated volumes.

PATIENTS AND METHODS: Thirty cT1-2N0-1 breast cancer patients underwent a CT-scan in radiation treatment position, prior to and after lumpectomy. Five observers delineated a boost-CTV, both with and without access to the Preop-CT. For each patient and for each observer pair, the conformity index (CI) and the distance between the centres of mass (COMd) for both boost volumes were calculated. In addition, all delineated volumes including the standard deviation (SD) with respect to the median delineation were calculated.

RESULTS: Using a Preop-CT reduced the mean COMd of the boost-CTV from 1.1cm to 1.0cm ( $p < 0.001$ ). No effect was seen on the CI, but the boost-CTV volume reduced from 42cc to 36cc ( $p = 0.005$ ), implying a reduction of interobserver variation. We saw no significant change in the SD.

CONCLUSION: Use of a Preop-CT in BCT results in a modest but statistically significant reduction in interobserver variation of the boost-CTV delineations and in a significant reduction in the boost-CTV volume.

Impactfactor: 5.580

### **Sangen MJ van der**

#### **Small but significant socioeconomic inequalities in axillary staging and treatment of breast cancer in the Netherlands**

Aarts MJ, Hamelinck VC, Bastiaannet E, Coebergh JW, Liefers GJ, Voogd AC, Sangen MJ van der\*, Louwman WJ

Br J Cancer. 2012 Jun 26;107(1):12-7

BACKGROUND: The use of sentinel node biopsy (SNB), lymph node dissection, breast-conserving surgery, radiotherapy, chemotherapy and hormonal treatment for breast cancer was evaluated in relation to socioeconomic status (SES) in the Netherlands, where access to care was assumed to be equal.

**METHODS:** Female breast cancer patients diagnosed between 1994 and 2008 were selected from the nationwide population-based Netherlands Cancer Registry (N=176 505). Socioeconomic status was assessed based on income, employment and education at postal code level. Multivariable models included age, year of diagnosis and stage.

**RESULTS:** Sentinel node biopsy was less often applied in high-SES patients (multivariable analyses, < 49 years: odds ratio (OR) 0.70 (95% CI: 0.56-0.89); 50-75 years: 0.85 (0.73-0.99)). Additionally, lymph node dissection was less common in low-SES patients aged e 76 years (OR 1.34 (0.95-1.89)). Socioeconomic status-related differences in treatment were only significant in the age group 50-75 years. High-SES women with stage T1-2 were more likely to undergo breast-conserving surgery (+radiotherapy) (OR 1.15 (1.09-1.22) and OR 1.16 (1.09-1.22), respectively). Chemotherapy use among node-positive patients was higher in the high-SES group, but was not significant in multivariable analysis. Hormonal therapy was not related to SES.

**CONCLUSION:** Small but significant differences were observed in the use of SNB, lymph node dissection and breast-conserving surgery according to SES in Dutch breast cancer patients despite assumed equal access to health care.

*Impactfactor: 4.023*

### **Sangen MJ van der**

#### **SUBMIT: Systemic therapy with or without up front surgery of the primary tumor in breast cancer patients with distant metastases at initial presentation**

Ruiterkamp J, Voogd AC, Tjan-Heijnen VC, Bosscha K, Linden YM van der, Rutgers EJ, Boven E, Sangen MJ van der\*, Ernst MF; Dutch Breast Cancer Trialists' Group (BOOG) *BMC Surg.* 2012 Apr 2;12:5

*Impactfactor: 1.333*

### **Toorn PP van der**

#### **High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers**

Meijer GJ\*, Toorn PP van der\*, Bal M, Schuring D\*, Weterings J\*, Wildt M de\* *Radiother Oncol.* 2012 Sep 27. pii: S0167-8140(12)00362-3

*Voor abstract zie: Radiotherapie - Meijer GJ*

*Impactfactor: 5.580*

### **Weterings J**

#### **High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers**

Meijer GJ\*, Toorn PP van der\*, Bal M\*, Schuring D\*, Weterings J\*, Wildt M de\* *Radiother Oncol.* 2012 Sep 27. pii: S0167-8140(12)00362-3.

*Voor abstract zie: Radiotherapie - Meijer GJ*

*Impactfactor: 5.580*

\* = Werkzaam in het Catharina Ziekenhuis



## **Spoedeisende Hulp**

## **Buenen N<sup>∞</sup>**

### **Compensatory activity in the extrastriate body area of Parkinson's disease patients**

Nuenen BF van\*, Helmich RC, Buenen N\*, Warrenburg BP van de, Bloem BR, Toni I  
J Neurosci. 2012 Jul 11;32(28):9546-53

*Voor abstract zie: Neurologie - Nuenen BF van*

*Impactfactor: 7.115*

## **Thijssen WA**

### **Emergency departments in The Netherlands**

Thijssen WA\*, Giesen PH, Wensing M

Emerg Med J. 2012 Jan;29(1):6-9. Epub 2011 Oct 28

Emergency medicine in The Netherlands is faced with an increasing interest by politicians and stakeholders in health care. This is due to crowding, increasing costs, criticism of the quality of emergency care, restructuring of out-of-hours services in primary care and the introduction of a training programme for emergency physicians in 2000. A comprehensive search was conducted of published research, policy reports and updated Dutch websites on acute care. Publications were included in this review if these referred to emergency care, including emergency departments (ED), general practitioner (GP) cooperatives and emergency medical services in The Netherlands and were written in English or Dutch. The literature search identified 14 eligible papers. The manual search identified 11 additional papers. Seven reports and two PhD theses were also included. Given the lack of relevant empirical research the review was liberal in its inclusion, but the analysis focused on research when available. ED in The Netherlands are in different stages of development. However, it is obvious that the presence of emergency physicians is increasing and more ED will be staffed by emergency physicians. Although this seems an important step, it does not necessarily imply a good position of the emergency physician in the ED. What the characteristics of the future patient of the Dutch ED will be is dependent on the development of different ED levels of care and GP cooperatives. The lack of empirical research also points out the need for research on quality of care in Dutch ED.

*Impactfactor: 1.439*

\* = *Werkzaam in het Catharina Ziekenhuis*

<sup>∞</sup> = *Ten tijde van publicatie werkzaam bij: Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen.*

**Urologie**

## **Brinkman WM**

### **Single versus multimodality training basic laparoscopic skills**

Brinkman WM\*, Havermans SY\*, Buzink SN, Botden SM, Jakimowicz JJ\*, Schoot BC\*

Surg Endosc. 2012 Aug;26(8):2172-8. Epub 2012 Feb 21

**INTRODUCTION:** Even though literature provides compelling evidence of the value of simulators for training of basic laparoscopic skills, the best way to incorporate them into a surgical curriculum is unclear. This study compares the training outcome of single modality training with multimodality training of basic laparoscopic skills.

**METHODS:** Thirty-six medical students without laparoscopic experience performed six training sessions of 45 min each, one per day, in which four different basic tasks were trained. Participants in the singlemodality group (S) (n = 18) practiced solely on a virtual reality (VR) simulator. Participants in the multimodality group (M) (n = 18) practiced on the same VR simulator (2x), a box trainer (2x), and an augmented reality simulator (2x). All participants performed a pre-test and post-test on the VR simulator (the four basic tasks + one additional basic task). Halfway through the training protocol, both groups performed a salpingectomy on the VR simulator as interim test.

**RESULTS:** Both groups improved their performance significantly (Wilcoxon signed-rank,  $P < 0.05$ ). The performances of group S and group M in the additional basic task and the salpingectomy did not differ significantly (Mann-Whitney U test,  $P > 0.05$ ). Group S performed the four basic tasks in the post-test on the VR faster than group M ( $P < 0.05$ ), which can be explained by the fact that they were much more familiar with these tasks.

**CONCLUSIONS:** Training of basic laparoscopic tasks on single or multiple modalities does not result in different training outcome. Both training methods seem appropriate for the attainment of basic laparoscopic skills in future curricula.

*Impactfactor: 4.013*

## **Hendriks AJ**

### **Designing simulator-based training: An approach integrating cognitive task analysis and four-component instructional design**

Tjiam IM\*, Schout BM, Hendriks AJ\*, Scherpbier AJ, Witjes JA, Merriënboer JJ van  
Med Teach. 2012;34(10):e698-707

*Voor abstract zie: Urologie - Tjiam IM*

*Impactfactor: 1.217*

## **Hendriks AJ**

### **Program for laparoscopic urologic skills: a newly developed and validated educational program**

Tjiam IM\*, Persoon MC\*, Hendriks AJ\*, Muijtjens AM, Witjes JA, Scherpbier AJ

Urology. 2012 Apr;79(4):815-20

*Voor abstract zie: Urologie - Tjiam IM*

*Impactfactor: 2.428*

**Koldewijn EL**

**Wat te doen als pillen niet werken bij urge-incontinentie? Nog veel vragen en onduidelijkheden [What to do if pills do not work for urge incontinence--still many questions and ambiguities]**

Koldewijn EL\*

Ned Tijdschr Geneeskd. 2012;156(33):A5099

Bladder training and antimuscarinics are first-line treatments for the symptoms of an overactive bladder. Unfortunately, many patients stop using drugs due to undesirable effects or limited efficacy. The paper by Smits et al. contains a summarisation of various neuromodulation treatments that can be offered to patients after first-line treatments have failed, e.g. sacral neuromodulation, posterior tibial nerve stimulation, pudendal neuromodulation and intravesical botulinum toxin A. An unambiguous treatment algorithm based on RCTs is lacking at this time; however, postulation of a patient's profile is possible. Research in the field of dysfunctional voiding should focus on comparing the different treatment options in order to create an algorithm based on science.

*Impactfactor: --*

**Persoon MC**

**Program for laparoscopic urologic skills: a newly developed and validated educational program**

Tjiam IM\*, Persoon MC\*, Hendriks AJ\*, Muijtjens AM, Witjes JA, Scherpbier AJ

Urology. 2012 Apr;79(4):815-20

*Voor abstract zie: Urologie - Tjiam IM*

*Impactfactor: 2.428*

**Tjiam IM**

**Designing simulator-based training: An approach integrating cognitive task analysis and four-component instructional design**

Tjiam IM\*, Schout BM, Hendriks AJ\*, Scherpbier AJ, Witjes JA, Merriënboer JJ van

Med Teach. 2012;34(10):e698-707

Most studies of simulator-based surgical skills training have focused on the acquisition of psychomotor skills, but surgical procedures are complex tasks requiring both psychomotor and cognitive skills. As skills training is modelled on expert performance consisting partly of unconscious automatic processes that experts are not always able to explicate, simulator developers should collaborate with educational experts and physicians in developing efficient and effective training programmes. This article presents an approach to designing simulator-based skill training comprising cognitive task analysis integrated with instructional design according to the four-component/instructional design model. This theory-driven approach is illustrated by a description of how it was used in the development of simulator-based training for the nephrostomy procedure.

*Impactfactor: 1.217*

## **Tjiam IM**

### **Program for laparoscopic urologic skills: a newly developed and validated educational program**

Tjiam IM\*, Persoon MC\*, Hendriks AJ\*, Muijtjens AM, Witjes JA, Scherpbier AJ

Urology. 2012 Apr;79(4):815-20

**OBJECTIVE:** To develop and evaluate a program for laparoscopic urologic skills (PLUS) to determine the face, content, and construct validation to achieve uniformity and standardization in training residents in urology.

**METHODS:** The PLUS consists of 5 basic laparoscopic tasks. Three tasks were abstracted from the Fundamentals of Laparoscopic Surgery program, and 2 additional tasks were developed under continuous evaluation by expert urologists. Fifty participants were recruited from different hospitals and performed the final PLUS training. They all completed a questionnaire after performance. Three outcome parameters were measured: performance quality, time, and dropped objects. The relationship between laparoscopic experience and the outcome parameters was investigated.

**RESULTS:** Of the 50 participants, 13 were students, 20 were residents, and 17 were urologists. Doublelog linear regression analysis for all 5 tasks showed a significant effect (effect size range 0.53-0.82;  $P < .0005$ ) for laparoscopic experience on performance time. Substantial correlations were found between experience and quality ratings (log-linear regression effect size 0.37;  $P = .012$ ) and the number of dropped objects (Spearman correlation effect size 0.49;  $P < .01$ ). The usefulness of the PLUS model as a training tool for basic laparoscopic skills was rated 4.55 on a scale from 1 (not useful) to 5 (useful) (standard deviation 0.58; range 3-5).

**CONCLUSION:** The results of the present study indicated the face, content, and construct validity for the PLUS. The training is considered appropriate for use as a primary training tool for an entry test or as part of a step-wise training program in which basic and procedural laparoscopic skills are integrated.

*Impactfactor: 2.428*

## **Wildt MJ de**

### **High precision bladder cancer irradiation by integrating a library planning procedure of 6 prospectively generated SIB IMRT plans with image guidance using lipiodol markers**

Meijer GJ\*, Toorn PP van der, Bal M\*, Schuring D\*, Weterings J\*, Wildt M de \*

Radiother Oncol. 2012 Sep 27. pii: S0167-8140(12)00362-3

*Voor abstract zie: Radiotherapie - Meijer GJ*

*Impactfactor: 5.580*

\* = *Werkzaam in het Catharina Ziekenhuis*

**Boeken**

## Anesthesiologie

Scheepers-Hoeks AM\*, Klijn F\*, Linden CM van der\*, Grouls RJ\*, Ackerman EW\*, Minderman N\*, Bergmans J, **Korsten HH\***

**Chapter 15: Clinical decision support systems for 'making it easy to do it right'.** – p. 324-335

In: Neonatal monitoring technologies : design for integrated solutions / Wei Chen, Sidarto Bambang Oetoma, Loe Feijs.

Hershey, PA : Medical Information Science Reference (IGI Global), 2012.

