DE LEESTAFEL

MEI 2019

Een Maandelijkse Selectie van Wetenschappelijke GE-nieuws

Coloproctologie

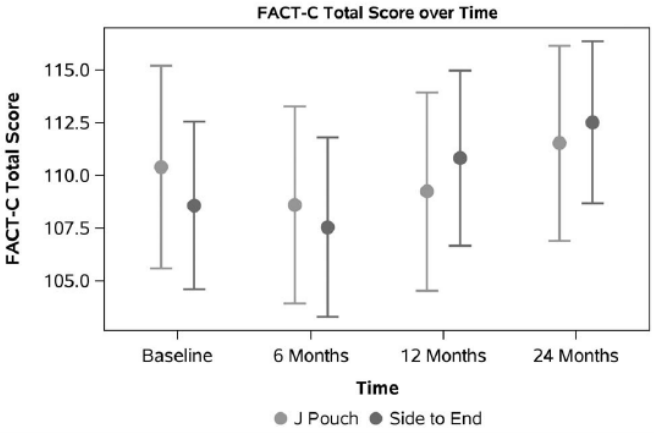
Gelijkwaardig QOL en functional outcome J-pouch en side-to-end anastomose na rectumchirurgie

Better Function With a Colonic J-Pouch or a Side-to-end Anastomosis? A Randomized Controlled Trial to Compare the Complications, Functional Outcome, and Quality of Life in Patients With Low Rectal Cancer After a J-Pouch or a Side-to-end Anastomosis. Y Parc et al. Annals of Surgery: May 2019 - Volume 269 - Issue 5 - p 815–826.
Pubmed ID: 30921049

BACKGROUND INFORMATION: We aimed to compare prospectively the complications and functional outcome of patients undergoing a J-Pouch (JP) or a side-to-end anastomosis (SE) for treatment of low rectal cancer at a 2-year time point after resection for rectal cancer.

METHODS: A multicenter study was conducted on patients with low rectal cancer who were randomized to receive either a JP or SE and were followed for 24 months utilizing SF-12 and FACT-C surveys to evaluate the quality of life (QOL). Fecal incontinence was evaluated using the Fecal Incontinence Severity Index (FISI). Bowel function, complications, and their treatments were recorded**.**

RESULTS: Two hundred thirty-eight patients (165 males) were randomized with 167 final eligible patients, 80 in the JP group and 87 in the SE group for evaluation. The mean age at surgery was 61 (range 29 to 82) years. The overall mean recurrence rate was 12 of 238, 5% and similar in both groups.



COMPLICATIONS: Overall, 37 of 190 (19%) patients reported complications, 14 of these were Clavien Dindo Grade 3b and 2 were 3a: leak 3 (2 JP,1 SE), fistula 4 (1 JP, 3 SE), small bowel obstruction 4 (3JP, 1 SE), stricture 4 (3 SE, 1 SA), pouch necrosis 2 (JP), and wound infection 5 (2 JP, 3 SE). QOL scores using either instrument between the 2 groups at 12 and 24 months were similar ($P > 0.05$). Bowel movements, clustering, and FISI scores were similar.

CONCLUSION: At time points of 1 and 2 years after a JP or a SE for low rectal cancer, QOL, functional outcome, and complications are comparable between the groups. Although choosing a particular procedure may depend on surgeon/patient choice or anatomical considerations at the time of surgery, SE functions similar to JP and may be chosen due to the ease of construction.

Pijnbestrijding na colorectale chirurgie? Intrathecale pijnstilling meest effectief

Randomized clinical trial of liposomal bupivacaine transverse abdominis plane block versus intrathecal analgesia in colorectal surgery. DT Colibaseanu et al. BJS, May 2019 – Volume 106 – Issue 6, pages 692-699.
Pubmed ID: 30919948

BACKGROUND: Transverse abdominis plane (TAP) block is considered an effective alternative to neuraxial analgesia for abdominal surgery. However, limited evidence supports its use over traditional analgesic modalities in colorectal surgery. This study compared the analgesic efficacy of liposomal bupivacaine TAP block with intrathecal (IT) opioid administration in a multicentre RCT.

METHODS: Patients undergoing elective small bowel or colorectal resection were randomized to receive TAP block or a single injection of IT analgesia with hydromorphone. Patients were assessed at 4, 8, 16, 24 and 48 h after surgery. Primary outcomes were mean pain scores and morphine milligram equivalents (MMEs) administered within 48 h after surgery. Secondary outcomes included duration of hospital stay, incidence of postoperative ileus and use of intravenous patient-controlled analgesia.

RESULTS: In total, 209 patients were recruited and 200 completed the trial (TAP 102, IT 98). The TAP group had a 1·6-point greater mean pain score than the IT group at 4 h after surgery, and this difference lasted for 16 h after operation. The TAP group received more MMEs within the first 24 h after surgery than the IT group (median difference in MMEs 10·0, 95 per cent c.i. 3·0 to 20·5). There were no differences in MME use at 24 and 48 h, or with respect to secondary outcomes.

