

DE LEESTAFEL

JANUARI 2020

Een Maandelijks Selectie van Wetenschappelijke GE-nieuws

Coloproctologie

Noorwegen stopt met TaTME: meer naadlekkages en hoger percentage local recurrence

Transanal total mesorectal excision for rectal cancer has been suspended in Norway. HH Wasmuth et al. *BJS*, Jan 2020 – Volume 107 – Issue 1, pages 121-130.

Pubmed ID: 31802481.

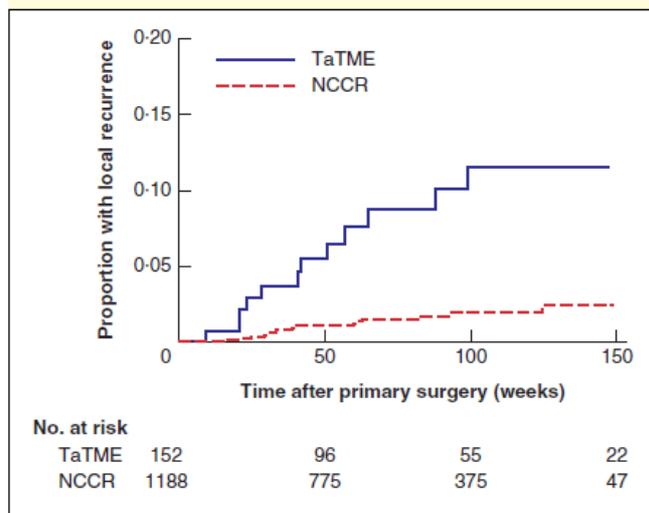
BACKGROUND: Transanal total mesorectal excision (TaTME) for rectal cancer has emerged as an alternative to the traditional abdominal approach. However, concerns have been raised about local recurrence. The aim of this study was to evaluate local recurrence after TaTME. Secondary aims included postoperative mortality, anastomotic leak and stoma rates.

METHODS: Data on all patients who underwent TaTME were recorded and compared with those from national cohorts in the Norwegian Colorectal Cancer Registry (NCCR) and the Norwegian Registry for Gastrointestinal Surgery (NoRGast). Kaplan-Meier estimates were used to compare local recurrence.

RESULTS: In Norway, 157 patients underwent TaTME for rectal cancer between October 2014 and October 2018. Three of seven hospitals abandoned TaTME after a total of five procedures. The local recurrence rate was 12 of 157 (7.6 per cent); eight local recurrences were multifocal or extensive. The estimated local recurrence rate at 2.4 years was 11.6 (95 per cent c.i. 6.6 to 19.9) per cent after TaTME compared with 2.4 (1.4 to 4.3) per cent in the NCCR ($P < 0.001$). The adjusted hazard ratio was 6.71 (95 per cent c.i. 2.94 to 15.32). Anastomotic leaks resulting in reoperation occurred in 8.4 per cent of patients in the TaTME cohort compared with 4.5 per cent in NoRGast ($P = 0.047$). Fifty-six patients (35.7 per cent) had a stoma at latest follow-up; 39 (24.8 per cent) were permanent.

CONCLUSION: Anastomotic leak rates after TaTME were higher than national rates; local recurrence rates and growth patterns were unfavourable.

Fig. 3 One-minus-survival Kaplan–Meier plot of estimated local recurrence rates in study cohort with rectal cancer treated with transanal total mesorectal excision compared with a corresponding national non-transanal total mesorectal excision cohort



TaTME, transanal total mesorectal excision. $P < 0.001$ (log rank test).

Geen return-to-work in 30% colorectaal carcinoom patiënten na 2 jaar. Een predictiemodel in de Nederlandse populatie.

Predicting return to work among patients with colorectal cancer. CM den Bakker et al. *BJS*, Jan 2020 – Volume 107 – Issue 1, pages 140-148.

Pubmed ID: 31654404.

BACKGROUND: The increase in prevalence of colorectal cancer among young patients coupled with an older retirement age in developed countries means that more patients are being diagnosed with colorectal cancer while still at work. The aim of this study was to develop prediction models for return to work by 1 and 2 years after the start of sick leave.