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**Dudink RL\***, **Kusters M\***, **Rutten HJ\***

**Which patients do benefit from extended resections in case of locally advanced rectal cancer?** - p. 275-290

In: Multidisciplinary management of rectal cancer: questions and answers / Valentini, Vincenzo; Schmoll, Hans-Joachim; Cornelis J. H. van de (Eds.)  
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**Laar EF van de**, Peil J

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**Promoties**

## **Cardiologie**

### **Vermeulen Windsant IC**

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Vermeulen Windsant, Iris Catharina

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## **Chirurgie**

### **Grootenboer N∞**

Gender differences in presentation of disease and clinical outcome after vascular surgery

Rotterdam : [s.n.], 2012

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*Copromotor: Sambeek MRHM van*

### **Klaver YL**

Peritoneal carcinomatosis from colorectal cancer : preclinical and clinical studies into surgical and medical treatment

[S.l. : s.n.], 2012

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*Copromotor: Hingh IHJT de*

## **Dermatologie**

### **Geer-Rutten S van der**

Disease management for chronic skin cancer

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*Copromotor: Krekels GAM*

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### **Cnossen TT∞**

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*Copromotor: Konings CJAM*

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### **Graat-Verboom, L**

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### **Utens CM**

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### **Maas-van Schaijk NM**

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[s.l. : s.n.], 2012

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## **Neurologie**

### **Nuenen BF van**

Cerebral reorganization in premotor parkinson

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## **Onderwijs & Onderzoek**

### **Pluyter JR**

Designing immersive surgical training against information technology-related overload in the operating room

[s.l. : s.n.], 2012

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*Promotor: Jakimowicz JJ*

## **Pamm**

### **Wulf MW**

Epidemiology of livestock-associated Methicillin resistant Staphylococcus aureus.

Mireille Wilhelmina Huberta Wulf\*

Epidemiology of Livestock-associated Methicillin resistant Staphylococcus aureus

[s.l. : s.n.], 2012

9789081867801

## **Urologie**

Persoon MC

Learning in urology : the influence of simulators and human factors

[s.l. : s.n.], 2012

9789461691828

*Co-promotor: Hendrikx AJ*

**Wetenschapsavond  
Catharina Ziekenhuis  
2012**

# Presentaties

## Algemeen Klinisch Laboratorium

### Deiman AL

#### Farmacogenetica in het CZE

Birgit Deiman, Rutger Nieuwenhuis, Volkher Scharnhorst, Nico Pijls

Achtergrond: Sinds kort is het mogelijk om in het laboratorium van het CZE farmacogenetica bepalingen uit te laten voeren.

Doelstelling: Aan de hand van retrospectieve en prospectieve studies wordt de toegevoegde waarde van farmacogenetica voor de patient op verschillende vakgebieden onderzocht.

Methode: Voor het aantonen van de variaties in het humane DNA wordt de real-time polymerase chain reaction methode gebruikt.

Resultaten en conclusies: Plavix is een plaatjes aggregatieremmer die voorgeschreven wordt aan patienten die een dotterbehandeling moeten ondergaan. Het gebruik van dit middel heeft het aantal gevallen van stenttrombose significant doen dalen. Plavix wordt als pro-drug ingenomen en moet door het CYP2C19 enzym worden omgezet in een actief metaboliet. Uit uitgebreide literatuur studies is gebleken dat bepaalde variaties in het CYP2C19 gen resulteren in plavix resistente wat resulteert in een significante verhoging van het aantal gevallen van stent-trombose. Sinds ruim een jaar worden alle patienten in het CZE die een dotterbehandeling moeten ondergaan preventief getest op variaties in het CYP2C19 gen. De resultaten van het eerst jaar laten zien dat plavix-resistente patienten aanzienlijk veel vaker terug komen in de kliniek voor een tweede dotter behandeling. Aan plavix-resistente patienten wordt momenteel een alternatief medicijn, prasugrel, voorgeschreven. In de psychiatrie heeft men juist te maken met de gevolgen van bijwerkingen van medicijnen. In een retrospectieve studie is gekeken of bijwerking kunnen worden verklaard op grond van variaties in de genen die betrokken zijn bij het metabolisme van de medicijnen. Aan de hand van een aantal casussen zal worden getoond dat dit voor sommige patienten inderdaad het geval is.

Vernieuwde elementen: Farmacogenetica is een nieuw vakgebied. Met moleculaire diagnostiek kan een genetisch profiel van de patiënt worden verkregen wat informatie geeft over de effectiviteit en verdraagzaamheid van medicijnen. Op grond van dit genetisch profiel kan gerichter een keuze gemaakt worden uit de medicijnen die voorhanden zijn.

## Cardiologie

### Schampaert S

#### Autoregulation of coronary blood flow in the isolated beating pig heart

S. Schampaert\*, M. van 't Veer\*, M.C.M. Rutten, S. van Tuijl, J. de Hart, F.N. van de Vosse, N.H.J. Pijls\*

Background: The isolated beating pig heart model is an accessible platform to investigate the coronary circulation in its truly morphologic and physiologic state, while allowing excellent control of the individual hemodynamic parameters. Moreover, the model is not categorized as animal experiment and decreases the necessity of scarifying large mammals for animal research. Ex vivo testing is therefore beneficial from a time, cost and ethical perspective. However, whether the coronary autoregulation is still intact is not known.

Purpose: To study the autoregulation of coronary blood flow in the working isolated beating pig heart in response to brief occlusions of the coronary artery, to step-wise changes in left ventricle loading conditions and contractile states, and to pharmacologic vasodilating stimuli.

Methods Six slaughterhouse pig hearts ( $473 \pm 40$  g) were isolated, prepared and connected to an external circulatory system. Through coronary reperfusion and controlled cardiac loading, physiological cardiac performance was achieved.

Results: The isolated beating pig heart was capable of generating flow patterns and pressure curves that closely mimic aortic and coronary in vivo flow and pressure. After release of a coronary occlusion, coronary blood flow rose rapidly to an equal (maximum) level as the flow during control beats (peak to basal ratio of approximately one), independent of the duration of occlusion. Moreover, a linear relation was found between coronary blood flow and coronary driving pressure for a wide variation of preload, afterload and contractility ( $R^2 = 0.94 \pm 0.03$ ,  $p < 0.001$ ). Zero flow pressure intercepts were estimated by extrapolation and found to vary between 10 and 32 mmHg. In addition, intracoronary administration of papaverine did not yield a transient increase in blood flow as it does in the in vivo coronary artery.

Conclusion: Together, this strongly indicates that the coronary circulation in the isolated beating pig heart is in a permanent state of maximum hyperemia, making the model excellently suitable for coronary physiology research in which steady-state hyperemia is paramount, such as studying fractional flow reserve, the most important intracoronary diagnostic technique in the human catheterization laboratory used for guiding revascularization procedures (European Society of Cardiology guidelines).

## Geriatric

### Linden CM van der

#### **Een elektronisch systeem om redenen van staken van medicatie vast te leggen en te waarschuwen bij herstart na bijwerking**

Carolien MJ van der Linden\*, Paul AF Jansen, Rob J van Marum, René JE Grouls\*,

Toine CG Egberts, Erik HM Korsten\*

Achtergrond: Uit eerder onderzoek bleek 27% van de middelen die eerder gestaakt werden vanwege een bijwerking opnieuw aan dezelfde patiënt voorgeschreven te worden (1). In een andere studie bleek bij 40% van gestaakte medicijnen geen reden van staken vastgelegd in het dossier (2).

Doelstelling: Ontwikkeling, implementatie en eerste resultaten van een elektronisch systeem om redenen van staken van medicatie vast te leggen en te bewaken op herstart na bijwerking.

Methode: Wij hebben met behulp van Gaston-software (3) een elektronisch systeem ontwikkeld waarmee artsen door middel van een pop-up-scherm redenen van staken vastleggen bij ieder klinisch gestaakt medicijn. Bij een mogelijke bijwerking als reden van staken wordt tevens een omschrijving van het verschijnsel, de ernst van de bijwerking en een advies bij eventuele represcriptie vastgelegd. Vervolgens waarschuwt dit systeem de voorschrijver wanneer een middel, dat eerder een bijwerking gaf, opnieuw wordt voorgeschreven. Het systeem is geïmplementeerd op een afdeling geriatric van 20 bedden en gedurende 11,4 maanden zijn data verzameld.

Resultaten: Gedurende 11,4 maanden werden 2228 geneesmiddelen gestaakt bij 403 opgenomen patiënten. Redenen van staken zijn in de tabel weergegeven.

Reden van staken	Aantal	Percentage
Niet langer geïndiceerd	1263	56,7%
Switch naar andere toedieningsvorm	294	13,2%
Palliatie	182	8,2%
Onvoldoende effect	145	6,5%
Mogelijk bijwerking of allergie	140	6,3%
Contraindicatie	53	2,4%
Interactie	7	0,3%
Anders	144	6,4%
Totaal	2228	100%

Meest voorkomende bijwerkingen waren nierfunctiestoornissen, elektrolytstoornissen en diarree. Twintig keer verscheen de waarschuwing voor opnieuw voorschrijven na een bijwerking. Het gegeven advies bij represcriptie was 19 keer *\_extra monitoring nodig\_*, dit advies werd 16 keer gevolgd. Het advies *\_middel niet meer voorschrijven\_* verscheen één keer en werd gevolgd.

Conclusies: Met dit systeem worden redenen van staken gedocumenteerd en volgt een waarschuwing bij opnieuw voorschrijven na een bijwerking. De gegeven adviezen werden in hoge mate gevolgd. Het systeem zal worden uitgerold naar meerdere afdelingen en gekoppeld worden aan de eerste lijn. Of dit systeem opnieuw optredende bijwerkingen kan voorkomen moet blijken uit vervolgonderzoek.

## Klinische Fysica

### Dries W

#### Een nieuwe infrastructuur voor research en innovatie: Het EuroCAT project

W.J.F. Dries\*, R. van de Bogaard, K. de Jaeger\*

Achtergrond: De klassieke strategie van de randomized controlled trial om tot beter inzicht te komen in factoren die de uitkomst van behandelingen bepalen werkt in de oncologie erg traag door een lage participatie van patiënten en lange follow-up tijden.

Doelstelling: Het gebruik van de digitale behandelgegevens en beelden, opgeslagen in bestaande ziekenhuissystemen, kan misschien wetenschap en individualisering van behandelingen sneller vooruit helpen. Software voor data mining, machine learning en beeldanalyse is hiervoor al beschikbaar. Een betere voorspelling van de uitkomst van verschillende behandelingen maakt het mogelijk om een betere keuze te maken tussen die mogelijke behandelingen en daarmee kunnen zowel gunstiger resultaten en als hogere kosteneffectiviteit worden bereikt. Dit werkveld wordt aangeduid met de term *\_Computer Aided Theragnostics\_*

Methode: De afdeling Radiotherapie van het CZE wil hieraan bijdragen door aan te haken bij het EuroCAT project van MAASTRO Clinic, samen met andere deelnemers uit Duitsland en België. Het Europees en regionaal gesubsidieerde project behelst het bouwen van de hiervoor nodige ICT infrastructuur en starten met onderzoek, in eerste instantie gericht op radiotherapie voor longkankerpatiënten. Een aparte database met niet-herleidbare gegevens wordt gebouwd en regelmatig via koppelingen met de klinische systemen geactualiseerd.

Resultaten en conclusies: Het project loopt tot oktober 2013, maar leidt al eerder tot beter inzicht in optimaal gebruik van onze klinische systemen voor registratie van gegevens en beelden. Het systeem lijkt ook bruikbaar voor onderzoek en innovatie binnen andere specialismen. Innovatieve aspecten zijn het direct gebruik van beelden en het vermijden van

privacy issues doordat de patiëntdata niet centraal opgeslagen worden maar binnen het deelnemende ziekenhuis blijven: niet de patiëntdata worden verspreid maar de applicaties.

## Urologie

### Berkers CH

#### How Useful and Realistic is the Symbionix TURP Simulator for Training Transurethral Prostate Resection Procedures?

I. Tjiam, C.H.J. Berkers, E.L. Koldewijn

**Purpose:** We evaluated the face and content validity (novices, residents and experts' opinions of realism and usefulness) and construct validity (performances of novices, residents and experts) of the TURP simulator (Symbionix and Virtamed, Beit Golan, Israel), a simulator for transurethral resection procedures, to assess the didactic value of the simulator in the training curriculum of residents.

**Material and Methods:** Between October 2011 and February 2012, students (n=22), residents (n=22) and experts (n=22) performed 2 complete TURP procedures on the VirtaMedTURP simulator. All participants rated simulator usefulness and realism on a 10-point scale (1: not at all useful/realistic, 10: very useful/realistic). The simulator measured performances by its metrics (resection time, amount of prostate and capsule resected, visuability, blood loss and amount of complications). Additionally, one observer checked the procedural steps using a validated checklist. Participants were classified as experts (more than 50 complete procedures performed), residents (1-50 complete procedures performed) or novices (no complete procedures performed).

**Results:** A total of 66 questionnaires were analysed. Mean general judgement (face and content) about the simulator was rated 7,4 (SD 1,07) on a ten-point scale. All participants qualified the VirtamedTURP simulator as a useful tool to learn TURP skills on. Haptic feedback scored a mean rate under 6,0 in all groups. Statistical analysis of the simulator's metrics (Kruskal Wallis test) showed significant faster resection time and less blood loss in experts and residents (construct). More experienced residents have better performances than less experienced residents.

**Conclusions:** Measured against criteria from other validation studies, VirtaMedTURP simulator's face and content validity appear to be moderately useful and realistic, but has a unsatisfactory score in haptic feedback. Construct validity is good for resection time and the amount of blood loss, but lacks in measuring visuability and cutting skills. With some modifications the VirtaMedTURP simulator can be a useful tool for residents TURP training.

*Beste presentatie wetenschapsavond Catharina ziekenhuis 2012*

## Posters

### Algemeen Klinisch Laboratorium

**Berkel M van**

#### **Interference of Howell-Jolly bodies in reticulocyte enumeration in splenectomysed patients**

Miranda van Berkel, Eveline Besselaar, Philip Kuijper and Volkher Scharnhorst

**Introduction:** Reticulocyte enumeration in peripheral blood is an important diagnosticum in the evaluation of erythropoiesis. In this case report, a splenectomysed patient with a marked reticulocytosis in combination with normal number of erythrocytes containing adequate haemoglobin content is presented. The erythrocytes of the patient contained a substantial number of Howell-Jolly bodies, which are RNA remnants in erythrocytes that are normally removed by the spleen. The patient's blood was analysed on three different automated haematology analysers. Each analyser displayed a different reticulocyte concentration, due to a dissimilar grade of interference of Howell-Jolly bodies in reticulocyte analysis.