Table 3 Primary and secondary outcomes

	Intrathecal opioid ($n = 98$)	Transversus abdominis plane block ($n = 102$)	Difference	*P*
Mean postoperative pain score*				
0–48 h (primary outcome)	2·4 (2·1, 2·7)	3·0 (2·7, 3·3)	0·6 (0·2, 1·0)	0·007§
4 h	1·8 (1·4, 2·2)	3·4 (2·9, 3·9)	1·6 (1·0, 2·3)	< 0·001§
8 h	1·4 (1·0, 1·8)	3·0 (2·5, 3·5)	1·5 (0·9, 2·2)	< 0·001§
16 h	2·2 (1·6, 2·8)	3·2 (2·6, 3·8)	1·0 (0·1, 1·8)	0·024§
POD 1	2·8 (2·3, 3·2)	2·8 (2·5, 3·1)	0 (–0·5, 0·5)	0·860§
POD 2	2·8 (2·3, 3·2)	2·5 (2·1, 2·9)	–0·2 (–0·8, 0·3)	0·410§
Discharge	2·3 (1·7, 2·8)	2·1 (1·6, 2·6)	–0·2 (–0·9, 0·5)	0·600§
Total MMEs†				
POD 0–2 (primary outcome)	32·5 (24·4, 42·0)	47·5 (35·6, 65·9)	15·0 (–0·5, 35·1)	0·102¶
POD 0	15·0 (7·5, 18·8)	25·0 (18·8, 33·0)	10·0 (3·0, 20·5)	0·002¶
POD 1	7·5 (0, 10·0)	7·5 (5·0, 15·0)	0 (–2·8, 11·4)	0·200¶
POD 2	7·5 (0, 10·5)	0 (0, 7·5)	–7·5 (–9·1, 2·5)	0·250¶
Secondary outcomes				
Duration of hospital stay (days)†	3 (3, 4)	3 (3, 3)	0 (–1, 0)	0·085¶
Intravenous patient-controlled analgesia on POD 0–2 (%)‡	1 (0, 6)	5·0 (2·0, 11·0)	4·0 (–1·0, 10·0)	0·212#
Postoperative ileus (%)‡	14 (7, 21)	11·0 (6·0, 18·0)	–4·0 (–13·0, 6·0)	0·454**

Values in parentheses are 95 per cent confidence intervals: *t-based, †estimated using 1000 bootstrap resamples and ‡estimated using the score method. POD, postoperative day; MME, morphine milligram equivalent. §Two-sample t test, ¶Wilcoxon rank-sum test, #Fisher's exact test and **χ^2 test.

CONCLUSION: IT opioid administration provided better immediate postoperative pain control than TAP block. Both modalities resulted in low pain scores in patients undergoing elective colorectal surgery and should be considered in multimodal postoperative analgesic plans. Registration number: NCT02356198 (http://www.clinicaltrials.gov).

UPPER GI

Naast dumping syndroom, ook veranderde glucose metabolisme na slokdarmresectie

Changes in gut hormones, glycaemic response and symptoms after oesophagectomy. JA Elliott et al. BJS. BJS, May 2019 – Volume 106 – Issue 6, pages 735-746.
Pubmed ID: 30883706

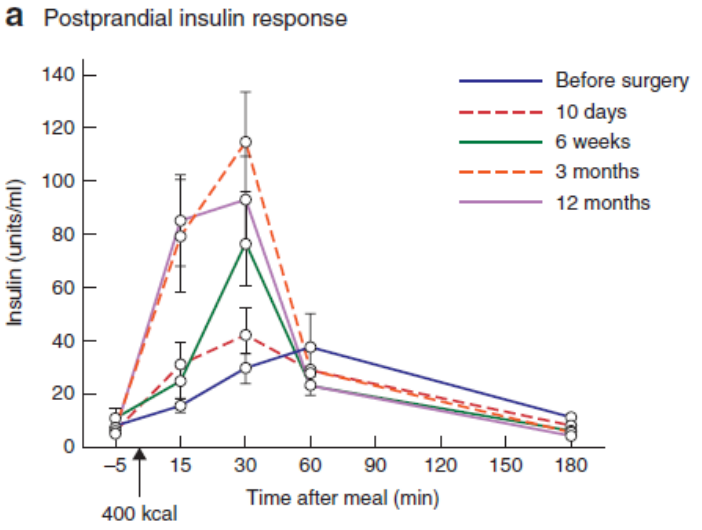
BACKGROUND: Oesophagectomy is associated with reduced appetite, weight loss and postprandial hypoglycaemia, the pathophysiological basis of which remains largely unexplored. This study aimed to investigate changes in enteroendocrine function after oesophagectomy.

METHODS: In this prospective study, 12 consecutive patients undergoing oesophagectomy were studied before and 10 days, 6, 12 and 52 weeks after surgery. Serial plasma total fasting ghrelin, and glucagon-like peptide 1 (GLP-1), insulin and glucose release following a standard 400-kcal mixed-meal stimulus were determined. CT body composition and anthropometry were assessed, and symptom scores calculated using European Organisation for Research and Treatment of Cancer (EORTC) questionnaires.