METHODS: This was a retrospective registry-based cohort study of data from a nationwide occupational health service in the Netherlands. Only employed patients with colonic or rectal cancer treated with curative intent were included. Two predictor variable models were developed using multivariable logistic regression with backward selection. Calibration, discrimination and explained variance were used to assess model performance, and internal validation by bootstrapping was performed.

RESULTS: Median time to return to work for 317 included patients was 423 (95 per cent c.i. 379 to 467) days. Two-thirds of patients had returned to work by 2 years after the start of the sick leave. Presence of metastases, adjuvant treatment, stoma, emotional distress and postoperative complications were predictors of not returning to work in the 1-year model. In the 2-year model, presence of metastases, emotional distress, postoperative complications, company size and the trajectory of the return-to-work process were predictors.

CONCLUSION: Almost 70 per cent of patients with colorectal cancer in this population returned to work within 2 years after the start of sick leave. The models can be used to guide patients early in colorectal cancer treatment about the likelihood of returning to work, and to identify and modify barriers that could facilitate this.

Table 5 Results of multivariable logistic regression analysis for return to work by 2 years						
	Before internal validation			After internal validation		
	Regression coefficient	Odds ratio	P	Regression coefficient	Odds ratio	P
Presence of metastases (yes versus no)	-0.95	0.39 (0.21, 0.72)	0.003	-0.95	0.39 (0.22, 0.67)	0.001
Emotional distress (yes versus no)	-0.95	0.39 (0.22, 0.67)	0.001	-0.95	0.39 (0.22, 0.67)	0.001
Postoperative complications (yes versus no)	-0.60	0.55 (0.32, 0.93)	0.026	-0.60	0.55 (0.31, 0.97)	0.039
Company size (no. of employees)						
10–50 versus < 10	-0.28	0.76 (0.41, 1.38)	0.362	-0.28	0.76 (0.39, 1.46)	0.403
51–250 versus < 10	-0.60	0.55 (0.25, 1.18)	0.125	-0.60	0.55 (0.24, 1.27)	0.162
≥ 251 versus < 10	-1.31	0.27 (0.07, 1.12)	0.070	-1.31	0.27 (0.07, 1.11)	0.069
Trajectory of return to work (direct versus phased)	1.26	3.52 (2.07, 6.00)	<0.001	1.26	3.52 (1.52, 5.62)	0.001
Constant		1.08			1.08	
P (Hosmer and Lemeshow test)		0.513				
Nagelkerke's R ²		0.20			0.12	
AUC		0.73 (0.67, 0.79)			0.71 (0.65, 0.77)	

Values in parentheses are 95 per cent confidence intervals. AUC, area under the curve.

UPPER GI

Naadlekkage na slokdarm/maag resectie heeft GEEN effect op de disease-free-survival

Impact of postoperative complications on disease recurrence and long-term survival following oesophagogastric cancer resection. JH Saunders et al. *BJS*, Jan 2020 – Volume 107 – Issue 1, pages 103-112.

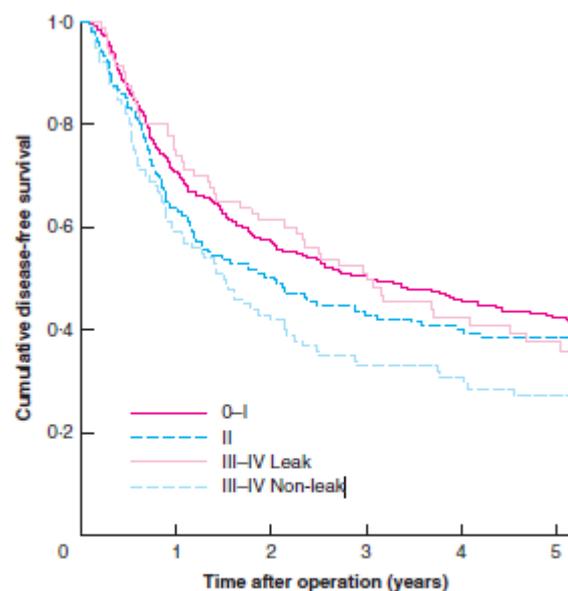
Pubmed ID: 31869460.