**Methods:** Blood was collected in K3EDTA containing tubes (vacutainer 3688610, Becton Dickinson) and blood counts were measured within 6 hours on a Beckman Coulter LH 750, a Sysmex XE-5000 and a CellDyn Sapphire automatic haematology analyser. As a reference method, reticulocytes were manually counted after supravital Brilliant Cresyl Blue (BCB) staining.

**Results:** In the presence of Howell Jolly bodies, a strong discrepancy between automatic reticulocyte counting on three systems using different methods was observed. Beckman Coulter LH 750 automated counter produced a reticulocyte number of 49/nl, resembling the BCB staining and manual counting (54/nl). In contrast, both Sysmex XE-5000 and CellDyn Sapphire counted false elevated numbers of reticulocytes (94/nl and 377/nl respectively).

**Conclusion:** Overall, use of state-of-the-art haematology analysers may produce falsely elevated Reticulocyte numbers due to the presence of Howell-Jolly bodies or other nucleic acid remnants. Therefore, reticulocyte numbers in hyposplenic or splenectomysed patients should be interpreted with care.

## Apotheek

**Scheepers-Hoeks AM**

#### **Retrospective Cross Sectional Study to Determine the Prevalence and Incidence of Severe Hypo- and Hypercalcaemia in Hospitalized Patients**

J. de Vries\*, M. Kokkelink\*, A.T.M. Wasylewicz, A.M.J.W.Scheepers-Hoeks, A.M.

Harmsze, B. Bravenboer, R.J.E.Grouls

**Background:** Few data exist on the prevalence of hypo- and hypercalcaemia in a general hospital setting. Clinical rules incorporated in a clinical decision support system (CDSS) can provide useful epidemiological data.<sup>1</sup>

**Aim:** To identify the prevalence, incidence and causes of severe hypo- and hypercalcaemia and to quantify the percentage of these patients using calcium concentration influencing drugs in a general hospital setting.

**Methods:** A clinical rule selecting patients with critical calcium levels (<1,8 and >2,8 mmol/l) and drugs influencing plasma calcium levels was developed.<sup>2</sup> Cut-off values and drugs

influencing plasma calcium levels were in consensus with the Department of Internal Medicine of the Catharina Hospital Eindhoven (CZE).<sup>3</sup> Data of all patients admitted to the CZE in 2011 (n=17.814) were retrospectively analyzed using a CDSS. The electronic medical records (EMR) of these selected patients were studied to determine the incidence and cause of hypo- and hypercalcaemia.

Results: The prevalence of severe hypo- and hypercalcaemia is 0.25% (n=44) and 0.44% (n=79) respectively. The incidence proportion for developing a hypo- and hypercalcaemia during admission is 0.16% and 0.07% respectively. In case of severe hypercalcaemia 19.0% of patients used calcium concentration increasing drugs. Patients presenting with severe hypocalcaemia used calcium concentration lowering in 18.2% of the cases.

Conclusion: Results of this retrospective study show that the prevalence and incidence proportion of severe calcium disturbances in a general hospital setting are low.

Approximately a fifth of the identified patients use calcium influencing drugs. The results also show the potential of CDSS to facilitate the conduct of epidemiological studies.

### **Scheepers-Hoeks AM**

#### **Propective Implementation of Clinical Rules on an Intensive Care Unit to Determine the Effect on Medication Safety in Practice**

A.M.J.W.Scheepers-Hoeks, H.H.M. Korsten, C. Neef, R.J.E.Grouls

Background: Clinical rules incorporated in a clinical decision support system (CDSS) are increasingly used as third generation medication safety systems to prevent Adverse Drug Events (ADEs). Although these systems can produce a wide spectrum of alerts, it is unclear how these alerts can be optimally presented in order to be most effective.

Aim: Determine the effect on guideline compliance after prospective implementation of different clinical rules on the ICU and the difference in this effect between four different alert mechanisms.

Methods: A randomised controlled clinical trial with historical case controls is performed. From October 2009 till December 2011, all patients admitted to the ICU of the Catharina-hospital were included. Four alert methods were compared on the percentage of guideline compliance (pharmacy intervention, physician Excel-list, EPD-section, pop-up alert).

Results: In total 3013 alerts were generated by the CDSS-system divided over: pop-up alert (1800x), pharmacy intervention (584x), physician Excel-list (629x). The EPD-section was never consulted. The users on the Intensive Care indicated that pharmacy intervention was the most preferred alerting method. Also a pop-up alert was useful, in contrast with a physician Excel-list and an EPD-section which were not found useful.

## **Cardiologie**

### **Heuvel M van den**

#### **Vectorcardiographic changes in the heart axis during left ventricular pacing The value of vectorcardiography in cardiac resynchronization therapy**

Madelon van den Heuvel BSc, Marcel van 't Veer MSc, PhD, Berry van Gelder PhD, Frank Bracke, MD, PhD

Introduction: One third of the patients having Cardiac resynchronisation therapy (CRT) as a therapy for heart failure, do not experience clinical benefit. This might be due to suboptimal position of the left ventricular (LV) lead. The purpose of this study was to examine whether the heart axis obtained from a vectorcardiogram (VCG) can be helpful in localising the left

ventricular stimulation site by determining the mutual position of the stimulation electrodes of a LV-lead.

Methods: The Frank VCG was calculated from a standard 12-lead employing the Kors method. This method was applied in 13 CRT patients with a standard dual unipolar or quadripolar LV-lead implanted in a coronary sinus tributary. The heart axis during unipolar stimulation was calculated in the frontal, sagittal and transversal plane and correlated with a position. The calculated position of the electrodes was compared with the position on chest X-ray.

Results: In 90 out of 93 two-dimensional VCGs the mutual position of the LV electrodes was correctly described compared to the X-ray: a more left oriented heart axis correlated with a position of the LV electrode to the right in the frontal plane; a more cranial orientated heart axis correlated with a caudal position in the sagittal plane (see figure 1); a more septal heart axis correlated with a lateral position in the transversal plane.

Conclusion: The VCG calculated using the Kors method is an adequate tool to determine the mutual position of the LV electrodes and might be useful to make an accurate determination of the lead position.

*Beste poster wetenschapsavond Catharina ziekenhuis 2012*

## **Wijnbergen I**

### **Gender Differences in Long-term Outcome after Primary Percutaneous Intervention for ST-segment elevation Myocardial Infarction**

Inge Wijnbergen, Marcel van 't Veer, Nico Pijls

Purpose To assess the influence of gender on long term outcome in patients with STEMI who underwent primary percutaneous intervention (PCI) between January 2006 and May 2008.

Methods Two-year follow-up data from 870 patients (23% female) were available from the DEBATER trial database. The primary endpoint was MACE, defined as the composite of death, myocardial infarction and target vessel revascularisation (TVR).

Results Women were older ( $64.7 \pm 11.7$  vs  $59.0 \pm 10.7$ ;  $p < 0.001$ ), and had more often diabetes mellitus (15% vs 9%;  $p = 0.01$ ) and hypertension (44% vs 25%;  $p < 0.001$ ). At two years the rate of MACE was significantly higher in women (21% vs 14%;  $p = 0.02$ ). The mortality rate in women was 8% versus 2.6% in men ( $p < 0.001$ ). However, multivariate analysis after adjustment for age and the baseline characteristics hypertension, smoking and diabetes mellitus showed similar MACE and mortality rates in men and women.

Conclusion Women have higher rates of both MACE and mortality after primary PCI for STEMI compared to men because of higher age with higher baseline risk profiles.

## **Inwendige geneeskunde**

### **Wlazlo N**

#### **Iron Metabolism Is Associated With Adipocyte Insulin Resistance and Plasma Adiponectin: The Cohort on Diabetes and Atherosclerosis Maastricht (CODAM) study**

Wlazlo N\*, van Greevenbroek MM, Ferreira I, Jansen EH, Feskens EJ, van der Kallen CJ, Schalkwijk CG, Bravenboer B\*, Stehouwer CD

Objective: Serum ferritin and transferrin are associated with muscle insulin resistance (IR), but little is known about the role of iron on the adipose tissue. Data in the literature suggest a direct role for iron and iron-metabolism related factors in adipose tissue function and

metabolism. For this reason, we investigated whether several markers of iron metabolism were associated with adipocyte IR and serum adiponectin.

Research design and methods: Serum ferritin (in g/L), transferrin (in g/L), total iron (in mol/L), nontransferrin-bound iron (NTBI) (in mol/L), transferrin saturation (in %), and adiponectin (in g/mL) were determined in 496 individuals (60% men). Adipocyte IR was defined by the product of fasting insulin and non-esterified fatty acids (NEFAs). Associations between iron metabolism parameters and adipocyte IR or serum adiponectin were investigated with multiple linear regression analyses.

Results: Serum ferritin ( $\beta=0.148$ ; 95%CI 0.093-0.202), transferrin ( $\beta=0.458$ ; 95%CI 0.326-0.590), Total iron ( $\beta=0.013$ ; 95%CI 0.006-0.021), and NTBI ( $\beta=0.048$ ; 95%CI 0.017-0.080) were associated with adipocyte IR (all  $p<0.005$ ) after adjustment for several covariates, including inflammatory markers. Notably, these associations should not be fully ascribed to insulin, as all markers of iron metabolism were associated with NEFAs as well (all  $p<0.02$ ). Finally, ferritin ( $\beta=-0.080$ ; 95%CI -0.129 to -0.031) and transferrin ( $\beta=-0.180$ ; 95%CI -0.299 to -0.062) were inversely associated with adiponectin (both  $p<0.01$ ).

Conclusions: The observed associations of several parameters of iron metabolism with adipocyte IR could suggest that iron accumulation in adipose tissue may play an important role early in the pathogenesis of IR and type 2 diabetes mellitus.

## Onderwijs & Onderzoek

### Pluyter JR

#### Immersive Surgical Training in a Simulated OR Setting: Towards Narrowing the Gap Between Simulation Training and Clinical Practice

Pluyter JR\*, Rutkowski A-F, Jakakimowicz JJ\*

Geen abstract beschikbaar



**Wetenschapsavond  
Catharina Ziekenhuis  
2013**

## Presentaties

### Algemeen Klinisch Laboratorium

**Berkel M van**

#### **Reference values and variation of cardiac troponin I and T measured with sensitive assays in hemodialysis patients without a history of cardiac disease**

Miranda van Berkel\*, Daniël A. Geerse\*, Volkher Scharnhorst\* and Constantijn J.A.M. Konings\*

Achtergrond : Myocardial infarction (MI) is defined as a change in cardiac troponin with appropriate clinical symptoms and at least one troponin result exceeding the 99th percentile. It is essential to discriminate acute cardiac damage from other causes of troponin elevation. In this study, we investigated inter-individual variation of troponin measured with a sensitive cTnI en hs-cTnT assay in hemodialysis patients.

Methode : This study included 206 chronic hemodialysis patients. cTnI and cTnT were determined using cTnI-ultra (Siemens) and hs-cTnT assays (Roche). Patients with a history of cardiac events were excluded from analysis. The 99th percentile of troponin concentration and the 95th percentile of change in troponin between samples drawn with a 3 monthly interval were calculated

Resultaat : Dialysis patients without known cardiac events had 99th percentiles of cTnI and cTnT concentrations of 0.215 ug/L and 232 ng/L, which highly exceed the 99th percentile reference values for healthy individuals (0.056 ug/L and 20 ng/L respectively). The 95th percentile of change for TnI was 0.128 ug/L and 94 ng/L for cTnT. Patients (n=5) diagnosed with MI exceeded this 95th percentile of variation significantly, with a minimal change from baseline of 146 ng/L for hsTnT.

Conclusie : We have established reference intervals for troponin concentration and change in hemodialysis patients without a history of cardiac disease. Data from 5 patients suggest that hs-cTnT levels in hemodialysis patients with an acute MI exceed the 99th percentile of change for cTnT. Our results suggest cTnI and hs-cTnT aid in triage of patients with symptoms of MI if population-specific 99th percentiles and troponin changes are used.

### Cardiologie

**Nunen LX van**

#### **Intra-aortic balloon counterpulsation in acute myocardial infarction with cardiogenic shock or persistent ischemia: 3-year experience in 4076 consecutive patients undergoing primary percutaneous coronary intervention**

Lokien X. van Nunen MD\*, Marcel van 't Veer PhD\*, Stéphanie Schampaert MSc\*, Boudewijn J.E.M. Steerneman RN\*, Marcel C.M. Rutten PhD , Frans N. van de Vosse PhD , Nico H.J. Pijls MD PhD\*

Background: Recent evidence questions the role of IABP in treatment of acute myocardial infarction complicated by CS. An area of increasing interest is the use of IABP for PI.

Objectives: To analyse the use of intra-aortic balloon pump (IABP) in patients with acute myocardial infarction complicated by cardiogenic shock (CS) or persistent ischemia (PI).

Methods: From 2008 to 2010, a total of 4076 patients were admitted to the hospital for primary percutaneous coronary intervention (PCI) for acute myocardial infarction. Out of

those patients, 239 patients received an IABP. Characteristics of those 239 patients and outcome are investigated in this study.

Results: Mean age of the study population was  $64 \pm 11$  years, 75% were male patients, 63% of the patients were in CS and 37% of the patients had PI. The patients who met the criteria of CS had a 30-day mortality rate of 36% and 1-year mortality of 41%. The patient subgroup treated because of PI, had a 30-day mortality rate of 7%; 1-year mortality was 11%. Independent predictors for higher 30-day mortality were CS (OR, 5.1; 95% CI, 1.8-13.8) and IABP running time  $\geq 1$  day (OR, 3.0; 95% CI, 1.4-6.2).

Conclusions: Mortality in patients admitted for primary PCI because of acute myocardial infarction complicated by CS is high despite IABP use. In contrast, outcome in patients in whom IABP was used to treat PI was favourable and mandates further prospective studies.

## Chirurgie

### Lee D van der

#### **The effect of chewing gum before and directly after surgery on postoperative ileus in colorectal surgery; a randomized controlled trial**

D. van der Lee BSc\*, T. van den Heijkant MD\*, B. Aerts MD\*, M. Osinga-de Jong MD, H. Rutten MD PhD\*, I. de Hingh MD PhD\*, G. Nieuwenhuijzen MD PhD\*, K. Hulsewé MD PhD, T. Hoofwijk MD PhD, W. Buurman PhD and M. Luyer MD PhD\*

Background: Nutritional stimulation of the autonomic nervous system ameliorates postoperative ileus in experimental models. Timing of the intervention is essential for these effects, however anaesthesiology guidelines advocate a pre-operative fast.

