DE LEESTAFEL

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Een Maandelijkse Selectie van Wetenschappelijke GE-nieuws

Coloproctologie

Kortere opname duur en minder complicaties na darmchirurgie gevolgd door een Enhanced Recovery Pathway voor patienten 65 jaar en ouder

High Compliance to an Enhanced Recovery Pathway for Patients ≥65 Years Undergoing Major Small and Large Intestinal Surgery Is Associated With Improved Postoperative Outcomes. OP Owodunni et al. Annals of Surgery, December 2019, Volume 270, Issue 6, p1117-1123.
Pubmed ID: 29923874.

OBJECTIVE: This study was performed to evaluate compliance to an Enhanced Recovery Pathway (ERP) among patients ≥65 years and determine the effect of compliance on postoperative outcomes.

SUMMARY BACKGROUND DATA: ERPs improve postoperative outcomes in patients undergoing major surgery. Given the inherent decline of the older surgical patient, the benefit of an ERP in this population has been questioned.

METHODS: Patients undergoing major small and large intestinal surgery prior to and following ERP implementation at the Johns Hopkins Medical Institutions were entered into the ACS-NSQIP database. Outcomes included ERP compliance rates, complications, length of stay (LOS), and 30-day readmission rates were determined for older patients.

RESULTS: Nine hundred seventy-four patients (693 < 65 yrs and 281 ≥ 65 yrs) were included. Of those ≥ 65 years, 142 (51%) were entered prior to and 139 (49%) were entered following ERP implementation. More ERP than pre-ERP patients underwent laparoscopic procedures (45.3% vs. 32.4%, P = 0.02), had disseminated malignancies (9.4% vs. 2.8%, P = 0.03), and smoked (14.4% vs. 4.9%, P = 0.01). Overall compliance was 74.5%, and 47% of older ERP patients achieved high compliance (≥75% compliance with ERP variables). High compliance was associated with a 30% decrease LOS (IRR: 0.7 P = 0.001) and 60% decrease in major (CD ≥ II) complications (OR: 0.4 P = 0.05).

CONCLUSION: LOS and complication rates following implementation of an ERP were significantly improved in highly compliant elderly patients. Interventions to further improve outcomes should target decreasing variability by increasing individual compliance with an effective clinical pathway.

Risicofactoren heroperatie en heropname na abdominale chirurgie vanwege de ziekte van Crohn

Risk factors for 90-day readmission and return to the operating room following abdominal operations for Crohn's disease. F Grass et al. Surgery: December 2019 – Volume 166 – Issue 6 – p 1068-1075.
Pubmed ID: 31548096.

BACKGROUND: This study aimed to determine timing and risk factors for 30- and 90-day unplanned hospital readmissions and return to the operating room.

METHODS: Retrospective case series, including consecutive adult patients with Crohn's disease, undergoing a major abdominal surgical procedure during a 3.5-year inclusion period was performed. The primary outcomes were 0- to 30-day and 30- to 90-day readmission and return to the operating room rates. Univariate and multivariable risk factors for both outcomes at 30 and 90 days were assessed through Cox regression analysis.

RESULTS: Of 680 included patients with Crohn's disease, 89 (13.1%) were readmitted within 30 days, 55 (8.1%) within 30-90 days, and 11 (1.6%) in both follow-up periods for a combined 90-day readmission rate of 24.4% (n = 166). Multivariable risk factors for 30-day readmissions were type of procedure performed, corticosteroid use (hazard ratio [HR] 1.71, P = .01), younger age (HR 0.98 per year, P = .01), and prolonged disease duration (HR 1.03 per year, P = .03). No significant risk factors identified for 30- to 90-day readmissions. By 90 days, 76 patients (11.2%) had a return to the operating room (of which 8.8% was within 30 days). Risk factors for 30-day return to the operating room included tobacco use (HR 1.86, P = .04), diabetes (HR 3.30, P = .01), corticosteroid use (HR 3.51, P <.001), and preoperative immunomodulator therapy (HR 2.70, P < .001).