BACKGROUND: Postoperative complications after resection of oesophagogastric carcinoma can result in considerable early morbidity and mortality. However, the long-term effects on survival are less clear.

METHODS: All patients undergoing intentionally curative resection for oesophageal or gastric cancer between 2006 and 2016 were selected from an institutional database. Patients were categorized by complication severity according to the Clavien-Dindo classification (grades 0-V). Complications were defined according to an international consensus statement. The effect of leak and severe non-leak-related complications on overall survival, recurrence and disease-free survival was assessed using Kaplan-Meier analyses to evaluate differences between groups. All factors significantly associated with survival in univariable analysis were entered into a Cox multivariable regression model with stepwise elimination.

RESULTS: Some 1100 patients were included, with a median age of 69 (range 28-92) years; 48.1 per cent had stage III disease and cancer recurred in 428 patients (38.9 per cent). Complications of grade III or higher occurred in 244 patients (22.2 per cent). The most common complications were pulmonary (29.9 per cent), with a 13.0 per cent incidence of pneumonia. Rates of atrial dysrhythmia and anastomotic leak were 10.0 and 9.6 per cent respectively. Patients with a grade III-IV leak did not have significantly reduced overall survival compared with those who had grade 0-I complications. However, patients with grade III-IV non-leak-related complications had reduced median overall survival (19.7 versus 42.7 months; $P < 0.001$) and disease-free survival (18.4 versus 36.4 months; $P < 0.001$). Cox regression analysis identified age, tumour stage, resection margin and grade III-IV non-leak-related complications as independent predictors of poor overall and disease-free survival.

CONCLUSION: Beyond the acute postoperative period, anastomotic leak does not adversely affect survival, however, other severe postoperative complications do reduce long-term overall and disease-free survival.



No. at risk				
0-I	705	493	298	185
II	151	95	63	53
III-IV Leak	81	59	39	21
III-IV Non-leak	100	59	33	24

Complications were graded according to the Clavien-Dindo classification.

Meten oraal belasten na minimaal invasieve slokdarmresectie? De gerandomiseerde NUTRIENT II trial

Direct Oral Feeding Following Minimally Invasive Esophagectomy (NUTRIENT II trial): An International, Multicenter, Open-label Randomized Controlled Trial. GHK Berkelmans et al. *Annals of Surgery*, January 2020, Volume 271, Issue 1, p41-47.

Pubmed ID: 31090563.

OBJECTIVE: Patients undergoing an esophagectomy are often kept nil-by-mouth postoperatively out of fear for increasing anastomotic leakage and pulmonary complications. This study investigates the effect of direct start of oral feeding following minimally invasive esophagectomy (MIE) compared with standard of care.

BACKGROUND: Elements of enhanced recovery after surgery (ERAS) protocols have been successfully introduced in patients undergoing an esophagectomy. However, start of oral intake, which is an essential part of the ERAS protocols, remains a matter of debate.

METHODS: Patients in this multicenter, international randomized controlled trial were randomized to directly start oral feeding (intervention) after a MIE with intrathoracic anastomosis or to receive nil-by-mouth and tube feeding for 5 days postoperative (control group). Primary outcome was time to functional recovery. Secondary outcome parameters included anastomotic leakage, pneumonia rate, and other surgical complications scored by predefined definitions.

RESULTS: Baseline characteristics were similar in the intervention (n = 65) and control (n = 67) group. Functional recovery was 7 days for patients receiving direct oral feeding compared with 8 days in the control group (P = 0.436). Anastomotic leakage rate did not differ in the intervention (18.5%) and control group (16.4%, P = 0.757). Pneumonia rates were comparable between the intervention (24.6%) and control group (34.3%, P = 0.221). Other morbidity rates were similar, except for chyle leakage, which was more prevalent in the standard of care group (P = 0.032).

CONCLUSION: Direct oral feeding after an esophagectomy does not affect functional recovery and did not increase incidence or severity of postoperative complications.