RESULTS: At 1 year, two of the 12 patients exhibited postprandial hypoglycaemia, with reductions in bodyweight (mean(s.e.m.) 17·1(3·2) per cent, P < 0·001), fat mass (21.5(2.5) kg versus 25.5(2.4) kg before surgery; P = 0·014), lean body mass (51.5(2.2) versus 54.0(1.8) kg respectively; P = 0·003) and insulin resistance (HOMA-IR: 0.84(0.17) versus 1.16(0.20); P = 0·022). Mean(s.e.m.) fasting ghrelin levels decreased from postoperative day 10, but had recovered by 1 year (preoperative: 621·5(71·7) pg/ml; 10 days: 415·1(59·80) pg/ml; 6 weeks: 309·0(42·0) pg/ml; 12 weeks: 415·8(52·1) pg/ml; 52 weeks: 547·4(83·2) pg/ml; P < 0·001) and did not predict weight loss (P = 0·198). Postprandial insulin increased progressively at 10 days, 6, 12 and 52 weeks (mean(s.e.m.) insulin AUC0-30 min : fold change 1·7(0·4), 2·0(0·4), 3·5(0·7) and 4·0(0·8) respectively; P = 0·001). Postprandial GLP-1 concentration increased from day 10 after surgery (P < 0·001), with a 3·3(1·8)-fold increase at 1 year (P < 0·001). Peak GLP-1 level was inversely associated with the postprandial glucose nadir (P = 0·041) and symptomatic neuroglycopenia (Sigstad score, P = 0·017, R^2 = 0·45). GLP-1 AUC predicted loss of weight (P = 0·008, R^2 = 0·52) and fat mass (P = 0·010, R^2 = 0·64) at 1 year.

CONCLUSION: Altered enteroendocrine physiology is associated with early satiety, weight loss and postprandial hypoglycaemia after oesophagectomy.

Fig. 5 Postprandial insulin and glucose levels after oesophagectomy



Slechtere overleving plaveiselcelcarcinoom slokdarm indien JMJD3 overexpressie

JMJD3 expression is an independent prognosticator in patients with esophageal squamous cell carcinoma. SH Li et al. Surgery: May 2019 – Volume 165 – Issue 5 – p 946-952.
Pubmed ID: 30678869.

BACKGROUND: The Jumonji-domain containing 3 has diverse roles in multiple cancers. Here, we investigated its prognostic significance in esophageal squamous cell carcinoma.

METHODS: By using immunohistochemistry, the Jumonji-domain containing 3 expression was examined in 109 surgically resected esophageal squamous cell carcinomas and correlated with treatment outcome. The functional role of Jumonji-domain containing 3 in esophageal squamous cell carcinoma cells was determined by Jumonji-domain containing 3-mediated small interfering ribonucleic acid.

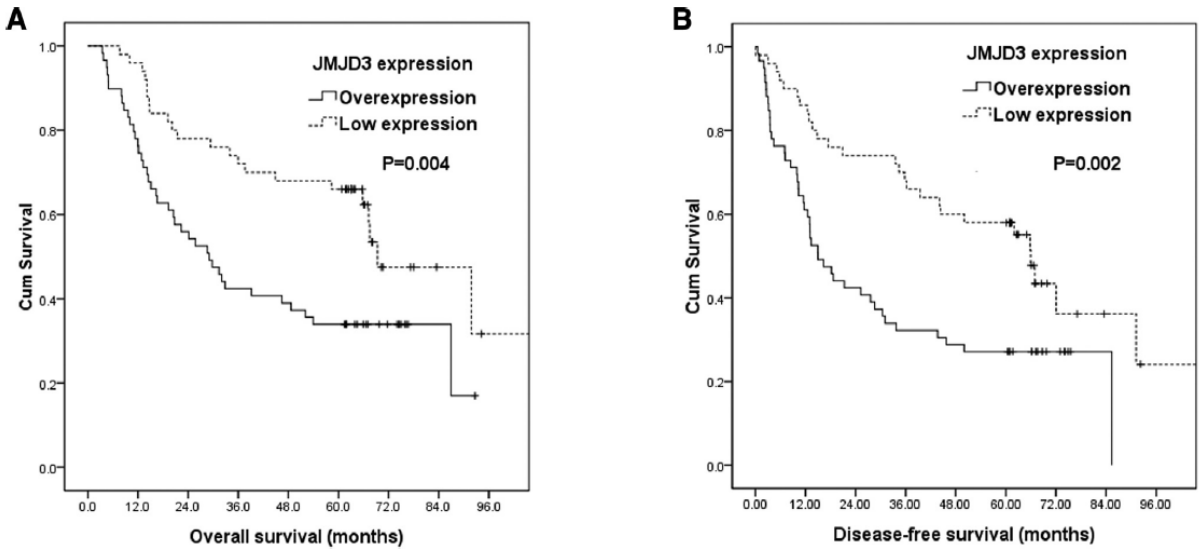


Fig 2. Kaplan-Meier curves according to JMJD3 status. (*A*) Overall survival according to JMJD3 status. (*B*) Disease-free survival according to JMJD3 status.