CONCLUSION: Type of surgery, corticosteroid use, younger age, and prolonged disease duration were associated with 30-day hospital readmission, and tobacco use, diabetes, corticosteroid use, and preoperative immunomodulator therapy were risk factors for 30-day return to the operating room. Postoperative biologic therapy did not increase hospital readmission or return to operating room rates within 90 days of surgery.

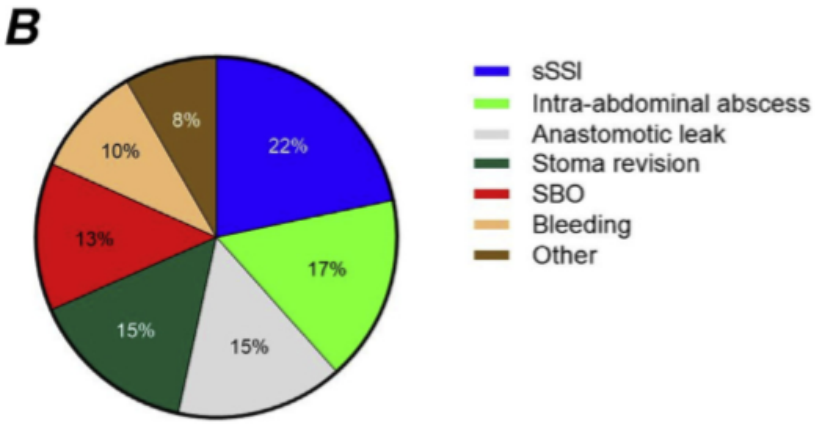


Fig 2. (*B*) Main indications for 30-day reoperation (n=60)

UPPER GI

Impact van centralisatie van zorg op de overleving van gereseceerde maagkanker patiënten

Effect of Hospital Volume With Respect to Performing Gastric Cancer Resection on Recurrence and Survival: Results From the CRITICS Trial. YHM Claassen et al. Annals of Surgery, December 2019, Volume 270, Issue 6, p1096-1102.
Pubmed ID: 29995679.

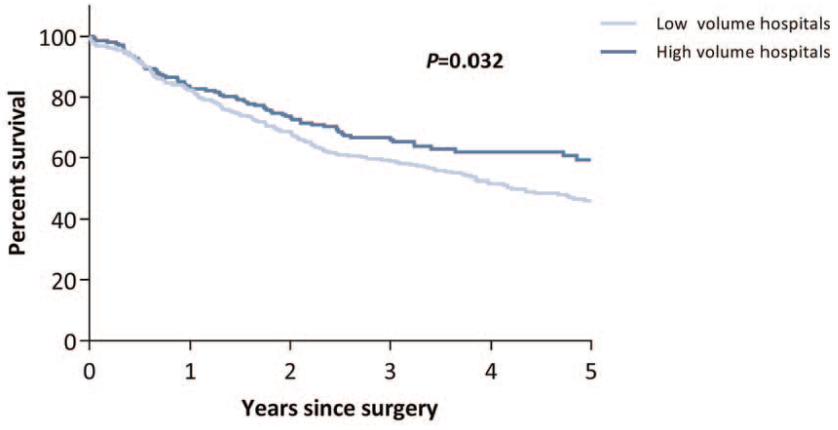
OBJECTIVE: We examined the association between surgical hospital volume and both overall survival (OS) and disease-free survival (DFS) using data obtained from the international CRITICS (ChemoRadiotherapy after Induction chemotherapy In Cancer of the Stomach) trial.

SUMMARY BACKGROUND DATA: In the CRITICS trial, patients with resectable gastric cancer were randomized to receive preoperative chemotherapy followed by adequate gastrectomy and either chemotherapy or chemoradiotherapy.

METHODS: Patients in the CRITICS trial who underwent a gastrectomy with curative intent in a Dutch hospital were included in the analysis. The annual number of gastric cancer surgeries performed at the participating hospitals was obtained from the Netherlands Cancer Registry; the hospitals were then classified as low-volume (1-20 surgeries/year) or high-volume (≥21 surgeries/year) and matched with the CRITICS trial data. Univariate and multivariate analyses were then performed to evaluate the hazard ratio (HR) between hospital volume and both OS and DFS.