TABLE 2. Primary Outcome; Time from Esophagectomy to Functional Recovery

	Direct Oral Feeding	Standard of Care	P
Intention-to-treat analysis	N = 65	N = 66*	
Functional recovery, days	7 [6–14]	8 [7–16]	0.436
Per-protocol analysis	N = 41	N = 41	
Functional recovery, days	6 [6–8]	7 [6–8]	0.455

Values are medians [lower quartile - upper quartile].

*One patient died during hospital admission and was therefore not able to achieve functional recovery.

Neuroendocrine pancreastumoren <2.0cm toch opereren?

Operative resection in early stage pancreatic neuroendocrine tumors in the United States: Are we over- or undertreating patients?. S.V. Chivukula et al; Surgery: January 2020 – Volume 167 – Issue 1 – p 180-186.

Pubmed ID: 31537303.

BACKGROUND: Many current guidelines recommend nonoperative management for pancreatic neuroendocrine tumors <2 cm. The objective of this study was to evaluate the utilization and outcomes of resection for these pancreatic neuroendocrine tumors in the United States.

METHODS: Using the National Cancer Database (2004-2014), 3,243 cases of T1 (≤ 2.0 cm) pancreatic neuroendocrine tumors were identified. Additional patient and tumor characteristics were examined. Multivariate models were used to identify factors that predicted resection and to assess patient survival after resection.

RESULTS: 75% of pancreatic neuroendocrine tumors measuring 0 to 1.0 cm and 80% of pancreatic neuroendocrine tumors measuring >1.0 and ≤ 2.0 cm were resected. Eighty-four pancreatic neuroendocrine tumors were functional, of which 82% were resected. Variables influencing resection included positive lymph nodes, tumor in body or tail of pancreas, well or moderately differentiated tumors, and resection at academic medical centers (odds ratio 1.5-4.9). When controlling for other variables, patients with pancreatic neuroendocrine tumors 1 to 2 cm who underwent resection had a prolonged 5-year survival rate (hazard ratio 0.51, confidence interval 0.34-0.75) when compared with those who did not undergo resection. This survival benefit of resection was not found for pancreatic neuroendocrine tumors 0 to 1 cm (hazard ratio = 0.63, confidence interval 0.36-1.11).

CONCLUSIONS: Contrary to many current recommendations, most patients with pancreatic neuroendocrine tumors ≤ 2.0 cm undergo surgical resection in the United States. A survival benefit was found for resection of pancreatic neuroendocrine tumors 1 to 2 cm, suggesting that current recommendations should perhaps be revised.

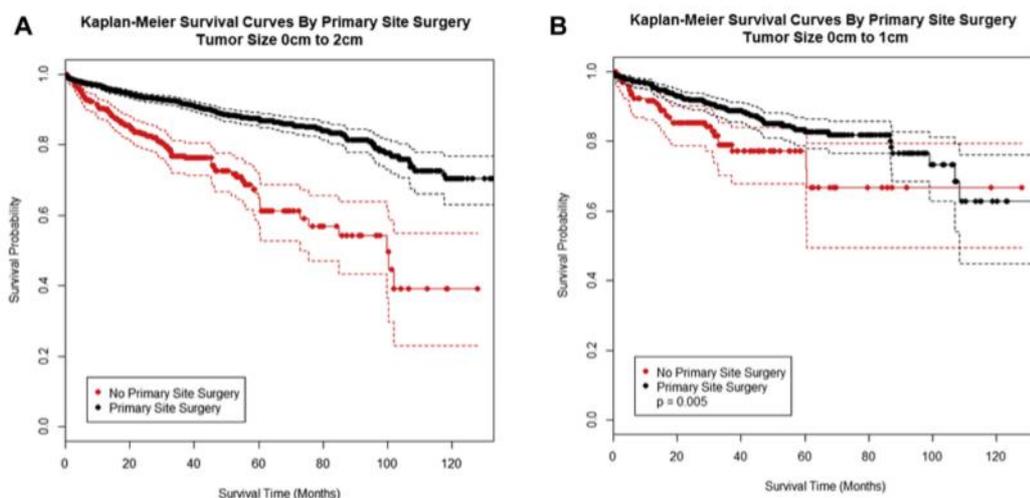


Fig 1. (A) Kaplan-Meier curve showing 5-year survival benefit on univariate analysis for patients with PanNETs ≤ 2 cm undergoing operative resection. (B) Kaplan-Meier curve showing 5-year survival benefit on univariate analysis of patients undergoing resection for PanNETs 0–1 cm, regardless of lymph node involvement. (C) Kaplan Meier curve showing 5-year survival benefit on univariate analysis for patients undergoing resection of PanNETs 1–2 cm, regardless of lymph node involvement.

