

# DE LEESTAFEL

## APRIL 2017

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### *Een Maandelijks Selectie van Wetenschappelijke GE-nieuws*

## Coloproctologie

### Functionele mucosalaag bevordert genezing van colonnaad

*Functional mucous layer and healing of proximal colonic anastomoses in an experimental model, J. W. A. M. Bosmans, BJS, April 2017 – Volume 104 – Issue 5, pages 619-630 .Pubmedid 28195642*

**BACKGROUND:** Anastomotic leakage (AL) is the most dreaded complication after colorectal surgery, causing high morbidity and mortality. Mucus is a first line of defence against external factors in the gastrointestinal tract. In this study, the structural mucus protein Muc2 was depleted in genetically engineered mice and the effect on healing of colonic anastomoses studied in an experimental model.

**METHOD:** Mice of different Muc2 genotypes were used in a proximal colonic AL model. Tissues were scored histologically for inflammation, bacterial translocation was determined by quantitative PCR of bacterial 16S ribosomal DNA, and epithelial cell damage was determined by assessing serum levels of intestinal fatty acid-binding protein.

**RESULTS:** Of 22 Muc2-deficient (Muc2<sup>-/-</sup>) mice, 20 developed AL, compared with seven of 22 control animals (P < 0.001). Control mice showed normal healing, whereas Muc2<sup>-/-</sup> mice had more inflammation with less collagen deposition and neoangiogenesis. A tendency towards higher bacterial translocation was seen in mesenteric lymph nodes and spleen in Muc2<sup>-/-</sup> mice. Intestinal fatty acid-binding protein levels were significantly higher in Muc2<sup>-/-</sup> mice compared with controls (P = 0.011).

**CONCLUSION:** A functional mucous layer facilitates the healing of colonic anastomoses. Colorectal anastomotic leakage remains the most dreaded complication after colorectal surgery. It is known that the aetiology of anastomotic leakage is multifactorial, and a role is suggested for the interaction between intraluminal content and mucosa.

## Helft van patienten met fecale incontinentie baat bij sacrale neurostimulatie op lange termijn

*Fecal incontinence treated by sacral neuromodulation: Long-term follow-up of 325 patient. Paul T.J. Jansse, Surgery: April 2017 Volume 161, Issue 4, Pages 1040–1048 pubmedid 28159117*

**BACKGROUND:** Long-term results of large patient cohorts with fecal incontinence treated by sacral neuromodulation are limited. This study shows the long-term results after a mean follow-up of 7.1 years in 325 patients with fecal incontinence treated by continuous sacral neuromodulation.

**METHODS:** All patients with fecal incontinence and eligible for sacral neuromodulation between 2000 and 2015 were evaluated retrospectively. Primary outcome was a decrease in episodes of fecal incontinence, which was defined as involuntary fecal loss at least once per week and documented by a 3 week bowel habit diary. Quality of life was assessed using the Short-Form 36 and the Fecal Incontinence Quality of Life Score.

**RESULTS:** In the study, 374 patients were included for sacral neuromodulation screening and 325 patients (32 male, 9.7%) received permanent, continuous sacral neuromodulation. Mean age was 56.5 years (17–82 years) and mean follow-up was 7.1 years (3.0–183.4 months). In the 325 patients with permanent sacral neuromodulation, fecal incontinence episodes decreased from a mean of  $16.1 \pm 14.5$  to  $3.0 \pm 3.7$  per 3-week period after sacral neuromodulation ( $P < .001$ ) according to the bowel habit diary. Sacral neuromodulation was removed due to unsatisfactory results in 81 patients. Quality of life (both Short-Form 36 and Fecal Incontinence Quality of Life Score) showed no significant difference compared with the Dutch population during follow-up.

**CONCLUSION:** Long-term efficacy of sacral neuromodulation can be maintained in about half (52.7%) of all patients screened with sacral neuromodulation for fecal incontinence after a mean follow-up of 7.1 years. Importantly, the quality of life of patients with sacral neuromodulation for fecal incontinence did not differ from the general population.