Aim: We investigated the hypothesis whether activation of the autonomic nervous system through sham feeding via chewing gum reduces postoperative ileus following colorectal surgery.

Methods: In this dual center placebo-controlled randomized trial 120 patients undergoing elective colorectal surgery were randomized for chewing gum ( $n = 58$ ) or a dermal patch placebo ( $n = 62$ ). Time to First flatus and first defaecation were assessed as well as gastric emptying, surgical complications and length of stay.

Results: Time to first flatus and first defaecation was significantly reduced in patients receiving chewing gum compared with the controls ( $P=0.006$  (flatus);  $P=0.04$  (defaecation)). Furthermore, chewing gum increased gastric emptying rate (median 25%, IQR 7-44% vs median 10%, IQR 2-27%;  $P=0.004$ ) and resulted in less reinterventions under general anaesthesia ( $n=2$  vs  $n=9$ ;  $P=0.048$ ). Finally, length of stay was reduced (mean of 8.5 days, SD 0.6 vs a mean of 11 days, SD 1.8;  $P=0.055$ ).

Conclusion: Chewing gum just before and directly after colorectal surgery reduces postoperative ileus, reduces the number of reinterventions under general anaesthesia and may shorten length of hospital stay. It is a simple and safe intervention to reduce postoperative complications and enhance recovery.

Innovation: This is the first study in which chewing gum is used to stimulate the autonomic nervous system to reduce postoperative ileus. Furthermore, postoperative ileus is objectivated by standardized ultrasound measurements of the gastric antrum to assess gastric emptying.

## Klinische Fysica

Unipan, M

### Minimizing the effect of rectal distension on prostate rotation during radiotherapy treatment

M. Unipan\*, F. van Aarle, A. Habraken, S. Barneveld, D. Schuring\*

**Purpose:** In prostate radiotherapy, accurate targeting is essential for a successful treatment. Prostates exhibit relatively frequent and large motion, mainly due to rectal filling. While translations of the prostate can be corrected for by online imaging, rotations cannot be corrected for and in general are managed by a variety of mostly invasive measures, e.g. insertion of a rectal balloon. We have developed a unique non-invasive monitoring protocol of prostate rotations based on imaging alone, used to select patients in need of re-planning. The purpose of this study is to assess the effectiveness of our monitoring protocol.

**Methods and materials:** From a population of 640 prostate cancer patients, 26 patients who exhibited frequent and large ( $>10^\circ$ ) prostate rotations were selected for a repeat CT scan and re-planning. The effectiveness of this strategy was assessed by evaluating the relative decrease in the frequency of large prostate rotations. The correlation between rectal filling and the frequency of large prostate rotations was also analyzed.

**Results:** For the re-planned patients, the frequency of large prostate rotations significantly decreased by 80.7% on average ( $p < 0.001$ ). No significant correlation was found between the rectal filling on the planning CT and the frequency of prostate rotations ( $p > 0.05$ ), however there seems to be a higher risk of large rotations in patients with a rectum diameter larger than 5 cm at the level of the prostate base ( $p = 0.03$ ).

**Conclusions:** A relatively simple, non-invasive prostate rotation monitoring protocol is sufficient to select the patients in need of adaptive replanning. Rectal filling on the planning CT scan is not a significant predictor of large prostate rotations, although patients with a large diameter of the rectum on the planning CT seem to have a higher chance of having large prostate rotations.

## Urologie

Kuppen MC

### Training status of residents in urology in the master-apprentice model

Kuppen M.C.P. \*, De Vries A.H. \*, Schout B.M.A., Koldewijn E.L. \*

**Introduction:** The current model for training of urology residents is the master-apprentice model. This model might become insufficient due to advances in educational theory, changes in clinical settings, and ethical perspectives.

**Purpose:** The purpose of this study is to investigate the current level of training of residents in urology to determine points of improvement.

**Methods:** 60 cystourethroscopy (UCS), 40 transrectal ultrasound of the prostate (TRUS), and 12 transurethral resection of bladder tumours (TURBT) performed by residents are analysed in two hospitals using observational surveys, semi-structured interviews, and questionnaires for patients. Main outcomes are residents' skills, completeness of registration, and patient comfort.

**Results:** in total 54 UCS, 42 TRUS, and 15 TURBT are observed in two hospitals. Residents score high in all procedures (85.5% in UCS, 91.7% in TRUS, and 83.7% in TURBT) supported by all interviewees. Scores on preparation (29.2% to 83.5%) and completion (22.6% to 64.0%) are low. Completion of registration is 58.3% for TRUS with biopsies and 52.5% for

TURBT. Patient comfort is 8.2 for UCS and TRUS, while experienced pain is 2.6 in UCS and 2.2 in TRUS.

Conclusion: Current training level of residents in the master-apprentice model is high. All residents are at the end of the learning curve, especially for UCS and TRUS. Areas of improvement are preparation, material usage, and completion of the procedures. Measurements should be carried out after implementation of a non-patient related training program in order to determine if these improvements can be achieved.

## Posters

### Algemeen Klinisch Laboratorium

#### Heuvel D van den en Boonen KJ

#### **Determination of dabigatran, rivaroxaban and apixaban using UPLC-MS/MS and comparison with coagulation assays for therapy monitoring**

E.M.H. Schmitz, D. van den Heuvel\*, K. Boonen\*, L. Brunsveld, D. van de Kerkhof\*

**Introduction:** Over the last several years, novel oral anticoagulants (NOACs) have been developed. Monitoring of NOACs was postulated to be obsolete. However, it appeared to be important for patients having deviating posture, diminished renal function or in emergency (bleeding) situations. Many new coagulation assays have been developed, because conventional coagulation assays are not suitable for adequate monitoring.

**Goal:** Our goal is the development of a reference UPLC-MS/MS technique for the quantification of dabigatran, rivaroxaban and apixaban, comparison with several coagulation tests and determination of target values for peak and trough plasma concentrations.

**Methods:** Plasma and full blood were spiked with dabigatran, rivaroxaban and apixaban for calibration (23-750 ng/mL) and quality control. A UPLC-MS/MS method and several coagulation assays were validated with standard protocols. Target values will be determined at several time points in an in-clinic orthopedic population and out-clinic cardiologic population.

**Results:** The UPLC-MS/MS technique met all the criteria as defined in the validation procedure. It can thus be used as a reference method to validate the different coagulation assays. Results of this validation will be available soon.

**Conclusion:** An adequate method for the measurement of dabigatran, rivaroxaban and apixaban was developed and validated. Target values will be determined and compared to coagulation assays in an in-clinic orthopedic and out-clinic cardiologic patient population.

#### Kerkhof D van de

#### **Platelet function and blood loss during coronary artery bypass surgery**

S. Mezger, A. van der Stokker, P. Lanen\*, A. van Straten\*, D. van de Kerkhof\*

**Inleiding:** Coronary artery bypass surgery (CABG) is associated to blood loss. Transfusion of platelets and plasma is often applied anticipating on heparinisation, extracorporeal circulation (ECC) and use of platelet inhibitors during surgery. To prevent blood loss during surgery, clopidogrel is often stopped at least 5 days before surgery. In this study coagulation and platelet function were monitored during the CABG procedure in a population that stopped clopidogrel use 5 days before the procedure (Group A) and in a population that continued clopidogrel through the procedure (Group B).

**Methode:** Patients undergoing standard CABG on ECC were included (n=60, Group A 38, Group B 22). Analysis was performed pre-surgery, during surgery and within 2 hours after arrival at the Intensive Care Unit. Thrombocyte function was analysed with Light Transmission Aggregometry (LTA), Multiple Electrode Aggregometry (MEA) and GPIIb/IIIa-expression with flowcytometry. Also, routine coagulation testing and thromboelastography was performed with platelet mapping. Blood loss and transfusion was registered.

**Resultaat:** No significant difference was present in hemoglobin concentration, blood loss and transfusion between Group A and B. Platelet aggregation with ADP was reduced in Group B, while strong agonists as collagen and TRAP was the same. The aggregation response of all

agonists was decreased during the surgical procedure and returned to pre-operative values at the time of arrival at the ICU. Coagulation assays showed no significantly different results during the procedure.

Conclusions: As most transfusions are applied at the ICU, this study shows that the use of clopidogrel during the procedure is a weak parameter for clinical decision making on transfusion. Platelet function is reduced during surgery, but is restored to pre-operation values at the time of arrival at the ICU.

## Cardiologie

### Broek M van den en Hiller D

#### Femoral artery complications after transfemoral coronary procedures

Maarten van den Broek\*, David Hiller\*

Preface: The femoral artery has been used as access site for coronary procedures since the 1960's. Serious adverse events are rare. However, haemorrhages, haematomas, pseudo aneurysms and arteriovenous fistulas are common, can cause discomfort, and sometimes even necessitate emergency surgery. There is a large number of variables that may influence the development of these complications. Vascular closure devices (VCD) are in an increasing rate replacing manual compression (MC) as a method of achieving haemostasis at the entry site. However, there is only marginal evidence that VCD's are superior to MC.

Goals: This registry aims to identify patient characteristics and procedure variables (e.g. the use of VCD) that influence the incidence of femoral complications and hopes to provide recommendations for optimal care.

Method: This study is designed as a prospective registry. Patients will be recruited on intermittent days, in two cathlabs of the Catharina hospital, during a 26 week period. Patient characteristics such as medication usage, laboratory values and cardiovascular risk factors are registered. Many values, such as; ease of puncture and method of closure, are noted during the procedure. The researchers themselves examine the patients both before and after the procedure to ensure little variability. After 4 weeks there is a telephonic follow-up. Incidence of major complications is the primary outcome, incidence minor complications and discomfort are secondary outcomes. Factors influencing these outcomes will be identified using statistical methods including multivariate analysis.

Results: At this point we have included approximately 340 patients and can only present descriptive data.

Conclusion: To follow at a later date.

### Lenders G

#### The Impact of Downstream Coronary Stenoses on Fractional Flow Reserve Assessment of Intermediate Left Main Disease in humans

Guy Lenders, Marcel van 't Veer, Nico Pijls

Background Fractional flow reserve (FFR) is a useful tool in assessing the functional significance of left main (LM) coronary artery stenosis. But the effect of downstream epicardial coronary artery disease remains unclear since the induced maximal hyperemia, could theoretically be incomplete.

Aim: The aim of this study is to assess the validity of measuring FFR of LM coronary artery stenosis in the setting of concomitant left anterior descending (LAD) or left circumflex (LCX) artery stenoses, both in an in vitro model and in humans.

Methods: Patients with an intermediate LM stenosis and a significant stenosis in the LAD or LCX, scheduled for percutaneous coronary intervention (PCI), were included. FFR was

measured in both `_downstream_` arteries before and after FFR-guided PCI of the stenotic artery.

Results: Inclusion is still running for this study and results are thereby preliminary. Data for the in vitro study will become available soon. For the human study, until now, data of only 6 patients is available. The difference in FFR before and after `_downstream_` PCI was between 0.00 and 0.02 in all patients, when measured in the non-stenotic artery. These data will be combined with the data of the in-vitro study.

Conclusion Patients with an intermediate LM-stenosis and a concomitant significant LAD or LCX stenosis are rare but these preliminary data confirm the results of the in vitro model. FFR assessment of intermediate LM stenosis is reliable, even when a significant `_downstream_` coronary artery stenosis is present.

## **Schampaert S**

### **Intra-aortic balloon pump support in the isolated beating pig heart**

Stéphanie Schampaert\*, Marcel van 't Veer\* Marcel C.M. Rutten,

Lokien X. van Nunen\* Sjoerd van Tuijl, Frans N. van de Vosse, Nico H.J. Pijls\*

Background: The intra augmentation as well as a systolic reduction in afterload. Although these blood pressure adaptations are expected to create clinical improvement in terms of coronary perfusion and myocardial oxygen consumption, the measured effect reported in literature is inconsistent and ambiguous among patients and animal experiments.

Methods: Six slaughterhouse pig hearts were isolated, prepared and connected to an external circulatory system. Through coronary reperfusion and controlled cardiac loading, physiological cardiac performance was achieved. IABP support was applied, while the support capabilities of the pump were evaluated.

Results: The IABP induced a diastolic blood pressure augmentation as well as a systolic reduction in afterload. The magnitude of these effects, however, strongly varied between the individual hearts. Both heart rate and systemic vascular resistance seemed to be strong determinants for this. For large values of systemic vascular resistance in combination with a pulse rate of moderate level, the IABP enhanced the amount of blood pressure augmentation pronouncedly. This resulted in a coronary blood flow increase of up to 40 %. On the other hand, the flow during IABP support remained unaltered in hearts beating at high pulse rate and where systemic vascular resistance was low. Independent of the magnitude of induced effects, myocardial oxygen consumption remained at baseline level during support.

Conclusion: The IABP is capable to support the endangered circulation by increasing hyperemic coronary blood flow. However, the magnitude of the induced effect strongly varies between the individual hearts.

Innovative elements: The isolated beating pig heart model is an accessible platform to investigate the coronary circulation in its truly morphological and physiological state. Besides the fact that its use is beneficial from a time, cost and ethical perspective, it allows testing of cardiovascular devices (i.e. ventricular assist devices) under well

## Chirurgie

Broos PP

### **Introducing the EAGLE Registry: Endovascular AAA Repair with the Endurant Stent Graft in Challenging Anatomy, a Global Experience**

P.P.H.L. Broos, MD\*; R.A. Stokmans, MD\*; P.W.M. Cuypers, MD, PhD\*; M.R.H.M. van Sambeek, MD, PhD\*; J.A.W. Teijink, MD, PhD\*

Introduction: In the past two decades, many technological advances have been introduced to improve feasibility and durability of endovascular aneurysm repair (EVAR). Also, operators have become more proficient with endovascular techniques. These developments have led to an increasing interest and confidence to extend treatment to challenging anatomies. Currently, approximately 30% of these patients are considered outside IFU criteria. The ENGAGE Registry, which describes the performance of a stent-graft with very liberal and extended IFU criteria, still reports 10-15% of patients with challenging anatomy of the proximal neck. Solid evidence on the effectiveness and safety of latest devices in challenging cases is missing.