Nederlandse “Textbook Outcome” pancreaschirurgie

Textbook Outcome: Nationwide Analysis of a Novel Quality Measure in Pancreatic Surgery. S.R. van Roessel et al. *Annals of Surgery*, January 2020, Volume 271, Issue 1, p155-162.

Pubmed ID: 31274651.

BACKGROUND: Textbook outcome (TO) is a multidimensional measure for quality assurance, reflecting the “ideal” surgical outcome.

METHODS: Post-hoc analysis of patients who underwent pancreatoduodenectomy (PD) or distal pancreatectomy (DP) for all indications between 2014 and 2017, queried from the nationwide prospective Dutch Pancreatic Cancer Audit. An international survey was conducted among 24 experts from 10 countries to reach consensus on the requirements for TO in pancreatic surgery. Univariable and multivariable logistic regression was performed to identify TO predictors. Between-hospital variation in TO rates was compared using observed-versus-expected rates.

RESULTS: Based on the survey (92% response rate), TO was defined by the absence of postoperative pancreatic fistula, bile leak, postpancreatectomy hemorrhage (all ISGPS grade B/C), severe complications (Clavien–Dindo \geq III), readmission, and in-hospital mortality. Overall, 3341 patients were included (2633 (79%) PD and 708 (21%) DP) of whom 60.3% achieved TO; 58.3% for PD and 67.4% for DP. On multivariable analysis, ASA class 3 predicted a worse TO rate after PD (ASA 3 OR 0.59 [0.44–0.80]), whereas a dilated pancreatic duct (>3 mm) and pancreatic ductal adenocarcinoma (PDAC) were associated with a better TO rate (OR 2.22 [2.05–3.57] and OR 1.36 [1.14–1.63], respectively). For DP, female sex and the absence of neoadjuvant therapy predicted better TO rates (OR 1.38 [1.01–1.90] and OR 2.53 [1.20–5.31], respectively). When comparing institutions, the observed-versus-expected rate for achieving TO varied from 0.71 to 1.46 per hospital after casemix-adjustment.

CONCLUSIONS: TO is a novel quality measure in pancreatic surgery. TO varies considerably between pancreatic centers, demonstrating the potential benefit of quality assurance programs.