RESULTS: From 2007 through 2015, 788 patients were included in the CRITICS trial. Among these 788 patients, 494 were eligible for our study; the median follow-up was 5.0 years. Five-year OS was 59.2% and 46.1% in the high-volume and low-volume hospitals, respectively. Multivariate analysis revealed that undergoing surgery in a high-volume hospital was associated with higher OS [HR = 0.69, 95% confidence interval (CI) = 0.50-0.94, P = 0.020] and DFS (HR = 0.73, 95% CI: 0.54-0.99, P = 0.040).

CONCLUSIONS: In the CRITICS trial, hospitals with a high annual volume of gastric cancer surgery were associated with higher overall and DFS. These findings emphasize the value of centralizing gastric cancer surgeries in the Western world.



Volume:							
Low	N at risk	287	236	196	159	122	90
High	N at risk	207	171	134	99	56	42

FIGURE 3. Kaplan-Meier curve of overall survival since surgery for all 494 patients who underwent gastrectomy for gastric cancer in low-volume and high-volume hospitals in the Netherlands.

Meten van skeletspier massa als voorspeller van response op neoadjuvante chemotherapie en postoperatieve complicaties?

Impact of measurement of skeletal muscle mass on clinical outcomes in patients with esophageal cancer undergoing esophagectomy after neoadjuvant chemotherapy. T Ishida et al. Surgery: December 2019 – Volume 166 – Issue 6 – p 1041-1047.
Pubmed ID: 31607486.

BACKGROUND: Some studies have reported that sarcopenia is linked to clinical outcomes in multiple types of malignancies, but this association has not been established in esophageal cancer. We assessed how sarcopenia affects clinical outcomes of multidisciplinary treatments for esophageal cancer.

METHODS: We included 165 esophageal cancer patients who had undergone neoadjuvant chemotherapy followed by esophagectomy. Computed tomography was used for cross-sectional measurement of the psoas muscle at the third lumbar vertebra; we then calculated the height-adjusted psoas muscle index. Pre- and postneoadjuvant chemotherapy psoas muscle indices were evaluated for associations with neoadjuvant chemotherapy response and neoadjuvant chemotherapy -related adverse events and postoperative complications, in addition to survival. Psoas muscle index cutoffs were 6.36 cm2/m2 for men and 3.92 cm2/m2 for women.

RESULTS: Psoas muscle index decreased after neoadjuvant chemotherapy (from 7.17 to 6.96 cm2/m2; P = .0008), and specifically in men (from 7.45 to 7.23 cm2/m2; P = .0001) but not in women (from 5.21 to 5.17 cm2/m2; P = .810). Preneoadjuvant chemotherapy psoas muscle index (low versus high) was associated with neoadjuvant chemotherapy response (response rate: 65.1% vs 80.3%; P = .0494) and neoadjuvant chemotherapy-related adverse events (neutropenia: 93.0% vs 78.7%; P = .0337; febrile neutropenia: 53.5% vs 34.3%; P = .0278; hyponatremia: 51.2% vs 31.2%; P = .0190). Post-neoadjuvant chemotherapy psoas muscle index correlated with postoperative rate of complications (56.9% vs 33.3%; P = .0046), especially pneumonia (31.4% vs 9.7% P = .0008). Psoas muscle index was not associated with survival.

Table V
Postoperative complications and surgical outcomes classified by post-NAC PMI and univariate and multivariate analysis on overall complications and pneumonia

Factors (≥grade 2)	Total ($N = 165$) (%)	Low PMI ($n = 51$) (%)	High PMI ($n = 114$) (%)	P value
Overall complications	67 (40.6)	29 (57)	38 (33.3)	.0046
Pneumonia	27 (16.4)	16 (31)	11 (9.7)	.0008
Anastomotic leak	7 (4.2)	3 (6)	4 (3.5)	.4845
Expectoration disorder	12 (7.3)	10 (22)	14 (12.7)	.1380
Arrhythmia	18 (10.9)	7 (14)	11 (9.7)	.4376

CONCLUSION: Cross sectional measures of sarcopenia before and after neoadjuvant chemotherapy could predict tumor response, neoadjuvant chemotherapy -related adverse events, and postoperative complications in multidisciplinary treatments for esophageal cancer.