## Upper GI

### Oogsten van lymfeklieren goed mogelijk na neoadjuvante chemotherapie bij patienten die een transthoracale oesophagusresectie ondergaan

*Impact of Extent of Lymphadenectomy on Survival, Post Neoadjuvant Chemotherapy and Transthoracic Esophagectomy, Phillips, Alexander W Annals of Surgery; April 2017 – Volume 265 – Issue 4 – p 750-756 PMID: 27467444*

**OBJECTIVE:** The aim of this study was to evaluate the influence of lymph node yield and the location of nodes on prognosis in patients with distal esophageal or gastroesophageal junction adenocarcinoma who have received neoadjuvant chemotherapy followed by transthoracic esophagectomy.

**BACKGROUND:** Debate continues regarding the extent of lymphadenectomy required when carrying out an esophagectomy. Lymph node yield has been used as a surrogate for extent of lymphadenectomy. Node location must, however, be reviewed to determine the true extent of lymphadenectomy.

**METHODS:** Data from consecutive patients with potentially curable adenocarcinoma of the lower esophagus or gastroesophageal junction were reviewed. Patients were treated with neoadjuvant chemotherapy, transthoracic esophagectomy, and 2-field lymphadenectomy. Outcomes according to lymph node yield were determined. Projected prognosis of carrying out less radical lymphadenectomies was calculated according to 3 groups: group 1-exclusion of proximal thoracic nodes, group 2-a minimal abdominal lymphadenectomy, and group 3-a minimal abdominal and thoracic lymphadenectomy.

**RESULTS:** Three hundred five patients were included. Median cancer-related survival was 37.7 months (confidence interval 29-46 mo). Absolute lymph node retrieval was not related to survival ( $P = 0.520$ ). An estimated additional 4 (2-6) cancer-related deaths were projected if group 1 nodes were omitted, 2 (1-4) additional deaths if group 2 nodes were omitted, and 9 (6-12) extra deaths if group 3 nodes were omitted. A minimal 24lymphadenectomy (groups 1, 2, and 3) was projected to lead to a 23% reduction in survival in patients with N1 or N2.

**CONCLUSION:** The present study demonstrates high lymph node yields are possible after transthoracic esophagectomy with en bloc 2-field lymphadenectomy in patients post neoadjuvant chemotherapy. This allows excellent postoperative staging. Furthermore, the extent of lymphadenectomy must be correlated with node location, which may have important implications in patients who have a less extensive lymphadenectomy.

## Voordeel van verrichten distale gastrectomie in oudere patienten ten opzichte van ‘supportive care’

*Survival benefit of gastrectomy for gastric cancer in patients ≥85 years old: A retrospective propensity score-matched analysis. Shunji Endo, Surgery: April 2017 Volume 161, Issue 4, Pages 984–994 PMID: 27894711*

**BACKGROUND:** The purpose of this study was to compare the long-term outcomes of patients ≥85 years old with gastric cancer who underwent curative distal gastrectomy or best supportive care alone.

**METHODS:** Among 241 consecutive patients aged ≥85 years who were diagnosed with gastric cancer, we retrospectively examined the cases of 56 patients that were treated with curative distal gastrectomy and 55 patients that were treated with best supportive care alone. To reduce selection bias, we conducted a propensity score-matching analysis. The patients’ propensity scores were estimated using a logistic regression model based on the following variables: sex, age, clinical cancer stage, performance status score, and each item of the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity score. Overall survival was compared using the Kaplan-Meier method and log-rank test.

**RESULTS:** Thirty pairs of patients were generated via propensity score matching. The clinical characteristics of the 2 groups were well matched. The median overall survival time was 57.3 months after distal gastrectomy, while it was 16.0 months after best supportive care ( $P = .0002$ ). Subgroup analyses of each sex showed that in males there was no significant difference in overall survival between distal gastrectomy and best supportive care ( $P = .37$ ) while the overall survival of females was significantly better after distal gastrectomy than after best supportive care ( $P < .0001$ ).

**CONCLUSION:** Our propensity score-matched study suggested that distal gastrectomy results in significantly better long-term survival than best supportive care alone in female patients with gastric cancer aged ≥85 years. In males, the indications for operation should be carefully determined.