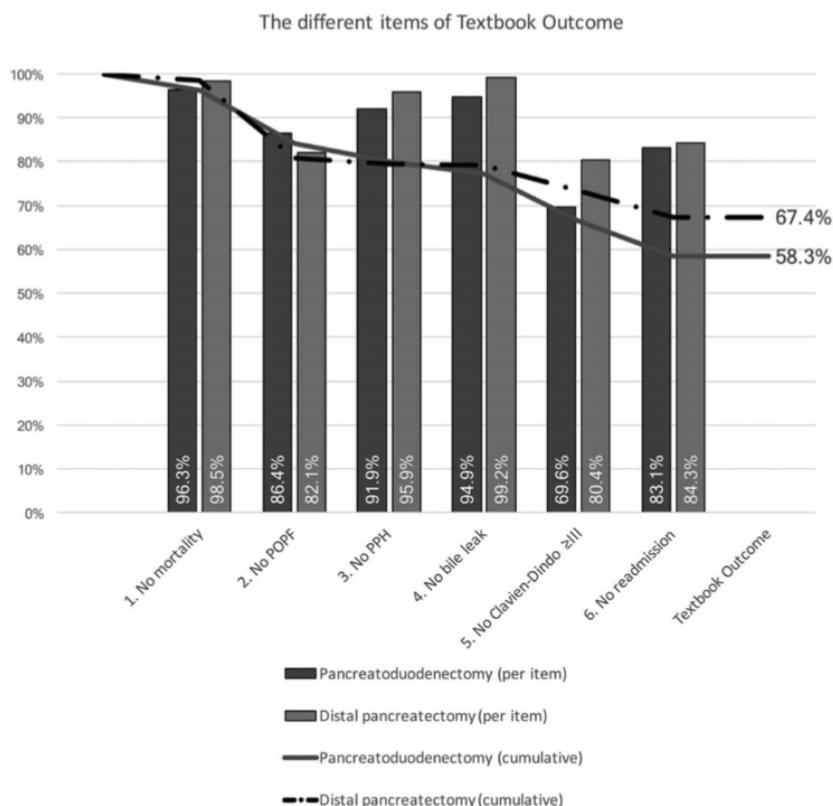


FIGURE 1. Textbook Outcome percentages (per item and cumulative) for pancreatoduodenectomy and distal pancreatectomy.

LEVERCHIRURGIE

BRAF mutante colorectale levermetastasen?

Is Hepatectomy Justified for BRAF Mutant Colorectal Liver Metastases?: A Multi-institutional Analysis of 1497 Patients. J. Gagnière et al; *Annals of Surgery*, January 2020, Volume 271, Issue 1, p147-154 Pubmed ID: 29995686.

OBJECTIVE: To analyze clinical outcomes and prognostic variables of patients undergoing hepatic resection for BRAF mutant (BRAF-mut) colorectal liver metastases (CRLM).

BACKGROUND: Outcomes following hepatectomy for BRAF-mut CRLM have not been well studied.

METHODS: All patients who underwent hepatectomy for CRLM with complete resection and known BRAF status during 2001 to 2016 at 3 high-volume centers were analyzed.

RESULTS: Of 4124 patients who underwent hepatectomy for CRLM, 1497 had complete resection and known BRAF status. Thirty-five (2%) patients were BRAF-mut, with 71% of V600E mutation. Compared with BRAF wild-type (BRAF-wt), BRAF-mut patients were older, more commonly presented with higher ASA scores, synchronous, multiple and smaller CRLM, underwent more major hepatectomies, but had less extrahepatic disease. Median overall survival (OS) was 81 months for BRAF-wt and 40 months for BRAF-mut patients ($P < 0.001$). Median recurrence-free survival (RFS) was 22 and 10 months for BRAF-wt and BRAF-mut patients ($P < 0.001$). For BRAF-mut, factors associated with worse OS were node-positive primary tumor, carcinoembryonic antigen (CEA) $> 200 \mu\text{g/L}$, and clinical risk score (CRS) ≥ 4 . Factors associated with worse RFS were node-positive primary tumor, ≥ 4 CRLM, and positive hepatic margin. V600E mutations were not associated with worse OS or RFS. A case-control matching analysis on prognostic clinicopathologic factors confirmed shorter OS ($P < 0.001$) and RFS ($P < 0.001$) in BRAF-mut.

CONCLUSIONS: Patients with resectable BRAF-mut CRLM are rare among patients selected for surgery and more commonly present with multiple synchronous tumors. BRAF mutation is associated with worse prognosis; however, long-term survival is possible and associated with node-negative primary tumors, CEA $\leq 200 \mu\text{g/L}$ and CRS < 4 .