HPB

Kwaliteit van leven na pancreatoduodenectomie: Canadese versie van PACAP

Population-Level Symptom Assessment Following Pancreaticoduodenectomy for Adenocarcinoma.
S. Tungs et al; JAMA Surg. 2019;154(11):e193348.
Pubmed ID: 31483457.

IMPORTANCE: Postoperative morbidity associated with pancreaticoduodenectomy (PD) for pancreatic adenocarcinoma (PA) remains as high as 70%. However, to our knowledge, few studies have examined quality of life in this patient population.

OBJECTIVE: To identify symptom burden and trajectories and factors associated with high symptom burden following PD for PA.

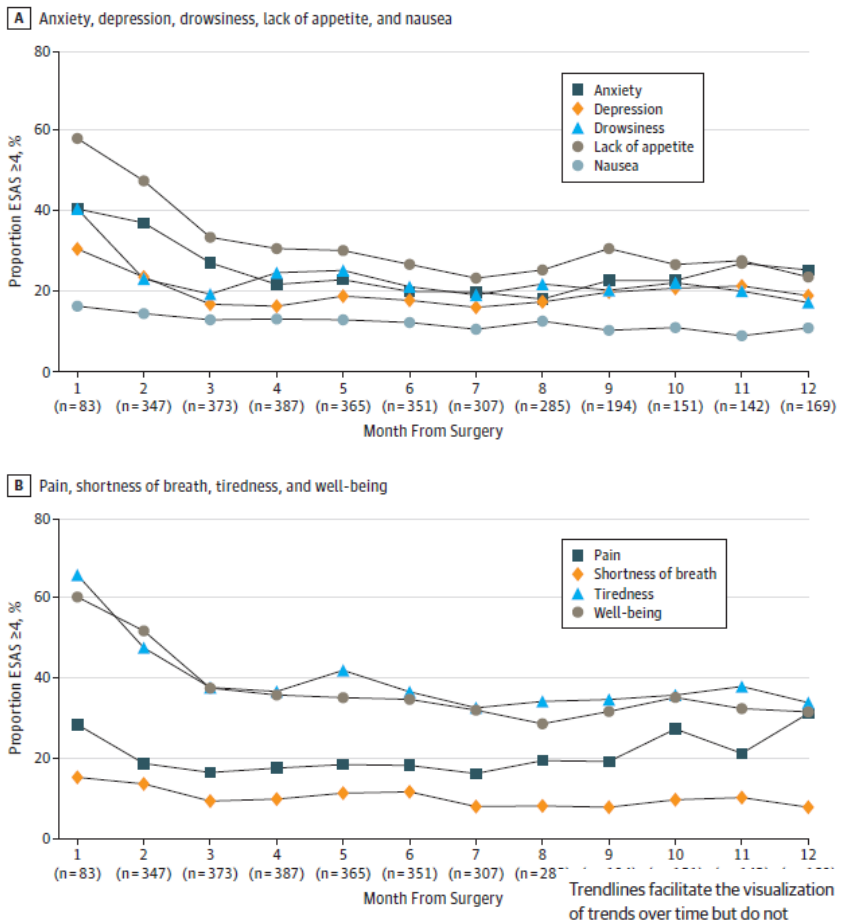
DESIGN, SETTING, AND PARTICIPANTS: This population-based cohort study of patients undergoing PD for PA diagnosed between 2009 and 2015 linked population-level administrative health care data to routinely prospectively collected Edmonton Symptom Assessment System (ESAS) scores from 2009 to 2015, with a data analysis undertaken in 2018.

EXPOSURES: Baseline characteristics, including age, sex, income quintile, rurality, immigration status, and comorbidity burden, as well as treatment characteristics, including year of surgery and receipt of chemotherapy.

MAIN OUTCOME AND MEASURES: The outcome of interest was moderate to severe symptoms (defined as ESAS ≥4) for anxiety, depression, drowsiness, lack of appetite, nausea, pain, shortness of breath, tiredness, and impaired well-being. The monthly prevalence of moderate to severe symptoms was presented graphically for each symptom. Multivariable regression models identified factors associated with the reporting of moderate to severe symptoms.