Method: EAGLE (Endurant for Challenging Anatomy: Global Experience) is designed to register the performance of the Endurant in challenging anatomy in a real-world setting, and to critically assess whether or not it is safe to expand current guidelines of anatomic eligibility for endovascular treatment. Initiated by doctors, EAGLE is a prospective, non-interventional study, aiming to enrol 350 patients in 20 experienced centres across countries worldwide. To minimize the risks of selection bias and enhance data quality, EAGLE eligibility will be determined by an independent core-lab and efforts will be made to secure consecutive enrolment of challenging cases. The EAGLE database is designed to merge with the on-going ENGAGE database, which enables comparative analysis of cases and results.

Conclusion: Studies on the performance of EVAR in challenging anatomy is necessary to demonstrate safety and effectiveness of the latest generation stent grafts, which is essential in making a balanced judgement in management of AAAs.

Broos PP

### **Performance of the Endurant Stent Graft in challenging anatomy: 30-day and 1-year analyses**

P.P.H.L. Broos, MD\*; R.A. Stokmans, MD1\*; P.W.M. Cuypers, MD, PhD\*; M.R.H.M. van Sambeek, MD, PhD\*; J.A.W. Teijink, MD, PhD\*

Objective: Dependent on anatomy of the proximal aortic neck we created three different groups; conservative (CON), stretched (STR) and challenging (CHA) anatomy to demonstrate safety and effectiveness of the latest generation stent-grafts in challenging anatomy.

Methods: Between 2009 and 2011, 1262 AAA patients were enrolled worldwide and treated with the Endurant Stent-Graft. 925 (75.9%) patients had CON anatomy, defined as AAAs with a proximal neck of  $\leq 15$  mm combined with an infrarenal neck angulation ( $\alpha$ )  $\leq 60^\circ$  and suprarenal angulation ( $\beta$ )  $\leq 45^\circ$ . 189 (15.5%) patients had STR anatomy, defined as AAAs with a proximal neck of 10-15 mm or  $>15$  mm combined with respectively  $<60^\circ$  and  $\beta <45^\circ$  or  $60-75^\circ$  and/or  $\beta 60-75^\circ$ . 104 patients (8.5%) patients were placed in the CHA group and had more challenging anatomy than the other two groups. Multivariate logistic regression was used to compare results, and to adjust for possible baseline differences.

Results: Operation time (119.2mins vs. 97.4mins,  $P = 0.000$ ) and use of contrast (74.3cc vs. 69.9cc,  $P = 0.002$ ) were significantly different between CHA and CON, but technical success ( $P = 0.112$ ) was similar between the three groups. No difference in the occurrence of mortality

and reinterventions within 30-days and 1-year post-implantation was seen between the groups. There was a significant higher rate of type-I endoleaks in CHA independently compared to CON and STR within 30-days ( $P = 0.000$  resp.  $P = 0.000$ ).

Conclusion: The results are promising and indicate that endovascular AAA repair with the Endurant Stent Graft is safe and effective in patients with challenging anatomy.

What this paper adds?: This study aimed to compare the differences in perioperative and postoperative outcome after endovascular repair of abdominal aortic aneurysms (AAA) with different morphology. Studies on the performance of EVAR in challenging anatomy is necessary to demonstrate safety and effectiveness of the latest generation stent grafts, which is essential in making a balanced judgement in management of AAAs.

## **Fokkenrood HJ**

### **Physical activity monitoring in patients with peripheral arterial disease: validation of a tri-axial accelerometer**

Fokkenrood HJP\*, Kuijlaars IAR, van den Tillart S, Scheltinga MR, de Bie RA, Teijink JAW\*

Introduction: Patients with peripheral arterial disease Fontaine II (PAD) may demonstrate less physical activity compared to individuals without PAD. Levels of daily activity are potentially quantified using an accelerometer. Aim of this pilot study was to evaluate the validity of a novel triaxial accelerometer (DynaPort MiniMod) in monitoring periods of activities in patients with PAD.

Materials & methods: Patients with diagnosed PAD were recruited ( $n=30$ ) during a routine visit at our vascular laboratory. Patients with restrictions to walking distance or gait other than PAD were excluded ( $n=9$ ). Participants were instructed to wear a MiniMod. They were video-recorded by two researchers who separately analysed the results according to an annotation protocol. Inter-rater reliability of annotations was studied with intraclass correlation coefficients (ICC). Total periods of postures were computed and compared between video observation and accelerometer data with ICC and Bland-Altman plots.

Results: A total of 29.5 hours of video observation in 21 participants (age:  $67 \pm 10$ ; 62% male) was used for analysis. Our video annotation method appeared reliable for most postures (lying: ICC=1; sitting: ICC=1; standing: ICC=0.98; walking: ICC=0.97; unable to score: ICC=1; not worn=1) except for shuffling (ICC=0.38). Accelerometer data correlated strongly with video annotations (lying: ICC=0.99); sitting: ICC=0.91; walking: ICC=0.85; not worn: ICC=0.97. However, no significant correlations ( $p > 0.05$ ) were found for standing (ICC=0.17) and shuffling (ICC=0.08).

Conclusions: The DynaPort MiniMod is a valid tool for quantifying periods of lying, sitting, walking and `_not worn_` in patients with IC but not for standing and shuffling. This may be explained by particular choices made in our annotation protocol as well as the low inter-rater variability of these postures.

## **Lauret GJ**

### **Physical activity monitoring in patients with intermittent claudication**

Lauret GJ\*, Fokkenrood HJP\*, Scheltinga MRM, Wittens CH, Teijink JAW\*

Introduction: Supervised exercise therapy is indicated for all patients with intermittent claudication (IC) in order to improve functional impairment and health-related quality of life. However, objective information about the physical activity of this population is lacking. The aim of this study was to quantify the level of physical activity of newly diagnosed patients with IC and compare them to current public health physical activity guidelines.

**Materials & methods:** Before initiating treatment, 90 patients with newly diagnosed IC were instructed to wear a tri-axial seismic accelerometer (Dynaport MoveMonitor, McRoberts B.V., The Hague, The Netherlands) during 1 week. If the device was worn correct for 5 days or more, the daily time spent in different activities, movement intensity and energy expenditure were determined. With these data the physical activity level, in metabolic equivalents (METs), was assessed and compared to the ACSM/AHA public health physical activity minimum recommendations (e 64 METs"min"day, in bouts of e 10 min).

**Results:** Data of 54 patients (351 days) were analysed. In total, only 52% of all patients with IC met the public health physical activity guidelines. The average daily physical activity level (103±106 METs"min"day) was influenced significantly by the baseline maximum walking distance, the SF-12 physical functioning score, the existence of pulmonary comorbidity and the number of legs affected. In total, 19±20 minutes a day were spent in moderate intensity activity (3-6 METs), compared to 1±3 minutes in vigorous intensity activity (>6 METs). Patients spent 125±105 minutes a day lying, 494±116 minutes sitting, 166 ±57 minutes standing, 23±12 minutes shuffling and 68±33 minutes in locomotion.

**Conclusions:** Half of the patients with IC do not meet the minimum public health recommendations for physical activity. These findings support the need for a well-structured supervised exercise programme aiming to improve not only functional impairment but also the level of physical activity.

## **Stokmans RA**

### **Challenging the evidence for pre-emptive coil embolisation of the internal iliac artery during endovascular aneurysm repair**

Rutger A. Stokmans, MD, PhD\*; Edith M. Willigendael, MD, PhD\*; Joep A.W. Teijink, MD, PhD\*; Jan A. Ten Bosch, MD\*; Marc R.H.M. van Sambeek, MD, PhD\*; Philippe W.M. Cuypers, MD, PhD\*

**Introduction.** When coverage of the internal iliac artery (IIA) during endovascular aneurysm repair (EVAR) is required, it is common practice to perform adjunctive coil embolisation of the IIA. There is, however, no solid evidence for the necessity of this strategy. We retrospectively analysed the results of a strategy in which coverage of the internal iliac artery during EVAR was routinely performed without coil embolisation.

**Methods.** From January 2010 until May 2012, 32 patients (96.9% men; mean age 73.0 years; range 52-89 years) underwent EVAR with stent-grafts extended into the external iliac artery (EIA), all without prior coil embolisation. Aneurysm morphology was determined on preoperative CT-images. During follow-up, patients were interviewed about buttock claudication, and the occurrence of endoleaks and evolution of aneurysm diameter were registered.

**Results.** At baseline, mid-CIA diameter was 33.5±16.8 mm, and 7 patients presented with ruptured aneurysms. Mean follow-up was 14.3±7.4 months. There were 8 deaths, none related to IIA coverage. Buttock claudication occurred in 7 (22.6%) patients, which persisted after 6 months in 2 cases of bilateral IIA coverage. No Type-I or -II endoleaks occurred related to IIA coverage. Aneurysm growth was not observed.

**Conclusion.** Endovascular treatment of aorto-iliac and iliac aneurysm without pre-emptive coil embolisation of the IIA appears safe and effective. No IIA-related endoleaks or reinterventions occurred in our series. This approach saves operating-time, contrast load and costs, and may reduce complications. However, a larger population and longer follow-up is required to confirm our findings.

**What this paper adds:** It has never been studied whether omission of coil embolisation leads to an increased risk for Type-II endoleak. This is the first study to describe the results of

EVAR without pre-emptive IIA coiling in a consecutive series of patients with aortoiliac aneurysms.

## **Stokmans RA**

### **Contemporary real-world EVAR outcomes in perspective: an early comparison of the ENGAGE and EUROSTAR registries**

Rutger A. Stokmans, MD\*; Pieter P.H.L. Broos, BSc\*; Joep A.W. Teijink, MD, PhD\*; Philippe W.M. Cuypers, MD, PhD\*; Jacob Buth, MD, PhD\*; M.R.H.M. van Sambeek, MD, PhD\*

**Introduction.** Endovascular AAA repair (EVAR) is continuously evolving. Registries are essential tools to closely monitor the performance of current devices in a real-world setting. However, margins in the outcomes of EVAR are small. Therefore, to detect obvious differences in the performance of current devices and care, long-term follow-up is required. Benchmarking with historic registries, such as EUROSTAR might be helpful to put early results of contemporary registries in perspective.

**Methods.** The original data of patients enrolled in the EUROSTAR registry was compared with patient level data from the ENGAGE registry. Data of 7321 EUROSTAR cases (Excluder, Talent or Zenith) was merged with data of 1263 ENGAGE cases (Endurant Stent Graft, Medtronic Vascular, Santa Rosa, California, USA). P-values <.05 were considered significant.

**Results.** Operation-time has decreased in ENGAGE compared to EUROSTAR, 103±47 vs. 127±58 minutes, p<.01. Perioperative conversion to open surgery occurred less often in ENGAGE (0.23% vs.0.74%, p=.04), and perioperative mortality rates declined (2.18% vs. 1.27%, p=.03). One-year all-cause survival did not differ between EUROSTAR and ENGAGE, respectively 92.21% versus 92.51%, but AAA-related mortality within 1-year decreased from 2.91% in EUROSTAR to 1.53% in ENGAGE, p<.01. The occurrence of secondary interventions within the first year also declined in ENGAGE, 1-year postoperatively 8.27%, whereas this was only 5.86% in ENGAGE, p<.01.

**Conclusion.** Results of this early comparison are promising for the Endurant Stent Graft, with less AAA-related mortality and fewer secondary interventions. However, long-term follow-up is needed to confirm durability of these results.

**What this paper adds:** A comparative analysis at patient level data between the landmark EUROSTAR (initiated by Catharina Hospital) and any recent registry has never been done. This study contributes in adding perspective to the results of ENGAGE, which is considered the most contemporary and largest on-going real-world EVAR registry.

## **Stokmans RA**

### **Endovascular versus Open Repair in Patients with Abdominal Aortic Aneurysms: a Meta-analysis of Randomised Controlled Trials**

Rutger A. Stokmans, MD, PhD\*; Joep A.W. Teijink, MD, PhD\*; Pieter P.H.L. Broos, BSc\*; B.L.W. Bendermacher, MD, PhD\*; Philippe W.M. Cuypers, MD, PhD\*; Martin H. Prins, MD, PhD\*; Marc R.H.M. van Sambeek, MD, PhD\*

**Introduction.** Surgical intervention is required in abdominal aortic aneurysm (AAA) patients to prevent them from lethal rupture. The objective of this meta-analysis is to assess the effectiveness of endovascular aneurysm repair (EVAR) versus conventional open surgical repair (OPEN) for AAA patients. Determined by the effects on 30-day, mid-term and long-term mortality, and the occurrence of secondary interventions.

**Methods.** A systematic literature search was conducted in PubMed, Medline, Embase and

ScienceDirect databases through May 2012, using (MeSH) keywords abdominal aortic aneurysm, endovascular, and open surgical. Articles on randomised controlled trials (RCTs) comparing EVAR with OPEN for non-ruptured, non-small AAAs were selected. The Delphi-list was used to assess the quality of the selected studies, and a description of the studies was given. The authors independently conducted both eligibility and quality assessments. Mantel-Haenszel\_s method was used for statistical pooling.

Results. A total of 11 articles describing 6 trials were used for extraction of data on 2899 patients. The pooling analysis showed a relative risk of 0.35 [95%CI, 0.20 to 0.61] concerning perioperative (30-day) mortality favouring EVAR compared to OPEN. Mid-term and long-term all-cause mortality rates, however, did not differ between the two methods ( $p=0.46$  and  $p=0.83$ , respectively). After the perioperative period, AAA-related deaths occurred 1.85 times more often in EVAR patients than in OPEN patients ( $p=0.03$ ). Also, approximately 2 times more secondary interventions were performed after EVAR compared to OPEN, but heterogeneity on this outcome effect was high ( $I^2=85\%$ ).

Conclusion. Endovascular repair is associated with lower perioperative mortality than open repair, but has not been shown to improve mid-term and long-term survival. Especially in the long-term, EVAR seems to be less effective than OPEN, since the likelihood for aneurysm related mortality and secondary interventions are higher after endovascular repair. Extended long-term trial data and trials comparing more contemporary devices with open surgical techniques are needed to validate these findings.