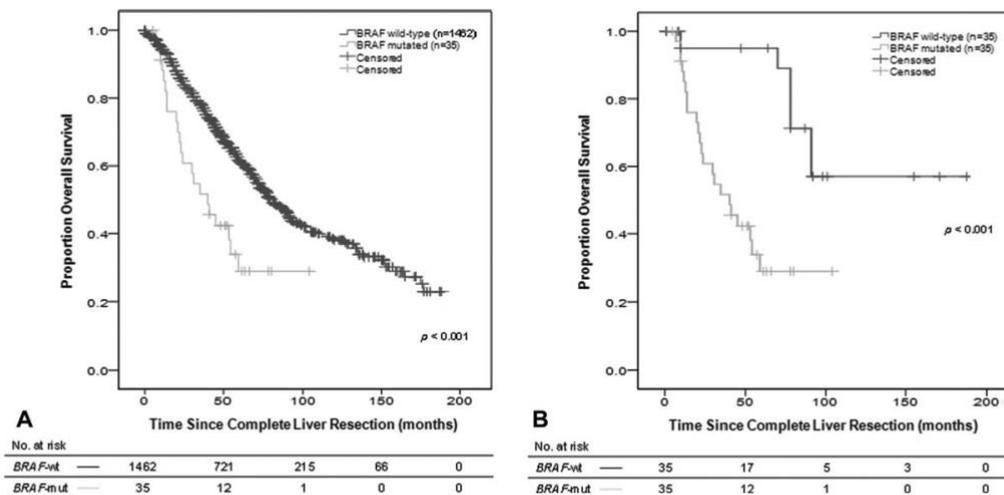


FIGURE 2. A, Overall survival after CRLM resection by BRAF mutation status, and (B) after case-control matching analysis (1:1) according to node-positive primary, synchronous CRLM, multiple CRLM, size of the largest CRLM > 5 cm, CEA > 200 ng/mL, the presence of extrahepatic disease at presentation, and the realization of a major hepatectomy.

Resectie marges relevant bij anatomische vs niet-anatomische leverresectie?

Significance of the surgical hepatic resection margin in patients with a single hepatocellular carcinoma. T. Aoki et al. *BJS*, Jan 2020 – Volume 107 – Issue 1, pages 113-120.
Pubmed ID: 31654406.

BACKGROUND: The impact of a wide surgical margin on the outcome of patients with hepatocellular carcinoma (HCC) has not been evaluated in relation to the type of liver resection performed, anatomical or non-anatomical. The aim of this study was to evaluate the impact of surgical margin status on outcomes in patients undergoing anatomical or non-anatomical resection for solitary HCC.

METHODS: Data from patients with solitary HCC who had undergone non-anatomical partial resection (Hr0 group) or anatomical resection of one Couinaud segment (HrS group) between 2000 and 2007 were extracted from a nationwide survey database in Japan. Overall and recurrence-free survival associated with the surgical margin status and width were evaluated in the two groups.

RESULTS: A total of 4457 patients were included in the Hr0 group and 3507 in the HrS group. A microscopically positive surgical margin was associated with poor overall survival in both groups. A negative but 0-mm surgical margin was associated with poorer overall and recurrence-free survival than a wider margin only in the Hr0 group. In the HrS group, the width of the surgical margin was not associated with patient outcome.

CONCLUSION: Anatomical resection with a negative 0-mm surgical margin may be acceptable. Non-anatomical resection with a negative 0-mm margin was associated with a less favourable survival outcome.