RESULTS: Univariate analysis showed that Jumonji-domain containing 3 overexpression was associated with inferior overall survival (P = .004) and disease-free survival (P = .002). In a multivariate comparison, Jumonji-domain containing 3 overexpression remained independently associated with worse overall survival (P = .017, hazard ratio = 1.898) and disease-free survival (P = .011, hazard ratio = 1.901). The 5-year overall and disease-free survival rates were 66% and 58% in patients with a low expression of Jumonji-domain containing 3 and 34% and 27% in patients with overexpression of Jumonji-domain containing 3. Silencing Jumonji-domain containing 3 in esophageal squamous cell carcinoma cells inhibited cell growth rate and bromodeoxyuridine incorporation ability. In contrast, a gain of function of Jumonji-domain containing 3 promoted esophageal squamous cell carcinoma cell proliferation. Furthermore, Jumonji-domain containing 3 expression contributes to Ras/MEK pathway.

CONCLUSION: Jumonji-domain containing 3 overexpression was independently associated with poor prognosis in patients with esophageal squamous cell carcinoma. In vitro, Jumonji-domain containing 3 expression regulated esophageal squamous cell carcinoma cell growth. These results may further elucidate the role of Jumonji-domain containing 3 in esophageal squamous cell carcinoma and provide a potential new therapeutic approach for patients with esophageal squamous cell carcinoma.

HPB

Overeenstemming betreft behandelstrategie maar 50% tussen verschillende MDO's

Multicentre study of multidisciplinary team assessment of pancreatic cancer resectability and treatment allocation. J. Kirkegard et al. BJS, May 2019 – Volume 106 – Issue 6, pages 756-764.
Pubmed ID: 30830974

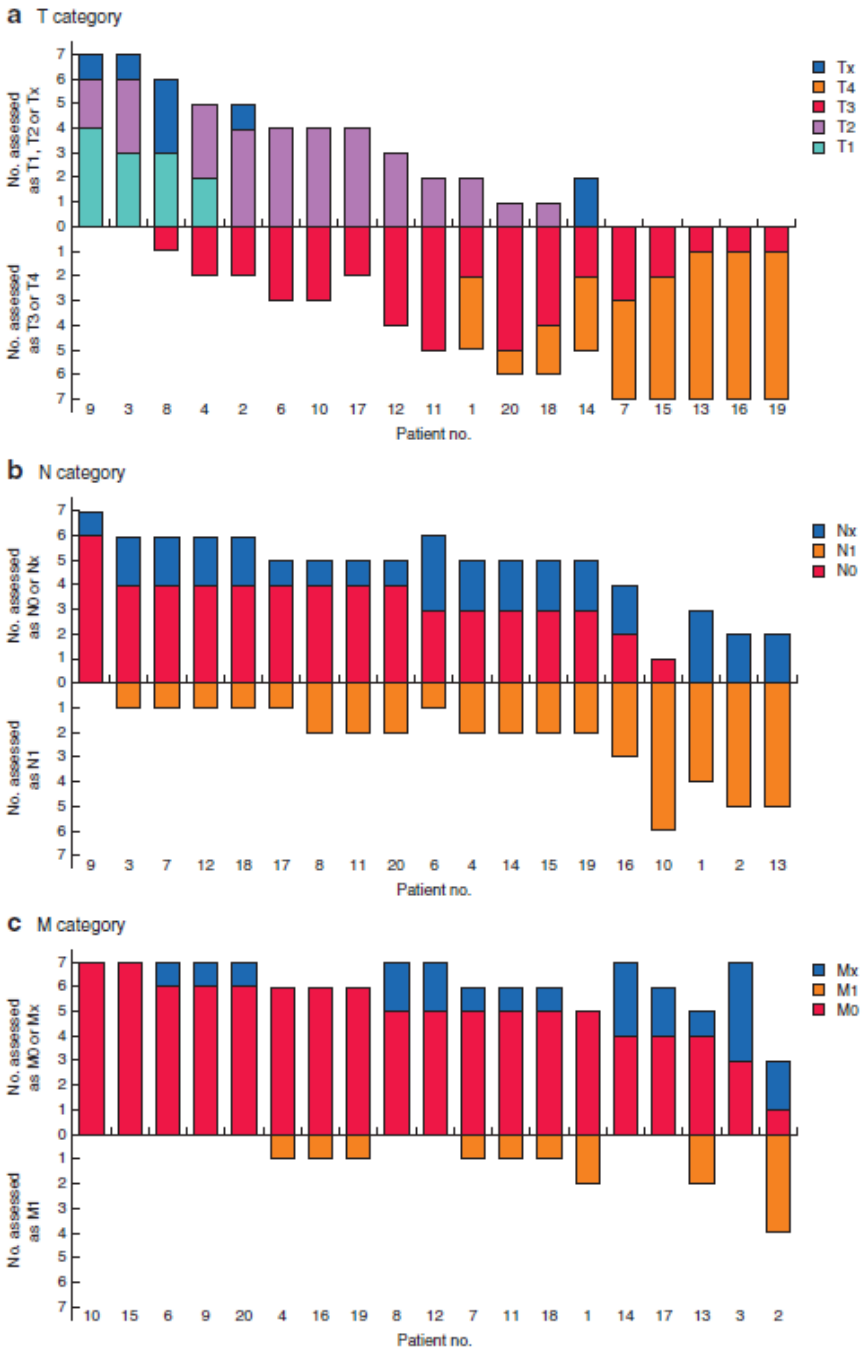
BACKGROUND: Multidisciplinary team (MDT) meetings have been adopted widely to ensure optimal treatment for patients with cancer. Agreements in tumour staging, resectability assessments and treatment allocation between different MDTs were assessed.