## HPB

## Geen effect ‘duct-to-mucosa’ pancreaticogastrostomie op fistelvorming na distale pancreatectomie.

*Randomized clinical trial of duct-to-mucosa pancreaticogastrostomy versus handsewn closure after distal pancreatectomy. K. Uemura, BJS, April 2017 – Volume 104 – Issue 5, pages 536-543. PMID: 28112814*

**BACKGROUND:** Postoperative pancreatic fistula (POPF) remains a major cause of morbidity after distal pancreatectomy. The aim of this study was to investigate whether duct-to-mucosa pancreaticogastrostomy of the pancreatic stump decreased clinical POPF formation compared with handsewn closure after distal pancreatectomy.

**METHODS:** This multicentre RCT was performed between April 2012 and June 2014. Patients undergoing distal pancreatectomy were assigned randomly to either duct-to-mucosa pancreaticogastrostomy or handsewn closure. The primary endpoint was the incidence of clinical POPF. Secondary endpoints were rates of other complications and length of hospital stay.

**RESULTS:** Some 80 patients were randomized, and 73 patients were evaluated in an intention-to-treat analysis: 36 in the pancreaticogastrostomy group and 37 in the handsewn closure group. The duration of operation was significantly longer in the pancreaticogastrostomy group than in the handsewn closure group (mean 268 versus 197 min respectively;  $P < 0.001$ ). The incidence of clinical POPF did not differ between groups (7 of 36 versus 7 of 37; odds ratio (OR) 1.03, 95 per cent c.i. 0.32 to 3.10;  $P = 1.000$ ). The rate of intra-abdominal fluid collection was significantly lower in the pancreaticogastrostomy group (6 of 36 versus 21 of 37; OR 0.15, 0.05 to 0.45;  $P < 0.001$ ). There were no statistically significant differences in the rates of other complications or length of hospital stay.

**CONCLUSION:** Duct-to-mucosa pancreaticogastrostomy did not reduce the incidence of clinical POPF compared with handsewn closure of the pancreatic stump after distal pancreatectomy.

## Tumorgrootte pancreastumoren alleen prognostisch in het geval van gelokaliseerde ziekte.

*Relationship between tumour size and outcome in pancreatic ductal adenocarcinoma. D. Ansari, BJS, April 2017 – Volume 104 – Issue 5, pages 600-607. PMID: 28177521*

**BACKGROUND:** The size of pancreatic ductal adenocarcinoma (PDAC) at diagnosis is an indicator of outcome. Previous studies have focused mostly on patients with resectable disease. The aim of this study was to investigate the relationship between tumour size and risk of metastasis and death in a

**METHODS:** Patients diagnosed with PDAC between 1988 and 2013 were identified from the Surveillance, Epidemiology, and End Results (SEER) database. Tumour size was defined as the maximum dimension of the tumour as provided by the registry. Metastatic spread was assessed, and survival was calculated according to size of the primary tumour using the Kaplan–Meier method. Cox proportional regression modelling was used to adjust for known confounders.

**RESULTS:** Some 58 728 patients were included. There were 187 patients (0.3 per cent) with a tumour size of 0.5 cm or less, in whom the rate of distant metastasis was 30.6 per cent. The probability of tumour dissemination was associated with tumour size at the time of diagnosis. The association between survival and tumour size was linear for patients with localized tumours, but stochastic in patients with regional and distant stages. In patients with resected tumours, increasing tumour size was associated with worse tumour-specific survival, whereas size was not associated with survival in patients with unresected tumours. In the adjusted Cox regression analysis, the death rate increased by 4.1 per cent for each additional 1-cm increase in tumour size.

**CONCLUSION:** Pancreatic cancer has a high metastatic capacity even in small tumours. The prognostic impact of tumour size is restricted to patients with localized disease.

## Leverchirurgie

### Geen conclusie mogelijk over duur van ziekenhuisopname en verminderde morbiditeit bij laparoscopische leversegmentresectie ten opzichte van open segmentresectie.