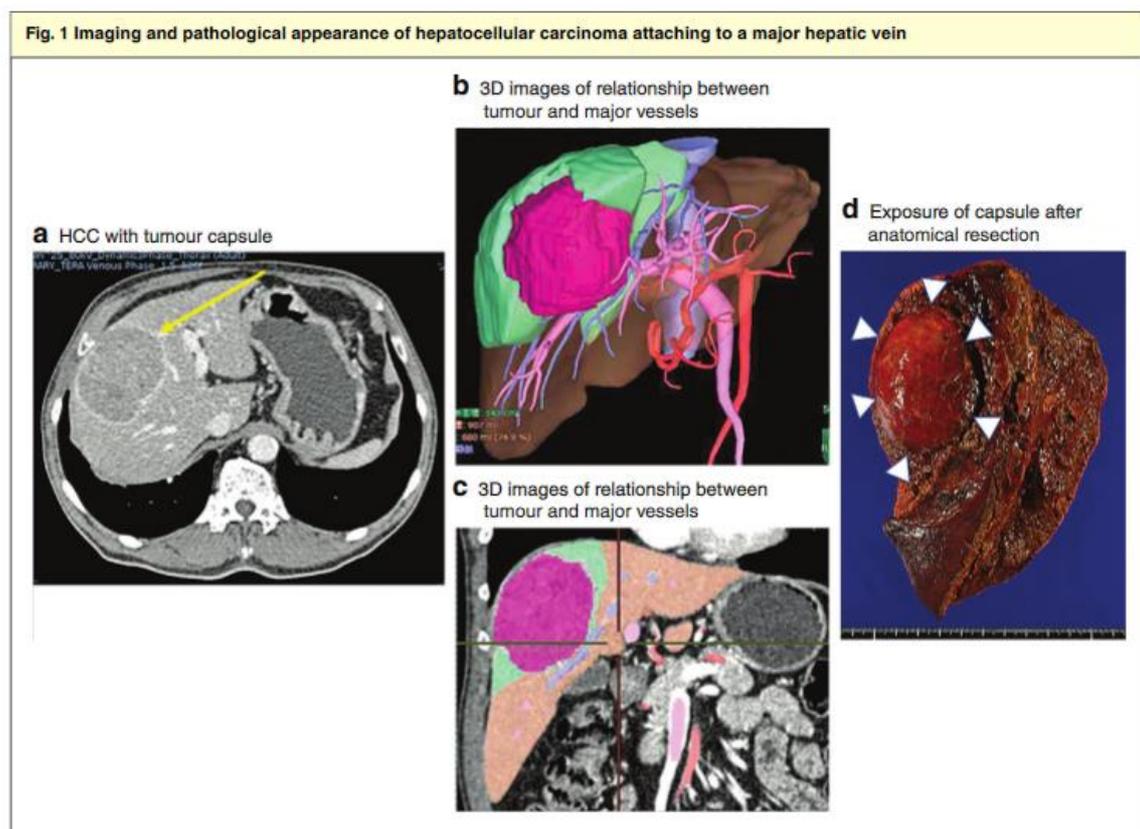


Fig. 1 Imaging and pathological appearance of hepatocellular carcinoma attaching to a major hepatic vein
a Hepatocellular carcinoma (HCC) with tumour capsule located adjacent to the middle hepatic vein (arrow). **b,c** The relationship between the tumour and major vessels is presented using simulation three-dimensional (3D) software (SYNAPSE VINCENT®; Fujifilm, Tokyo, Japan). **d** After performing an anatomical resection, the tumour capsule is exposed on the raw surface of the resected specimen (arrows).

BARIATRISCHE CHIRURGIE

Wel of geen stent als behandeling van naadlekkage na bariatrische chirurgie?

Incidence and Efficacy of Stent Placement in Leak Management After Bariatric Surgery: An MBSAQIP Analysis. AE Kanters et al. *Annals of Surgery*, January 2020, Volume 271, Issue 1, p134-139.

Pubmed ID: 30247333.

OBJECTIVE: The aim of this study was to evaluate the rates of use and efficacy of stent placement for postoperative leak following bariatric surgery.

SUMMARY OF BACKGROUND DATA: Endoscopically placed stents can successfully treat anastomotic and staple line leaks after bariatric surgery. However, the extent to which stents are used in the management of bariatric complications and rates of reoperation remain unknown.

METHODS: Data from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program participant use files were analyzed for patients who experienced anastomotic or staple line leaks after bariatric surgery, and then evaluated for use of an endoscopically placed stent. Patient and procedure-level data were compared between those who underwent stent placement versus those who required reoperation. Multivariable logistic regression was used to compare outcomes between groups.

RESULTS: A total of 354,865 bariatric cases were captured in 2015 to 2016. One thousand one hundred thirty patients (0.3%) required intervention for a leak, of whom 275 (24%) were treated with an endoscopically placed stent. One hundred seven (39%) of the patients who received stents required reoperation as

part of their care pathway. Patient characteristics were statistically similar when comparing leaks managed with stents to those treated with reoperation alone. Those treated with stents, however, had a higher likelihood of readmission (odds ratio 2.59, 95% confidence interval -1.59 to 4.20).

CONCLUSION: Placement of stents for management of leaks after bariatric surgery is common throughout the United States. The use of stents can be effective; however, it does not prevent reoperation and is associated with an increased likelihood of readmission. Both technique and resource utilization should be considered when choosing a management pathway for leaks.