## **ECC / Bloedmanagement**

**Hees JW van**

### **Healthcare Failure Mode Effect Analysis of a Miniaturized Extracorporeal Bypass Circuit**

Jeroen W.H. van Hees\*, Eduard P. Overvest\*, Vera Lagerburg\*, Carla Kloeze\*, A.H.M. van Straten\*

Background: The introduction of new and more advanced technology in healthcare occurs rapidly. Therefore more attention is needed to optimize the safe introduction and use of new devices and techniques. One example of new technology is a miniaturized extracorporeal bypass circuit. The most important improvement in this system compared to a conventional heart-lungmachine is a lower priming volume, which requires extra prospective risk assessment to ensure proper air-emboli handling. A proven technique for this is a 'failure mode effect analysis\_ (FMEA)1, which can be adapted for use in healthcare (hFMEA)2.

Methods: The hFMEA was initiated by the department of extracorporeal circulation and was performed in a multidisciplinary team including clinical perfusionists, clinical physicists and a technician. The hFMEA was performed in three 1.5h sessions. The first session was used to define a flow diagram of the process, the second to identify the potential failure modes and the third to describe adequate measures.

Results: The hFMEA demonstrated that failure of the bubble sensor for the electric remote clamping system, had the highest risk score of all failure modes. Without proper measures and/or training, this could result in irreversible morbidity or mortality of the patient.

Conclusion: The hFMEA demonstrated that implementing an additional low-level sensor in the miniaturized Extracorporeal bypass system was required to ensure patient safety. This qualitative analysis is an example of early identification of possible technology failures in any process or device, which can avoid adverse patient outcomes. Therefore, to address

and/or increase the safety of the use of high-risk apparatus in patient treatment, all physicians who use these devices should incorporate hFMEA into their clinical practice.

## **Gynaecologie**

### **Kuijsters N en Methorst W**

#### **Transvaginal electrohysteroigraphy for recording endometrial waves in non-pregnant uteri**

Nienke Kuijsters\*, Willem Methorst\*, Mady Kortenhorst\*, Matteo Santini, Chiara Rabotti, Massimo Mishi, Dick Schoot

Background: Contractions in a non-pregnant uterus play an important role in both natural and technically-assisted conception. Recent literature shows that endometrial waves influence pregnancy chances and can be modulated. Developing a reliable tool to measure these uterine movements is therefore of paramount importance. Current techniques to monitor these uterine movements are expensive, invasive, observer-dependent or not able to measure for a prolonged period. A transvaginal electrode (TVE), placed against the cervix, measuring uterine action potentials (electrohysterography = EHG) might solve these shortcomings.

Objectives: In this study we evaluate a novel tool to measure endometrial waves. Using a transvaginal electrode placed against the cervix, we measure myometrial micropotentials and compare these signals with trans-vaginal ultrasound imaging of endometrial waves (TVUS).

Materials and methods: Twenty-one women, age 18-40 years, visiting the fertility clinic of the Catharina Hospital were included. Measurements with the TVE and TVUS were performed simultaneously. The TVE recordings were analyzed by the Technical University Eindhoven and compared to the TVUS recordings.

Results: EHG data reliably visualize endometrial waves in a non-pregnant uterus.

Conclusion: EHG shows to be a reliable, observer-independent and easy measurement tool of endometrial waves, offering fertility patients an affordable, non-invasive and objective monitoring system that can be of aid in their treatment plan.

Innovatory elements:

- Novel method to measure contractions in a non-pregnant uterus
- Non-invasive, observer-independent and inexpensive measurement tool
- Measurement of both frequency and intensity

### **Raps M**

#### **TBG, TSH, free T4 levels and the risk of venous thrombosis in users of hormonal contraceptives**

M Raps#, J Curvers\*, FM Helmerhorst, BEPB Ballieux, J Rosing, S Thomassen, FR Rosendaal, HAAMvan Vliet\*

Background: Use of combined hormonal contraceptives is associated with a three- to six-fold increased risk of venous thrombosis relative to non-use, dependent on the estrogen dose as well as the progestogen type. Use of hormonal contraceptives lead to resistance to Activated Protein C (APC), which also serves as marker for venous thrombosis. Hyperthyroidism is also associated with an increased risk of venous thrombosis due to increased free Thyroxine (FT4) levels which cause a hypercoagulable state. Objective: Our hypothesis was that different hormonal contraceptives lead to different levels of FT4, thyroid stimulating hormone (TSH) and thyroxine binding globulin (TBG). The aim of this study was to evaluate this effect and

investigate the correlation with the known relative risk of venous thrombosis. Methods: We conducted an observational study in 254 users of different contraceptives and measured FT4, TBG and TSH levels and APC resistance. Results: Users of hormonal contraceptives with a higher risk of venous thrombosis, i.e. containing desogestrel, cyproterone acetate or drospirenone, had higher TBG levels than users of hormonal contraceptives with a low risk of venous thrombosis, i.e. the levonorgestrel containing intrauterine device. TSH levels are slightly elevated and FT4 levels did not change. TBG levels correlate with APC resistance and with the risk according to the literature.

Conclusion: Use of different hormonal contraceptives lead to elevated TBG levels, slightly elevated TSH levels and unchanged FT4 levels. There seems to be no correlation between the increased risk of venous thrombosis during use of hormonal contraceptives and the hypercoagulable state in hyperthyroid patients.

Vernieuwende elementen: De TBG, FT4 en TSH levels zijn gemeten in een groep van gebruiksters van diverse anticonceptiva met verschillende toedieningswegen.

Op basis van deze studie en de beschikbare kennis uit de literatuur werd een nieuwe hypothese geformuleerd over het ontstaan van veneuze trombose tijdens gebruik van hormonale anticonceptiva.

## **Zalm M van der**

### **Determinanten van de pijnbeleving bij uitwendige versie \_ De EBIS studie**

M van der Zalm\*, S Truijens, E Ciliacus, SMI Kuppens\*, VJM Pop

Achtergrond: Uitwendige versie van een foetus in stuit naar hoofdligging wordt door vrouwen als zeer pijnlijk ervaren. Onduidelijk is echter wat de determinanten zijn van deze pijnbeleving.

Doelstelling: Wij onderzochten welke factoren geassocieerd zijn met pijnbeleving bij versie.

Methode: In de Eindhoven Breech Intervention Study (EBIS: 2007-2012; prospectief, observationeel onderzoek; n= 249; leeftijd 31,4 jaar) werden demografische, obstetrische (o.a. uterustonius, buikspiertonus, amniotischvloeistof index) en psychologische (emotionele stress; Edinburgh Depression Scale [EDS]) gegevens verzameld van vrouwen die een versie ondergingen. De pijnbeleving werd gemeten door middel van een VAS pijnscore op een schaal van 0 tot 10 (0: geen pijn; 10: ondraaglijke pijn). Lineaire regressie werd uitgevoerd.

Resultaten: De belangrijkste determinanten van de pijnbeleving waren het niet slagen van de versie, een hoge EDS score, het aantal versie pogingen en een hoge uterustonius. Bij het niet slagen van de versie nam de VAS score toe met 1.4 (0.6; 2.1); per 1 eenheid toename op de EDS score, nam de VAS score toe met 0.1 (95% CI 0.03; 0.2); per mislukte poging nam de VAS score toe met 0.4 en (0.2; 0.7); en bij een hoge vs. lage uterustonius was de VAS score 0.6 (0.1; 1.1) hoger.

Conclusie: De belangrijkste determinanten van pijnbeleving bij uitwendige versie zijn het wel/niet slagen van de versie, emotionele stress, het aantal versie pogingen en een hoge uterustonius. Deze studie biedt mogelijke aangrijpingspunten voor het verminderen van de pijn rondom de versie.

## Intensive Care

### Vonken HJ en Zwaveling S

#### **Standard dosing of low molecular weight heparin (LMWH) based on weight leads to subtherapeutic anti-factor Xa levels in intensive care patients. An observational study**

Vonken H.J.C.\*, Zwaveling S.\*, van de Kerkhof D.H.\*, Houterman S.\*, Bindels A.J.G.H\*., Roos A.N\*

*Purpose:* LMWH is the first-choice anticoagulant in intensive care (ICU) patients. Dosage is based on admission weight, according to current guidelines of the Dutch Society of Intensive Care Medicine (NVIC). Monitoring anti-factor Xa levels (aFXa) is only advised in ICU patients with renal insufficiency. The target range for aFXa levels in literature, albeit unproven, is 0.2-0.6 IU/ml. The aim of this study was to observe if recommended aFXa levels are being achieved in ICU patients.

*Materials and methods:* We conducted an observational, prospective study in a 25-bed ICU and an 8-bed medium care unit (MCU). Patients were included between September 15<sup>th</sup> and December 15<sup>th</sup>, 2012 and received LMWH subcutaneous. Patients with an ICU stay less than 24 hours were excluded. Patients received 2500 IU Dalteparin if admission weight < 80kg, and 5000 IU if admission weight ≥ 80kg. The aFXa levels were measured four hours after administration using the validated chromogenic method (STA<sup>®</sup> Liquid Anti-Xa assay).

*Results:* We collected data from 190 patients of whom 101 < 80kg and 89 ≥ 80kg. The median aFXa of the entire population was 0.170 IU/ml (IQR 0.05-0.48). The median aFXa of patients < 80kg was significantly lower compared to patients ≥ 80kg (0.15 IU/ml (IQR 0.05-0.37) vs. 0.19 IU/ml (IQR 0.05-0.48), P < 0.001). In patients < 80kg 14% (n = 14) did reach the lower limit of the target range (0.2IU/ml) each day compared to 36% (n = 32) in patients ≥ 80kg (P < 0.001). In patients < 80 kg 63% (n = 64) never reached the lower limit compared to 35% (n = 31) in patients ≥ 80kg (P < 0.001).

*Conclusion:* Dosing of LMWH based on admission weight, according to current guidelines, leads only in a small minority to adequate aFXa activity. Monitoring of the aFXa levels should be considered in all ICU patients.

## Inwendige geneeskunde

### Dekker MJ

#### **Monthly cholecalciferol administration in chronic hemodialysis patients: consequences on biochemical parameters and prescribed medication**

Marijke J.E. Dekker MD\*, Daniël A. Geerse MD\*, Miranda van Berkel PhD\*, Marieke C.H.M. Kerskes\*, Maaïke Hengst\*, Constantijn J.A.M. Konings MD, PhD\*, Volkher Scharnhorst PhD\*

*Introduction:* Vitamin D plays a central role in normal calcium metabolism and bone mineralisation. Recent studies found that vitamin D deficiency is associated with cancer [1], auto-immune disease [2], cardiovascular disease [3] and increased mortality [4, 5]. In patients with ESRD, vitamin D deficiency has a higher prevalence than in the general population [6], due to the lack of ability to convert vitamin D to its active form, 1,25 hydroxy vitamin D. Suppletion of vitamin D is recommended in hemodialysis patients [10]. In this study we evaluated the effects of monthly cholecalciferol suppletion on the serum 25 hydroxy vitamin D levels, other laboratory measurements and prescribed medication.

Methods: In this single centre observational study we screened all our 161 hemodialysis patients for vitamin D insufficiency, defined as a 25-hydroxyvitamin D level < 50 nmol/L, and when deficiency was present colecalciferol 50.000 IU monthly was described. At baseline and every three months there after serum vitamin D, calcium, phosphate, PTH and AF levels were measured as well as the use of alfacalcidol, phosphate binders and cinacalcet. The follow up was 12 months.

Results: After 6 months 25-hydroxy vitamin D levels were raised from  $28.3 \pm 10.4$  to  $66.3 \pm 27.5$ , which reflexes a sufficient level of vitamin D in 70.2% of the patients. The serum calcium ( $2.28 \pm 0.17$  and  $2.29 \pm 0.133$ ), phosphate ( $1.54 \pm 0.50$  and  $1.45 \pm 0.41$ ) and AF ( $93.8 \pm 51.8$  and  $97.0 \pm 68.4$ ) levels were at baseline comparable with the serum levels after 12 months. The PTH levels showed a slight decrease, with  $29.9 \pm 22.5$  at baseline and  $22.8 \pm 20$  not statistically significant. The alfacalcidol usage was decreased in 23.1% (n=24) of the patients after 12 months.

Conclusion: Colecalciferol suppletion treated 25-hydroxyvitamin D deficiency in hemodialysis patients effective but has no significant effects on serum calcium, phosphate and alkaline phosphatase levels.

## Wlazlo N

### **Diabetes in patients with cirrhosis is associated with higher incidence of spontaneous bacterial peritonitis, but not with increased mortality**

Nick Wlazlo\*, Marleen M. van Greevenbroek, Joyce Curvers\*, Erik J. Schoon\*, Pieter Friederich\*, Jos W.R. Twisk, Bert Bravenboer\*, Coen D.A. Stehouwer

Background: Diabetes mellitus (DM) is present in 20-40% of patients with liver cirrhosis. Although DM may predispose to fatal bacterial infections, or may accelerate fibrosis, the prognostic impact of its high prevalence is yet unclear. Therefore, we investigated whether the presence of DM in patients with cirrhosis was associated with increased mortality, and/or with an increased incidence of spontaneous bacterial peritonitis (SBP), a common and serious infection in patients with cirrhosis.

Methods: We reviewed medical and laboratory data of 230 patients with cirrhosis from the period 2001-2011, of whom data were complete in n=226. Severity of liver cirrhosis was classified using the Child-Pugh and the Model for End-stage Liver Disease (MELD) score. Follow-up was performed until May 2012, with only 12 patients lost to follow-up. SBP was defined as the presence of ascites with an ascitic fluid polymorphonuclear count  $\geq 250$  cells/mm<sup>3</sup> and/or a positive culture. We used Cox regression analyses to investigate the associations between DM and mortality and incident SBP.