METHODS: Of all patients referred to one hospital, 19 patients considered to have non‐metastatic pancreatic cancer for evaluation were selected randomly for a multicentre study of MDT decisions in seven units across Northern Europe. Anonymized clinical information and radiological images were disseminated to the MDTs. All patients were reviewed by the MDTs for radiological T, N and M category, resectability assessment and treatment allocation. Each MDT was blinded to the decisions of other teams. Agreements were expressed as raw percentages and Krippendorff's α values, both with 95 per cent confidence intervals.

RESULTS: A total of 132 evaluations in 19 patients were carried out by the seven MDTs (1 evaluation was excluded owing to technical problems). The level of agreement for T, N and M categories ranged from moderate to near perfect (46·8, 61·1 and 82·8 per cent respectively), but there was substantial variation in assessment of resectability; seven patients were considered to be resectable by one MDT but unresectable by another. The MDTs all agreed on either a curative or palliative strategy in less than half of the patients (9 of 19). Only fair agreement in treatment allocation was observed (Krippendorff's α 0·31, 95 per cent c.i. 0·16 to 0·45). There was a high level of agreement in treatment allocation where resectability assessments were concordant.

CONCLUSIONS: Considerable disparities in MDT evaluations of patients with pancreatic cancer exist, including substantial variation in resectability assessments.

Fig. 1 Distribution of T, N and M category assessment in 19 patients



a T category, **b** N category and **c** M category. Each bar represents one patient. Patients are ordered by increasing T, N or M category.

Thromboprofylaxe na pancreatectomy: balance the risk

Outcomes following pancreatic surgery using three different thromboprophylaxis regimens. RG Hanna-Sawires et al. BJS May 2019 – Volume 106 – Issue 6, pages 765-773.
Pubmed ID: 30776085

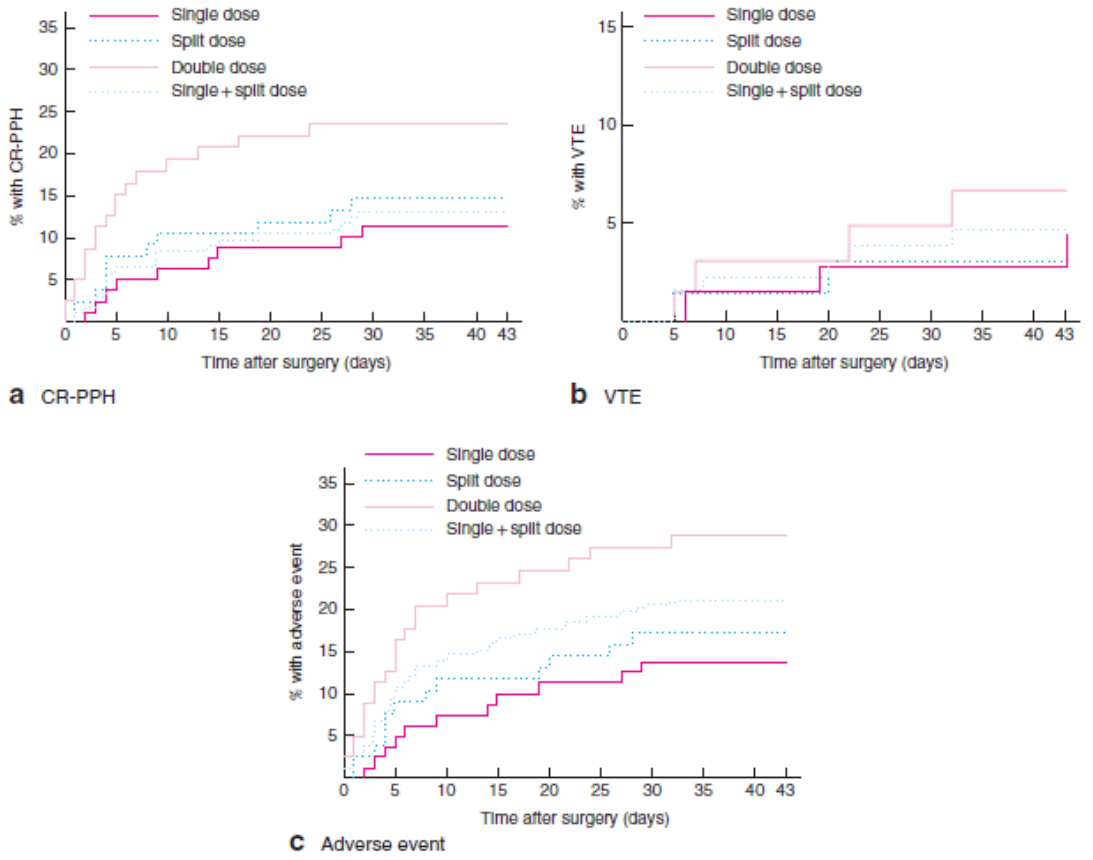
BACKGROUND: Postpancreatectomy haemorrhage (PPH) and venous thromboembolism (VTE) are serious complications following pancreatic surgery. The aim was to assess the timing, occurrence and predictors of PPH and VTE.