RESULTS: We analyzed 6058 individual symptom assessments among 615 patients with PA who underwent resection (285 women [46.3%]) with ESAS data. Tiredness (443 [72%]), impaired well-being (418 [68%]), and lack of appetite (400 [65%]) were most commonly reported as moderate to severe. The proportion of patients with moderate to severe symptoms

Figure 3. Proportion of All Patients Reporting Moderate to Severe Edmonton Symptom Assessment Scores (ESAS) for All Symptoms by Month of Assessment Following Surgery



Trendlines facilitate the visualization of trends over time but do not represent continuous data. Numbers under the x-axis indicate the denominator for each month. A moderate to severe ESAS is a score of more than 4.

was highest immediately after surgery (range, 14%-66% per symptom) and decreased over time, stabilizing around 3 months (range, 8%-42% per symptom). Female sex, higher comorbidity, and lower income were associated with a higher risk of reporting moderate to severe symptoms. Receipt of adjuvant chemotherapy was not associated with the risk of moderate to severe symptoms.

CONCLUSIONS AND RELEVANCE: There is a high prevalence of symptoms following PD for PA, with improvement over the first 3 months following surgery. In what to our knowledge is the largest cohort reporting on symptom burden for this population, we have identified factors associated with symptom severity. These findings will aid in managing patients' perioperative expectations and designing strategies to improve targeted symptom management.

''Recurrence patterns'' in ESPAC-4 studie

Patterns of Recurrence After Resection of Pancreatic Ductal Adenocarcinoma: A Secondary Analysis of the ESPAC-4 Randomized Adjuvant Chemotherapy Trial. R.P. Jones et al. JAMA Surg. 2019;154(11):1038-1048. Pubmed ID: 31483448.

MPORTANCE: The patterns of disease recurrence after resection of pancreatic ductal adenocarcinoma with adjuvant chemotherapy remain unclear.

OBJECTIVE: To define patterns of recurrence after adjuvant chemotherapy and the association with survival.

DESIGN, SETTING, AND PARTICIPANTS: Prospectively collected data from the phase 3 European Study Group for Pancreatic Cancer 4 adjuvant clinical trial, an international multicenter study. The study included 730 patients who had resection and adjuvant chemotherapy for pancreatic cancer. Data were analyzed between July 2017 and May 2019.

INTERVENTIONS: Randomization to adjuvant gemcitabine or gemcitabine plus capecitabine.

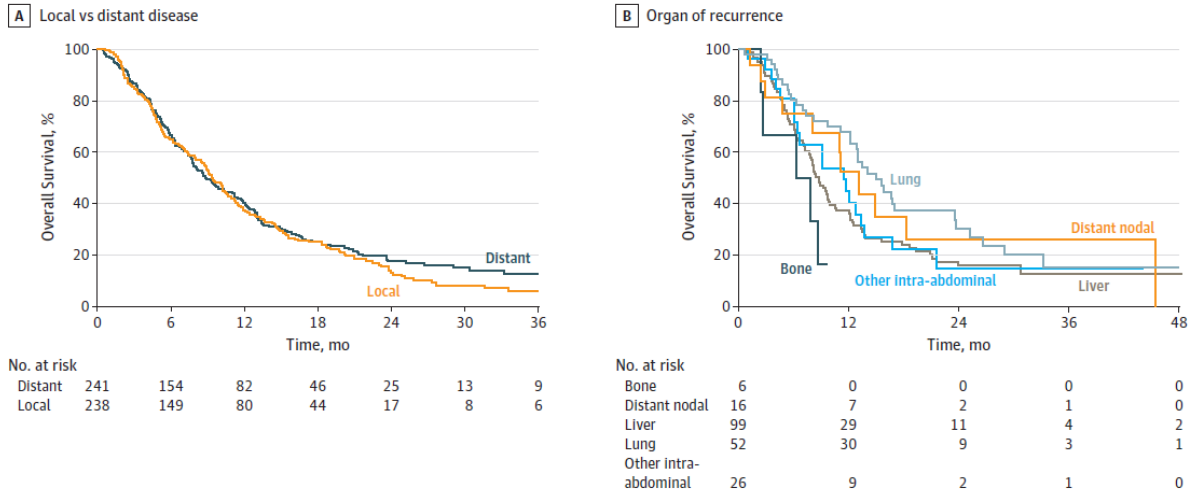
MAIN OUTCOMES AND MEASURES: Overall survival, recurrence, and sites of recurrence.