Results: DM was present at baseline in 78 patients (35%). Median follow up was 6.2 years [IQR 3.1-9.3], during which 118 patients died (47/78 with DM (60%) and 71/148 without DM (48%)). Median survival was 4.2 years (95%CI 2.5-5.8) for patients with DM, and 7.2 years (95%CI 4.5-9.9) for patients without DM (HR 1.45; 95%CI 1.00-2.10). However, DM was no longer associated with mortality after adjustment for age (HR 1.00; 95%CI 0.67-1.50). Further adjustment for sex, aetiology of cirrhosis, platelet count, and the Child-Pugh score or MELD score did not change this finding. During follow-up, 37 patients developed incident SBP (19 with DM and 18 without DM). The presence of DM at baseline was associated with incident SBP (HR 2.39; 95%CI 1.24-4.60), even after adjustment for age, sex, aetiology of cirrhosis, platelet count, and the Child-Pugh score (HR 2.37; 95%CI 1.09-5.14) or MELD score (HR 2.47; 95%CI 1.14-5.33).

Conclusions: The presence of DM in patients with cirrhosis was associated with an increased risk of SBP, which may represent an increased susceptibility to infections. On the other hand, DM was not associated with increased mortality in these patients.

## Klinische Fysica

### Kloeze C

#### Significante dosisreductie door gebruik van stroostralingswerend afdek materiaal bij EVAR procedures

Carla Kloeze\*, Lisa Klompenhouwer\*, Peter Brands\*, Marc van Sambeek\*,  
Philippe Cuypers\*, Joep Teijink\*

Achtergrond en doel: Jaarlijks worden in het Catharina Ziekenhuis ruim 160 EVAR (EndoVascular Aneurysm Repair) procedures uitgevoerd. Deze procedures vinden plaats onder Röntgendoorlichting, waarbij naast de patiënt ook de arts en het instrumenterende personeel blootgesteld worden aan straling. Vanwege het toenemende aantal interventies onder Röntgendoorlichting en de verlaging van de Europese richtlijn (ICRP 2011) voor de ooglensdosis naar 20 mSv/jaar is een extra stralingsbeschermende maatregel wenselijk. Bij andere interventies onder Röntgendoorlichting zijn dosisreducties van 33-88% gemeten door gebruik van stroostralingswerend afdek materiaal (Radpad, Wit inc., US) [1,2]. Het doel van deze studie is het bepalen van de dosisreductie voor de vaatchirurg (interventionalist) en het instrumenterende personeel door gebruik van de Radpad tijdens EVAR procedures. Methode: 36 Opeenvolgende EVAR procedures werden gerandomiseerd tussen uitvoering met en zonder Radpad. Dosismetingen werden verricht op de hand en borst van de vaatchirurg en de borst van de instrumenterende OK-assistent. De dosis op de borst is een goede maat voor de ooglensdosis.

Resultaten: De jaardosis op de borst en ooglens verkregen tijdens EVAR procedures wordt door gebruik van de Radpad verlaagd van 12,6 mSv naar 6,5 mSv voor de interventionalist en van 3,4 mSv naar 1,5 mSv voor de OK-assistent, overeenkomend met een gemiddelde dosisreductie per procedure van respectievelijk 52% en 57%. De handdosis van de interventionalist is verlaagd van 38 mSv naar 19 mSv; dit betekent een gemiddelde dosisreductie van 50% per procedure.

Conclusie: De Radpad is een effectieve dosisreducerende maatregel voor interventionalisten en instrumenterend personeel tijdens EVAR procedures.

### Velden FH van

#### Evaluation of half-time SPECT myocardial perfusion imaging

N Braakman\*, A de Vries\*, FHP van Velden\*, T Has\* PJM Jaegers\*, AJ Arends\*,  
DNJ Wyndaele\*

Background: The use of iterative reconstruction algorithms incorporating 3D collimator beam modelling, e.g. Flash3D, could potentially enable faster single-photon emission computed tomography (SPECT), reducing acquisition time up to 50% of current clinical acquisition time (half-time imaging).

Aim: The aim of this study was to evaluate half-time imaging for myocardial perfusion SPECT.

Methods: The Jaszczak phantom (Data Spectrum) with myocardial insert was acquired on a dual-head gamma camera (e.cam, Siemens Medical Solutions). The phantom was filled with <sup>99m</sup>Tc using a myocardium-to-background ratio of 12.5:1. Eight different acquisitions were performed with a varying number of projection views (8, 12 or 16) and time per view (5, 10, 20, 25, 30 and 40 sec/view). Data were reconstructed using Flash3D (8 iterations, 4 subsets) and currently clinically used filtered-backprojection (FBP). Bulls eye plots were derived from reconstructed images and were evaluated using the Siemens reference database.

Results: For a male reference database similar results were observed between Flash3D and FBP. However, for a female reference database a large artefact was observed in the right

coronary artery when Flash3D was used. This artefact was not visible when FBP was used. Sufficient image quality was observed while using FBP with 40, 30 or 25 sec/view, demonstrating the possibility to reduce scan time.

**Conclusion:** Half-time imaging may be feasible for SPECT myocardial perfusion imaging, reducing acquisition time up to 37% when FBP is used to reconstruct the data. Although Flash3D reconstructions may further decrease acquisition time, further research is required to investigate the potential value of Flash3D.

**Vernieuwende elementen:** The present study shows that acquisition time for single-photon emission computed tomography (SPECT) myocardial perfusion imaging can be reduced up to 37% when using standard FBP reconstruction techniques. However, caution should be taken before introducing the iterative Flash3D reconstruction technique as reconstruction artefacts may be introduced (under investigation).

## Longgeneeskunde

Arkel C van

### Predicting factors for early and long term mortality after thoracotomy in patients with primary lung cancer

C. van Arkel\*, D.W. Dumoulin\*, P. van der Lee\*, A.H.M.van Straten\*, F.J. Ter Woort\*, S. Houterman\*, B.E.E.M van den Borne\*

**Background:** To determine factors predicting early and long term mortality in patients who underwent a thoracotomy because of primary lung cancer.

**Methods:** Data of patients who underwent a thoracotomy in the Catharina Hospital Eindhoven between 1 January 1995 and 1 January 2011 have been collected retrospectively from the medical files. Early mortality was defined as mortality <30 days after surgery. Last date of follow up was 1 January 2013. Patients were divided in three periods according to date of surgery (1: 1995-1999, 2: 2000-2004 and 3: 2005-2010). Predicting factors for early mortality were assessed with uni- and multivariate logistic regression analysis. For long-term mortality and survival predicting factors were assessed using the Cox proportional hazards model and Kaplan-Meier survival curves.

**Results:** In total 501 patients underwent a thoracotomy due to primary lung cancer. Overall 30 day mortality was 5.6% (n=28). Early mortality was 5.2% for lobectomy (n=290), 2.9% for bilobectomy (n=29) and 10% for pneumonectomy (n=110). Multivariate analysis showed that age over 70 (p=0.002), pneumonectomy (p=0.004) and a pre-operative VO<sub>2</sub>max of <15 ml/kg/min (p=0.02) were significant predictors of early mortality. With respect to long term survival, 308 (62%) patients had died at the end of the follow-up period. Median survival time was 44 months, with an overall 5- and 10- year survival of 45% and 27% respectively. The 5- and 10-year survival for stage I, II and III-IV was 61% and 37%; 46% and 30%;16% and 6.6%, respectively (p<0.0001, log rank test). Finally Cox regression analysis showed that stage (stage I (HR 0.30; 95% CI 0.22-0.42), stage II (HR 0.38; 95% CI 0.26-0.57) compared to stage III-IV, FEV<sub>1</sub>% ≤70% (HR 1.57; 95% CI 1.16-2.11), a history of cerebrovascular disease (CVD) (HR 1.97; 95% CI 1.20-3.23) and surgery in an earlier time period (1 (HR 1.50; 95% CI 1.04-2.17); 2 (HR 1.46; 95% CI 1.05-2.02) compared to 3 were significant predictors of long term mortality.

**Conclusion:** In this cohort age, pneumonectomy and pre-operative VO<sub>2</sub>max are significant predictors of early mortality. Significant predictors of long term mortality are disease stage, FEV<sub>1</sub>%, a history of CVD and surgery in an earlier time period.

## Maag-darm-leverziekten

### Sommen F van der

#### Computer-aided Delineation of Early Neoplasia in Barrett's Esophagus Using High Definition Endoscopic Images

F. van der Sommen#, S. Zinger, P. H. N. de With, E. J. Schoon\*

**BACKGROUND:** Adenocarcinoma of the esophagus is the fastest rising type of cancer in the Western world. The recent development of High Definition endoscopy has enabled the specialist physician to identify Barrett's cancer at an early stage. Nevertheless, it still requires considerable effort, training and expertise to be able to recognize these irregularities associated with early cancer.

**GOAL:** Investigate the technical feasibility of a system that supports the gastroenterologist in finding early Barrett's cancer.

**METHODS:** An algorithm has been developed for finding early cancer in endoscopic images. We divide the image into small regions, where we quantify color and texture (surface irregularity) information of each region. This information is put into a vector, so we obtain a vector for each region in the image. Next, we employ a Support Vector Machine (SVM) in order to classify each region as being either cancerous, or non-cancerous. The classified regions are used to annotate the early cancerous tissue in the endoscopic image.

**RESULTS:** For training and testing the SVM classifier, 103 images of 30 patients have been selected. We have evaluated different region sizes and color spaces. The SVM achieved a maximum regionbased classification accuracy of 94.2% and similar sensitivity and specificity.

**CONCLUSION:** Our experiments show that our approach is promising for a computer-aided detection system that helps the endoscopist in finding early Barrett's Cancer. However, further research is needed to investigate the feasibility of such a real-time support system.

### Sommen F van der

#### Colonoscopy Pit-Pattern Classification Based on Shape Features

F. van der Sommen#, S. Zinger, P. H. N. de With, E. J. Schoon\*

**BACKGROUND:** With magnifying endoscopy, specialist physicians are able to make a presumptive tissue diagnosis by studying the pit pattern of a lesion in the colon (Kudo et al.), since this pattern corresponds with the histology. This could enable the endoscopist to directly remove adenomatous polyps and leave the hyperplastic polyps in situ, hereby reducing the risk and costs of colonoscopies.

**GOAL:** Investigate the technical feasibility of a system, that supports the endoscopist in classifying the pit pattern type of colonic lesions.

**METHODS:** We propose an algorithm, that uses shape information of the pits to identify the type of pit pattern of the lesion. We define four descriptive measures: Elongation, Circularity, Irregularity and Convexity. These measures are computed for every pit in an image obtained with magnifying colonoscopy. For each pit, the pit type is determined using a trained Support Vector Machine (SVM). The pit pattern is classified as the most occurring pit type in the image, using the occurring percentage as a reliability parameter.

**RESULTS:** We have yet tested the proposed algorithm using 36 clinically validated pit pattern images acquired by a magnifying colonoscope. The system achieved an classification accuracy of 88.9% and similar sensitivity and specificity.

**CONCLUSION:** Our first experiments show that the proposed measures are able to capture the shape of the mucosal pits relatively well and that the pit pattern type can be derived from classified pits. Research is ongoing to further develop and validate the proposed system.

## Spoeisende Hulp

**Timmermans JJ**

### **Efficiency of the Emergency Department of the Catharina Hospital in Eindhoven**

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ir. M. Wolleswinkel-Schriek\*, drs. A.v.d. Waarsenburg\*

Introduction: The ED is a multidisciplinary department that operates 24/7 and delivers high quality critical, emergent and urgent care.

Objective: Develop model to provide insights in efficiency and effect of improvements for waiting time reduction. The simulation model, is developed in Chi 3.0. Patients are created by the generator G and transported to the waiting room W. The traige T is used to determine the urgency. The ED has 18 treatment rooms Rn to examine and treat the patient. The simulated patient flow is similar to the real-life situation. Distributions for patient arrivals and treatment times are derived from historical data. Tools have been developed for the analysis of historical data and simulation output. A patient group and time interval can be selected via the user-friendly interface. The simulation model can be used to evaluate:

- The effect of opportunities for efficiency improvement.
- Future scenarios, such as the effects of an aging population or closure of neighboring EDs.

Conclusion:

- The simulation model represents the reality relatively close.
- Improvement opportunities can be evaluated.
- Future scenarios can be investigated.

## Urologie

**Brinkman WM**

### **How did the first generation of robot urologists train robot assisted laparoscopy and what can we learn from their experience?**

Willem Brinkman\*, Barbara Schout, Evert Koldewijn\*, John Rietbergen, Fred Witjes, Jeroen van Merriënboer

Introduction: The da Vinci robot is since its introduction in 1999 rising in popularity worldwide, especially in urology. The first generation of robot urologists that started robot assisted laparoscopy trained by self-guided learning. There are still limited training programs developed to train robot-assisted laparoscopy. Aim of this study was to get insight in the way training of the first generation was organized and to formulate recommendations for the next generation.

Method: An online questionnaire containing 19 multiple choice and Likert scale questions, was sent by a European robotic urology section mailing. Subject of the questions were: demographics, experience in robot-assisted laparoscopy, experience in training and opinion on training of a future generation of urologists.

Results: 94 robot urologists completed the questionnaire. Median year of start with robot-assisted laparoscopy was 2009 (2000-2012). Median number of supervised procedures at start of robot-assisted laparoscopy was 5 (range 0-100). 72% of the urologists did not complete any exam on knowledge or skills before starting robot assisted laparoscopy. Most important training components for a future generation according to the respondents were supervision (average score 4.7 on 5-points scale), live observations (4.4) video observations (4.3) and table assisting (4.4). Respondents indicated that the minimum training components before start of patient related learning were: live observations (94% indicated this as

essential) video observations (90%) knowledge training (88%) table assisting (87%) and basic skills training (69%).

Conclusion: The first generation of robot urologists did train but did not complete an exam on knowledge or skills. Besides, only a limited number of procedures were supervised. Observations, knowledge training and basic skills training are indicated as minimum training components for a future generation of robot urologists.

Vernieuwende aspecten: Er is nog niet eerder beschreven hoe bij de de eerste generatie van robot urologen de training heeft plaats gevonden.

## **Brinkman WM**

### **Trends and results of the European Basic Laparoscopic Urological Skills Exam**

Brinkman WM\*, Tjiam IM, Schout BMA, Koldewijn EL\*, Witjes JA

Introduction: The European Basic Laparoscopic Urological Skills (E-BLUS) program is implemented as an elective basic laparoscopy exam for last year urology residents. This exam and norm of the exam are extensively validated and set as a mandatory exam for second year residents in the Netherlands. Main research question of this study was: Do the European participants of the E-BLUS pass the exam according to the Dutch norm?