METHODS: Elective pancreatic resections undertaken in a single university hospital between November 2013 and September 2017 were assessed. Three intervals were reviewed, each with a different routine regimen of nadroparin: 2850 units once daily (single dose) administered in hospital only, or 5700 units once daily (double dose) or 2850 units twice daily (split dose) administered in hospital and continued for 6 weeks after surgery. Clinically relevant PPH (CR‐PPH) was classified according to International Study Group of Pancreatic Surgery criteria. VTE was defined according to a number of key diagnostic criteria within 6 weeks of surgery. Cox regression analyses were performed to test the hypotheses that the double‐dose group would experience more PPH than the other two groups, the single‐dose group would experience more VTE than the other two groups, and the split‐dose group would experience the fewest adverse events (PPH or VTE).

RESULTS: In total, 240 patients were included, 80 per group. The double‐dose group experienced significantly more CR‐PPH (hazard ratio (HR) 2·14, 95 per cent c.i. 1·16 to 3·94; P = 0·015). More relaparotomies due to CR‐PPH were performed in the double‐dose group (16 versus 3·8 per cent; P = 0·002). The single‐dose group did not experience more VTE (HR 1·41, 0·43 to 4·62; P = 0·570). The split dose was not associated with fewer adverse events (HR 0·77, 0·41 to 1·46; P = 0·422). Double‐dose low molecular weight heparin (LMWH), high BMI and pancreatic fistula were independent predictors of CR‐PPH.

CONCLUSIONS: A double dose of LMWH prophylaxis continued for 6 weeks after pancreatic resection was associated with a twofold higher rate of CR‐PPH, resulting in four times more relaparotomies. Patients receiving a single daily dose of LMWH in hospital only did not experience a higher rate of VTE.

Fig. 1 Time-to-event analyses for clinically relevant postpancreatectomy haemorrhage, venous thromboembolism and adverse events



a Clinically relevant postpancreatectomy haemorrhage (CR-PPH), b venous thromboembolism (VTE) and c adverse events. a $P = 0{\cdot}015$, b $P = 0{\cdot}570$, c $P = 0{\cdot}422$ (Cox regression analysis).

LEVERCHIRURGIE

Lever resectie voor perihilair cholangiocarcinoom: gevaarlijker in het Westen dan in het Oosten?

Morbidity and mortality after major liver resection in patients with perihilar cholangiocarcinoma: A systematic review and meta-analysis. LC Franken et al; Surgery: May 2019 – Volume 165 – Issue 5 – p 918-928

Pubmed ID: 30871811

BACKGROUND AND OBJECTIVE: Morbidity and mortality after hepatectomy for perihilar cholangiocarcinoma are known to be high. However, reported postoperative outcomes vary, with notable differences between Western and Asian series. We aimed to determine morbidity and mortality rates after major hepatectomy in patients with perihilar cholangiocarcinoma and assess differences in outcome regarding geographic location and hospital volume.

METHODS: A systematic review was performed by searching the MEDLINE and EMBASE databases through November 20, 2017. Risk of bias was assessed and meta-analysis and metaregression were performed using a random effects model.

RESULTS: A total of 51 studies were included, representing 4,634 patients. Pooled 30-day and 90-day mortality were 5% (95% CI 3%–6%) and 9% (95% CI 6%–12%), respectively. Pooled overall morbidity

and severe morbidity were 57% (95% CI 50%–64%) and 40% (95% CI 34%–47%), respectively. Western studies compared with Asian studies had a significantly higher 30-day mortality, 90-day mortality, and overall morbidity: 8% versus 2% (P < .001), 12% versus 3% (P < .001), and 63% versus 54% (P = .048), respectively. This effect on mortality remained significant after correcting for hospital volume. Univariate metaregression analysis showed no influence of hospital volume on mortality or morbidity, but when corrected for geographic location, higher hospital volume was associated with higher severe morbidity (P = .039).