*Randomized clinical trial of open versus laparoscopic left lateral hepatic sectionectomy within an enhanced recovery after surgery programme (ORANGE II study). E. M. Wong - Lun-Hing, BJS, April 2017 – Volume 104 – Issue 5, pages 525-535. PMID: 28138958*

**Background** Laparoscopic left lateral sectionectomy (LLLS) has been associated with shorter hospital stay and reduced overall morbidity compared with open left lateral sectionectomy (OLLS). Strong evidence has not, however, been provided.

**Method** In this multicentre double-blind RCT, patients (aged 18–80 years with a BMI of 18–35 kg/m<sup>2</sup> and ASA fitness grade of III or below) requiring left lateral sectionectomy (LLS) were assigned

randomly to OLLS or LLLS within an enhanced recovery after surgery (ERAS) programme. All randomized patients, ward physicians and nurses were blinded to the procedure undertaken. A parallel prospective registry (open non-randomized (ONR) versus laparoscopic non-randomized (LNR)) was used to monitor patients who were not enrolled for randomization because of doctor or patient preference. The primary endpoint was time to functional recovery. Secondary endpoints were length of hospital stay (LOS), readmission rate, 19 overall morbidity, composite endpoint of liver surgery-specific morbidity, mortality, and reasons for delay in discharge after functional recovery.

**Results** Between January 2010 and July 2014, patients were recruited at ten centres. Of these, 24 patients were randomized at eight centres, and 67 patients from eight centres were included in the prospective registry. Owing to slow accrual, the trial was stopped on the advice of an independent Data and Safety Monitoring Board in the Netherlands. No significant difference in median (i.q.r.) time to functional recovery was observed between laparoscopic and open surgery in the randomized or non-randomized groups: 3 (3–5) days for OLLS versus 3 (3–3) days for LLLS; and 3 (3–3) days for ONR versus 3 (3–4) days for LNR. There were no significant differences with regard to LOS, morbidity, reoperation, readmission and mortality rates.

**Conclusion** This RCT comparing open and laparoscopic LLS in an ERAS setting was not able to reach a conclusion on time to functional recovery, because it was stopped prematurely owing to slow accrual.

## Resectiepercentage in Noorwegen van colorectale levermetastasen 20% met veel variabiliteiten binnen regio's, patientkarakteristieken en ziekte-specifieke eigenschappen.

*Population-based study on resection rates and survival in patients with colorectal liver metastasis in Norway J.-H. Angelsen, BJS, April 2017 – Volume 104 – Issue 5, pages 580-589.*

[Pmid 28181674](#)

### Background

Detailed knowledge about the proportion of patients with colorectal liver metastases (CLM) undergoing resection is sparse. The aim of this study was to analyse cumulative resection rates and survival in patients with CLM.

**Method** For this population-based study of patients developing CLM during 2011–2013, data were extracted from the Norwegian Patient Registry and the Cancer Registry of Norway.

**Results** A total of 2960 patients had CLM; their median overall survival was 10.9 months. Liver resection was performed in 538 patients. The cumulative resection rate was 20.0 per cent. The cumulative resection rate was 23.3 per cent in patients aged less than 40 years, 31.1 per cent in patients aged 40–59 years, 24.7 per cent in those aged 60–74 years, 17.9 per cent in those aged 75–79 years and 4.7 per cent in patients aged 80 years or more ( $P < 0.001$ ). In multivariable analysis, resection rate was associated with age, extrahepatic metastases, disease-free interval and geographical region. Overall survival after diagnosis of CLM was affected by liver resection (hazard ratio (HR) 0.54, 95 per cent c.i. 0.34 to 0.86), rectal cancer (HR 0.82, 0.74 to 0.90), metachronous disease (HR 0.66, 0.60 to 0.74), increasing age (HR 1.32, 1.28 to 1.37), region, and extrahepatic metastases (HR 1.90, 1.74 to 2.07). Three- and 4-year overall survival rates after hepatectomy were 73.2 and 54.8 per cent respectively.

**Conclusion** The cumulative resection rate in patients with CLM in Norway between 2011 and 2013 was 20 per cent. Resection rates varied across geographical regions, and with patient and disease characteristics.