Method: The E-BLUS exam consists of 5 tasks validated for training of urological laparoscopic basic skills. [1,2] Participants of the exam were last year urology residents from different European countries during the European Urology Residents Education Program (EUREP) in September 2011 and 2012. Tutors during the exam were European urologists with experience in laparoscopy who completed the teach the teacher training of the E-BLUS. After the exam all participants completed a questionnaire with regards to demographics, experience in laparoscopy and training.

Results: 104 participants from 20 countries completed the exam in 2011 and 2012. Only 2 participants passed according to the validated Dutch norm. According to the questionnaire 65% of all participants did not have a skills lab in their hospital. 61 % did not train any basic skills in the 4 weeks prior to the exam. The last year urology residents performed on average 12 (part of) laparoscopic procedures.

Conclusion: The first results of the E-BLUS are disappointing. A possible cause can be internal and external motivation, including insufficient preparation. Better instructions and better training facilities should improve the results in the upcoming years.

Vernieuwende aspecten: Deze studie beschrijft de resultaten van de introductie van het eerste gestandaardiseerde Europese laparoscopie urologische vaardigheden examen

## **Vries AH de**

### **Het 40-uren project: door training in skillslabs& Urologische operaties veiliger en beter**

A.H. de Vries\*, C. Wagner, E. Koldewijn\*, R. Pelger, M. Boute, B. Schout

Binnen de opleiding Urologie is het niet meer acceptabel om een AIOS alleen volgens het klassieke meester-gezel model operatieve vaardigheden te leren, waarbij de patiënt het belangrijkste oefenmedium is. Dit vanwege ethische redenen, de behoefte om efficiënter gebruik te maken van tijd en geld op de operatiekamer en het streven naar verbetering van kwaliteit van de opleiding en zorg. Dit heeft geresulteerd in de ontwikkeling van een nationaal gestandaardiseerd trainingsprogramma van praktische vaardigheden voor AIOS Urologie, welke op dit moment in Nederland wordt geïmplementeerd: het 40 uren project.

Doelstelling: Evaluatie van de (kosten) effectiviteit van de implementatie van een nationaal gestandaardiseerd trainingsprogramma met praktische vaardigheden voor AIOS urologie.

Methode Het 40-uren project bestaat uit 40 trainingsmodules van een uur, onderverdeeld in een theoretisch en praktisch deel. Drie modules, te weten cystoscopie, echo prostaat, en de TURP, zullen worden geëvalueerd. Dit gebeurt in zes centra (4 interventie centra, 2 controle centra). Begonnen wordt met een nulmeting, waarin deze ingrepen geobserveerd worden en semigestructureerde interviews afgenomen worden (AIOS, supervisor, verpleegkundige). Hiernaast zal de patiënt gevraagd worden een vragenlijst in te vullen. Na het doorlopen van de trainingsmodules zal de evaluatie in deze zes centra herhaald worden.

Resultaten: Beoogde resultaten van dit project zijn:

- Verbetering van kennis en skills van de AIOS
- Verkorting van interventie tijd
- Verbetering van volledigheid registratie
- Verhoging van het patiëntcomfort tijdens de diagnostische procedures

Conclusie. Het 40-uren project richt zich op verbetering van kwaliteit van onderwijs voor AIOS Urologie en hierdoor verbetering van kwaliteit van zorg. \_Dát wat je kunt leren buiten de patiënt om, moet ook zo gedaan worden.

Vernieuwende element van de studie± Het 40-uren project is binnen de Urologie wereldwijd het eerste project waarin landelijk een gestructureerd trainingsprogramma voor praktische vaardigheden wordt uitgerold. Indien dit programma een succes wordt, zal dit hoogstwaarschijnlijk wereldwijd binnen de Urologie, maar mogelijk ook binnen de Chirurgie/Gynaecologie volgelingen krijgen.



## Tabellen

**Tabel 1: Overzicht aantal publicaties**

<b>Specialisme</b>	<b>Tijdschrift artikelen</b>	<b>Promoties</b>	<b>Boeken</b>	<b>Hoofstuk</b>	<b>Totaal</b>
Algemeen Klinisch					
Laboratorium	8				8
Anesthesiologie	15			2	17
Apotheek	1			1	2
Cardiologie	41	1		1	43
Cardiothoracale chirurgie	11				11
Chirurgie	66	2	1	5	74
Dermatologie	6				6
ECC en Bloedmanagement	1				1
Geestelijke verzorging	2			2	4
Geriatric	2				2
Gynaecologie	13				12
Intensive care	1				1
Inwendige geneeskunde	20	1			21
Kindergeneeskunde	5			1	6
Klinische Fysica	11			1	12
Longgeneeskunde	12	2		1	15
Maag, darm en leverziekten	6				6
Medische psychologie		1			1
Mondziekten en kaakchirurgie	1				1
Neurologie	13	1			14
Onderwijs en Onderzoek	8	1		1	10
Operatie Kamers	2			1	3
Pamm	11	1			12
Plastische chirurgie	5				5
Radiologie	8				8
Radiotherapie	11				11
SEH	1		1		2
Urologie	4	1			5
<b>Totaal</b>	<b>285</b>	<b>11</b>	<b>2</b>	<b>16</b>	<b>314</b>

**Tabel 2 Wetenschapsavonden**

<b>Specialisme</b>	Wetenschaps avond 2012	Wetenschaps avond 2012	<b>Totaal</b>	Wetenschaps avond 2013	Wetenschaps avond 2013	<b>Totaal</b>
	Presentaties	Posters		Presentaties	Posters	
Algemeen Klinisch Laboratorium	1	1	2	1	2	3
Apotheek		2	2		1	1
Cardiologie	1	2	3	1	3	4
Chirurgie				1	7	8
ECC en Bloedmanagement					1	1
Geriatric	1		1			
Gynaecologie					3	3
Intensive care					1	1
Inwendige geneeskunde		1	1		2	2
Klinische Fysica	1		1	1	2	3
Longgeneeskunde					1	1
Maag, darm en leverziekten					2	2
Onderwijs en Onderzoek		1	1			
SEH					1	1
Urologie	1		1	1	2	3
<b>Totaal</b>	<b>5</b>	<b>7</b>	<b>12</b>	<b>5</b>	<b>28</b>	<b>33</b>

**Tabel 3: Overzicht aantal aantal artikelen en gemiddelde impactfactor per specialisme**

Specialisme	Artikelen met impactfactor	Artikelen zonder impactfactor	Totaal aantal artikelen	Gemiddelde impactfactor	Standaard deviatie
Algemeen Klinisch					
Laboratorium	6	2	8	2.388	2.453
Anesthesiologie	10	5	15	1.759	1.614
Apotheek	1		1	3.485	0
Cardiologie	35	6	41	5.992	8.869
Cardiothoracale chirurgie	7	4	11	1.553	1.566
Chirurgie	56	10	66	3.372	6.749
Dermatologie	6		6	3.503	0.619
ECC en Bloedmanagement	1		1	0.918	0
Geestelijke verzorging		2	2	0	0
Geriatricie	2		2	8.382	8.077
Gynaecologie	9	4	13	3.774	4.344
Intensive care	1		1	2.072	0
Inwendige geneeskunde	19	1	20	3.678	2.098
Kindergeneeskunde	5		5	3.733	2.174
Klinische Fysica	10	1	11	3.590	2.039
Longgeneeskunde	6	6	12	1.685	2.070
Maag, darm en leverziekten	5	1	6	4.757	2.465
Mondziekten en kaakchirurgie	1		1	1.506	0
Neurologie	10	3	13	4.613	3.237
Onderwijs en Onderzoek	6	2	8	2.239	1.495
Operatie Kamers	1	1	2	1.643	2.324
Pamm	10	1	11	3.170	1.522
Plastische chirurgie	5		5	1.729	0.681
Radiologie	8		8	4.007	1.867
Radiotherapie	11		11	3.609	1.902
SEH	1		1	1.439	0
Urologie	3	1	4	3.063	2.967
<b>Totaal</b>	<b>235</b>	<b>50</b>	<b>285</b>	<b>3.589</b>	<b>5.153</b>

**Tabel 4: Impactfactor per tijdschrift**

Titel	Impact factor	Titel	Impact factor
Acta Anaesthesiol Belg	-	Circulation	14.739
Acta Anaesthesiol Scand	2.188	Clin Chem	7.905
Aliment Pharmacol Ther	3.769	Clin Chem Lab Med	2.150
Am J Cardiol	3.368	Clin Gastroenterol Hepatol	--
Am J Clin Pathol	2.598	Clin Oncol (R Coll Radiol)	2.072
Am J Gastroenterol.	7.282	Clin Vaccine Immunol.	2.546
Am Surg	1.285	Crit Care	4.607
Anaesth Intensive Care	1.279	Curr Opin Lipidol	6.086
Anaesthesia	2.958	Curr Pharm Biotechnol	-
Anaesth Analg	3.286	Dermatol Surg	1.798
Ann Oncol	6.425	Dev Med Child Neurol	2.918
Ann Surg Oncol	4.166	Diabetes Technol Ther	1.931
Ann Surg	7.492	Dis Colon Rectum	3.132
Ann Thorac Surg.	3.741	Drugs Aging	2.671
Ann Vasc Surg	1.035	EJC Supplements	-
Arch Pathol Lab Med	2.577	Emerg Med J	1.439
Asean Heart Journal	-	Endoscopy	5.210
Asian Cardiovasc Thorac Ann.	-	Epidemiol Infect	2.843
Atherosclerosis	3.794	Eur Heart J.	10.478
Biochim Biophys Acta	-	Eur J Cancer.	5.536
BJOG	3.407	Eur J Cardiothorac Surg.	2.550
Blood Purif	2.104	Eur J Clin Microbiol Infect Dis.	2.859
BMC Cancer	3.011	Eur J Radiol	2.606
BMC Cardiovasc Disord	1.517	Eur J Surg Oncol	2.499
BMC Med Inform Decis Mak	1.477	Eur J Vasc Endovasc Surg	2.991
BMC Neurol	2.167	Eur Radiol	3.222
BMC Res Notes	-	Euro Surveill	6.150
BMC Surg.	1.333	EuroIntervention	3.285
BMJ	14.093	Europace	1.980
BMJ Open	-	European Surgery	0.283
Bone	4.023	Fertil Steril.	3.775
Br J Anaesth	4.243	Gen Thorac Cardiovasc Surg	-
Br J Cancer	4.023	Gynecol Oncol.	3.888
Br J Dermatol	3.666	Health Psychol	3.873
Br J Surg	4.606	Heart Rhythm	4.102
Brain	9.457	Hernia	1.843
Breast	2.491	Hum Brain Mapp	5.880
Breast Cancer Res	5.245	Hum Reprod	4.475
Breast Cancer Res Treat.	5.245	Hypertension	6.207
Cancer Causes Control	2.877	Immunohematology	-
Cardiovasc Diabetol	3.346	Int J Artif Organs	1.861
Case Reports in Anesthesiol	--	Int J Cancer	5.444
Circ Arrhythm Electrophysiol	--	Int J Gynecol Obstet	2.045
Circ Cardiovasc Interv	6.058	Int J Integr Care	--
Circ J	3.766	Int J Oral Maxillofac Surg	1.506

Int J Radiat Oncol Biol Phys	4.105	Neurobiol Aging	6.189
Int J Surg	-	Neurology	8.312
Interact Cardiovasc Thorac Surg	-	Neurourol Urodyn	2.958
ISRN Surg	-	NTOG: Ned tijdschr Obst Gyn	-
J Affect Disord	3.517	NTvAA: Ned Ts Allerg Astma	-
J Alzheimers Dis	3.745	Nucl Med Commun	1.404
J Am Coll Cardiol	14.156	Obes Surg	3.286
J Am Soc Nephrol	9.663	Open J of Internal Med	-
J Anesth	0.831	Pancreas	2.386
J Bone Miner Res	6.373	Patient Educ Couns	2.305
J Cardiothorac Vasc Anesth.	1.640	Perfusion	0.918
J Cardiovasc Surg (Torino).	1.559	Pharmacogenet genomics	3.485
J Clin Endocrinol Metab.	5.967	PLoS Med	16.269
J Clin Gastroenterol	3.159	Plos One	-
J Clin Microbiol	4.153	Pol Przegl Chir	-
J Clin Oncol	18.372	Pulm Pharmacol Ther	2.800
J Crohns Colitis	2.566	Qual Life Res	2.300
J Eur Acad Dermatol Venereol.	2.980	Radiat Oncol	2.321
J Heart Valve Dis	0.811	Radiother Oncol	5.580
J Infect	4.126	Reg Anesth Pain Med.	4.079
J Inherit Metab Dis	3.577	Respir Med	2.475
J Multidiscip Healthc	-	Respir Res	-
J Neurosci	7.115	Revista portuguesa de cirurgia	-
J Obstet Gynaecol Res	0.942	Stroke.	5.729
J Occup Rehabil	-	Surg Endosc	4.013
J Pediatr (Rio J)	1.013	Thorac Cardiovasc Surg	0.882
J Physiol	-	Thromb Res	2.440
J Plast Reconstr Aesthet Surg	1.494	Tijdschr Neurol Neurochir	-
J Proteome Res	5.113	Transplantation	4.003
J Surg Oncol	2.100	Trials	2.496
J Surg Res	2.247	Ultrasound Obstet Gynecol	3.007
J Thromb Haemost	5.731	Urology	2.428
J Vasc Surg	3.153	Vasc Health Risk Manag.	-
JACC Cardiovasc Interv.	6.800	Vascular	0.891
Journal of Gynecologic Surgery	-	Verpleegkunde	-
Knee	1.736	Wideochir Inne Tech Malo Inwazyjne	-
Med Care	3.411	World J Gastroenterol.	2.471
Med Teach	1.217	World J Surg	2.362
Metabolism	2.664		
Microsurgery	1.605		
Minerva Urol Nefrol	-		
Mult Scler	4.255		
N Engl J Med	53.298		
Ned Tijdschr Allergie & Astma	-		
Ned Tijdschr Geneesk	-		
Ned Tijdschr Klin Chem Lab gen	-		
Nephrol Dial Transplant.	3.396		
Neth Heart J.	1.438		
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