CONCLUSION: Morbidity and mortality rates after major hepatectomy for perihilar cholangiocarcinoma are high. The Western series showed a higher mortality compared with the Asian series, even when corrected for hospital volume. Standardized reporting of outcomes is necessary. Underlying causes for differences in outcomes between Asian and Western centers, such as differences in treatment strategies, should be further analyzed.

Is een additionele resectie zinvol bij een positieve snijrand op vriescoupe bij perihilair cholangiocarcinoom?

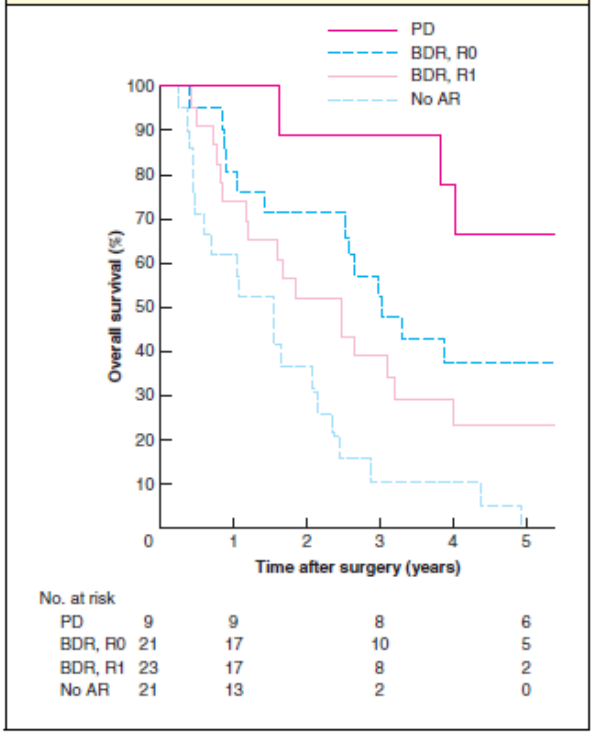
Clinical value of additional resection of a margin‐positive distal bile duct in perihilar cholangiocarcinoma. S Otsuka et al. BJS, May 2019 – Volume 106 – Issue 6, pages 774-782.
Pubmed ID: 30889275

BACKGROUND: Little is known about the effect of additional resection for a frozen-section-positive distal bile duct margin (DM) in perihilar cholangiocarcinoma.

METHODS: Patients who underwent surgical resection for perihilar cholangiocarcinoma between 2001 and 2015 were analysed retrospectively, focusing on the DM.

RESULTS: Of 558 consecutive patients who underwent frozen-section examination for a DM, 74 (13·3 per cent) had a frozen-section-positive DM with invasive cancer or carcinoma in situ. Eventually, 53 patients underwent additional resection (bile duct resection in 44 and pancreatoduodenectomy in 9), whereas the remaining 21 patients did not. Ultimately, R0 resection was achieved in 30 of the 53 patients (57 per cent). No patient who underwent additional resection died from surgical complications. The 44 patients with additional bile duct resection had a 5-year overall survival rate of 31 per cent. Overall survival of the nine patients who had pancreatoduodenectomy was better, with a 10-year rate of 67 per cent. Survival of the 21 patients without additional resection was dismal: all died within 5 years. Multivariable analyses identified nodal status and additional

Fig. 2 Kaplan–Meier analysis of overall survival of patients with frozen-section-positive distal bile duct margin, according to type of additional resection



P = 0·025 (pancreatoduodenectomy (PD) *versus* bile duct resection (BDR), R0), *P* = 0·254 (BDR, R0 *versus* BDR, R1), *P* = 0·019 (BDR, R1 *versus* no additional resection (AR)) (log rank test).

resection as independent prognostic factors (lymph node metastasis: hazard ratio (HR) 2·26, 95 per cent c.i. 1·26 to 4·07; bile duct resection versus no additional resection: HR 0·32, 0·17 to 0·60; pancreatoduodenectomy versus no additional resection: HR 0·08, 0·02 to 0·29).
CONCLUSIONS: Additional resection for frozen-section-positive DM in perihilar cholangiocarcinoma frequently yields R0 margins. It offers a better chance of long-term survival, and thus should be performed in carefully selected patients.