## Bariatrische chirurgie

### Medicatiegebruik neemt af onder patienten die een Roux-en-Y gastric bypass ondergaan

*Changes in Prescription Drug Use After Gastric Bypass Surgery: A Nationwide Cohort Study*  
Gribsholt, Sigrid, *Annals of Surgery*; April 2017 – Volume 265 – Issue 4 – p 757-765 PMID:  
28124974

**Objective** To evaluate changes over time in drug use among patients undergoing Roux-en-Y gastric bypass (RYGB) surgery and a matched population-based comparison cohort.

**Background** A little is known about the prescription drug use before and after RYGB surgery.

**Methods** Nationwide population-based cohort study included 9908 patients undergoing RYGB in Denmark during 2006 to 2010 and 99,080 matched general population members. We calculated prevalence ratios (PRs) comparing prescription drug use 36 months after RYGB/index date with use 6 months before this date (baseline).

**Results** At baseline, more RYGB patients (median 40 years, 22% males) used a prescription drug (81.5% vs 49.1%). After 3 years, the use had decreased slightly among RYGB patients [PR = 0.93; 95% confidence interval (CI) = (0.91, 0.94)], but increased in the comparison cohort (PR = 1.05; 95% CI = 1.04-1.06). In the RYGB cohort, large, sustained decreases occurred for treatment of metabolic syndrome-related conditions, such as any glucose-lowering drug (PR = 0.28; 95% CI = 0.25-0.31) and lipid-modifying drugs PR = 0.50; 95% CI = 0.46-0.55). Use of inhalants for obstructive airway diseases (PR = 0.79; 95% CI = 0.74-0.85) also decreased. Use of neuropsychiatric drugs was two-fold higher at baseline in the RYGB cohort (22.8% vs 10.9%) and increased further after RYGB—that is, antidepressants (PR = 1.13; 95% CI = 1.07-1.19), antipsychotics (PR = 1.39; 95% CI = 1.21-1.60), and potential treatment of neuropathy (PR = 1.39; 95% CI = 1.28-1.51).

## Effecten van het sluiten van defecten in het mesenterium hetzelfde in RCT als in nationale registratie

*Outcomes of laparoscopic gastric bypass in a randomized clinical trial compared with a concurrent national database, E. Stenberg, BJS, April 2017 – Volume 104 – Issue 5, pages 562-569. PMID: 28239833*

### Background

RCTs are the standard for assessing medical interventions, but they may not be feasible and their external validity is sometimes questioned. This study aimed to compare results from an RCT on mesenteric defect closure during laparoscopic gastric bypass with those from a national database containing data on the same procedure, to shed light on the external validity of the RCT.

### Method

Patients undergoing laparoscopic gastric bypass surgery within an RCT conducted between 1 May 2010 and 14 November 2011 were compared with those who underwent the same procedure in Sweden outside the RCT over the same time interval. Primary endpoints were severe complications within 30 days and surgery for small bowel obstruction within 4 years.

### Results

Some 2507 patients in the RCT were compared with 8485 patients in the non-RCT group. There were no differences in severe complications within 30 days in the group without closure of the mesenteric defect (odds ratio (OR) for RCT versus non-RCT 0.94, 95 per cent c.i. 0.64 to 1.36;  $P = 0.728$ ) or in the group with closure of the defect (OR 1.34, 0.96 to 1.86;  $P = 0.087$ ). There were no differences between the RCT and non-RCT cohorts in reoperation rates for small bowel obstruction in the mesenteric defect non-closure (cumulative incidence 10.9 versus 9.4 per cent respectively; hazard ratio (HR) 1.20, 95 per cent c.i. 0.99 to 1.46;  $P = 0.065$ ) and closure (cumulative incidence 5.7 versus 7.0 per cent; HR 0.82, 0.62 to 1.07;  $P = 0.137$ ) groups. The relative risk for small bowel obstruction without mesenteric defect closure compared with closure was 1.91 in the RCT group and 1.39 in the non-RCT group.

### Conclusion

The efficacy of mesenteric defect closure was similar in the RCT and national registry, providing evidence for the external validity of the RCT.