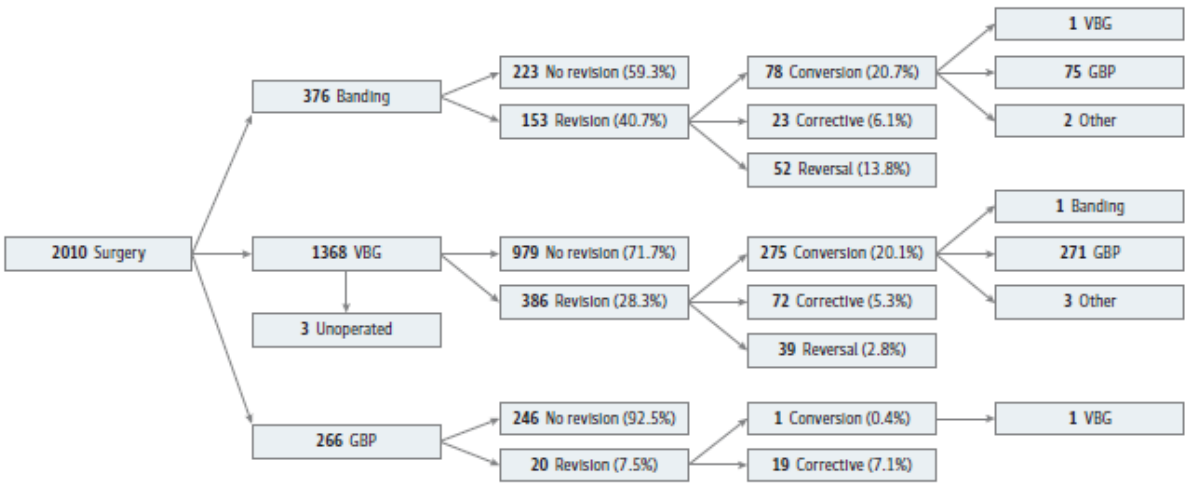
BARIATRISCHE CHIRURGIE

Minder revisie chirurgie na gastric-bypass?

Reoperations After Bariatric Surgery in 26 Years of Follow-up of the Swedish Obese Subjects Study. S Hjorth et al. JAMA Surg. 2019;154(4):319-326.
Pubmed ID: 30601881

IMPORTANCE: Bariatric surgery is an established treatment for obesity, but knowledge on the long-term incidence of revisional surgery is scarce.
OBJECTIVE: To determine the incidence and type of revisional surgery after bariatric surgery in 26 years of follow-up of participants in the Swedish Obese Subjects (SOS) study.
DESIGN, SETTING, AND PARTICIPANTS: The SOS study is a prospective nonrandomized controlled study comparing bariatric surgery (banding, vertical banded gastroplasty [VBG], and gastric bypass [GBP]) with usual care. The bariatric surgeries in the SOS study were conducted at 25 public surgical departments in Sweden. Men with body mass index values of 34 or higher and women with body mass indexes of 38 or higher were recruited to the surgery group of the SOS study between September 1, 1987, and January 31, 2001, and follow-up continued until December 31, 2014. Data analysis occurred from November 2016 to April 2018.
INTERVENTIONS: Banding, VBG, or GBP.
MAIN OUTCOMES AND MEASURES: Revisional surgeries, analyzed using data from questionnaires, hospital records, and the Swedish National Patient register through December 31, 2014.

Figure 1. Overview of SOS Surgery Cohort at Baseline (Index) and First-Time Revisional Surgery Follow-up Status in the Surgery Subgroups



The absolute numbers and percentages of index numbers in subgroups at baseline are shown. Other procedures include sleeve gastrectomy (including gastric plication), duodenal switch (including biliopancreatic diversion), and jejunoileal bypass. GBP indicates gastric bypass; VBG, vertical banded gastroplasty.

RESULTS: A total of 2010 participants underwent surgery. The age range was 37 to 60 years. A total of 376 participants underwent banding (18.7%), while 1365 had VBG (67.9%) and 266 had GBP (13.2%). During a median follow-up of 19 years, 559 participants (27.8%) underwent first-time revisional surgery, including 354 conversions to other bariatric procedures (17.6%), 114 corrective surgeries (5.6%), and 91 reversals to normal anatomy (4.5%). Revisional surgeries (conversions, corrective surgery, and reversals) were common after banding (153 of 376 [40.7%]) and VBG (386 of 1365 [28.3%]) but relatively rare after GBP (20 of 266 [7.5%]). Patients who had banding and VBG primarily underwent conversions to GBP or reversals. Incidence of reversals was 5 times higher after banding than after VBG (40.7% vs 7.5%; unadjusted hazard ratio, 5.19 [95% CI, 3.43-7.87]; P < .001). Corrective surgeries were equally common irrespective of the index surgery (72 of 1365 patients who had VBG [5.3%]; 23 of 376 patients who had banding [6.1%]; 19 of 266 patients who had GBP [7.1%]). Revisional surgery indications, including inadequate weight loss, band-associated complications (migration, stenosis, and slippage), staple-line disruptions, and postsurgical morbidity, varied depending on index surgery subgroup. Most corrections occurred within the first 10 years, whereas conversions and reversals occurred over the entire follow-up period.

CONCLUSIONS AND RELEVANCE: Corrective surgeries occur mainly within the first 10 years and with similar incidences across all 3 surgical subgroups, but indications varied. Conversions (mainly to GBP) and reversals occurred after many years and were most frequent after banding and VBG, reflecting a higher overall revisional surgery demand after these operations.

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