RESULTS: Of the 730 patients, median age was 65 years (range 37-81 years), 414 were men (57%), and 316 were women (43%). The median follow-up time from randomization was 43.2 months (95% CI, 39.7-45.5 months), with overall survival from time of surgery of 27.9 months (95% CI, 24.8-29.9 months) with gemcitabine and 30.2 months (95% CI, 25.8-33.5 months) with the combination (HR, 0.81; 95% CI, 0.68-0.98; P = .03). The 5-year survival estimates were 17.1% (95% CI, 11.6%-23.5%) and 28.0% (22.0%-34.3%), respectively. Recurrence occurred in 479 patients (65.6%); another 78 patients (10.7%) died without recurrence. Local recurrence occurred at a median of 11.63 months (95% CI, 10.05-12.19 months), significantly different from those with distant recurrence with a median of 9.49 months (95% CI, 8.44-10.71 months) (HR, 1.21; 95% CI, 1.01-1.45; P = .04). Following recurrence, the median survival was 9.36 months (95% CI, 8.08-10.48 months) for local recurrence and 8.94 months (95% CI, 7.82-11.17 months) with distant recurrence (HR, 0.89; 95% CI, 0.73-1.09; P = .27). The median overall survival of patients with distant-only recurrence (23.03 months; 95% CI, 19.55-25.85 months) or local with distant recurrence (23.82 months; 95% CI, 17.48-28.32 months) was not significantly different from those with only local recurrence (24.83 months; 95% CI, 22.96-27.63 months) (P = .85 and P = .35, respectively). Gemcitabine plus capecitabine had a 21% reduction of death following recurrence compared with monotherapy (HR, 0.79; 95% CI, 0.64-0.98; P = .03).

CONCLUSIONS AND RELEVANCE: There were no significant differences between the time to recurrence and subsequent and overall survival between local and distant recurrence. Pancreatic cancer behaves as a systemic disease requiring effective systemic therapy after resection.

TRIAL REGISTRATION: Clinicaltrials.gov Identifier: NCT00058201, EudraCT 2007-004299-38, and ISRCTN 96397434.

Figure 2. Kaplan-Meier Curves Showing Survival From Time of Recurrence



No. at risk

Distant	241	154	82	46	25	13	9
Local	238	149	80	44	17	8	6

No. at risk

Bone	6	0	0	0	0
Distant nodal	16	7	2	1	0
Liver	99	29	11	4	2
Lung	52	30	9	3	1
Other intra-abdominal	26	9	2	1	0

A, Recurrence stratified by local vs distant disease. B, Recurrence stratified by organ of recurrence.

LEVERCHIRURGIE

Kans op ''cure'' voor HCC patienten?

Defining the chance of cure after resection for hepatocellular carcinoma within and beyond the Barcelona Clinic Liver Cancer guidelines: A multi-institutional analysis of 1,010 patients. D.I. Tsilimigras et al; Surgery: December 2019 – Volume 166 – Issue 6 – p 967-974.
Pubmed ID: 31606196.

BACKGROUND AND OBJECTIVE: Surgery is considered the only potentially curative treatment option for patients with hepatocellular carcinoma. However, the chance that patients will eventually be "cured" after liver resection for hepatocellular carcinoma remains ill defined.

METHODS: Patients who underwent curative-intent hepatectomy for hepatocellular carcinoma between 1998 and 2017 were identified using an international multi-institutional database. A nonmixture cure model was used with disease-free survival as a primary measure to estimate cure fractions after matching patients with the general population by age, race, and sex.

RESULTS: Among 1,010 patients, the median and 5-year disease-free survival were 2.8 years and 36.6%, respectively. The probability of being cured after hepatocellular carcinoma resection was 42.2% and the median time to cure was 3.35 years. The multivariable cure model revealed preoperative alpha-fetoprotein level, tumor size, tumor number, and margin status as independent predictors of cure. The cure fraction for patients with an alpha-fetoprotein level ≤ 10 ng/mL, largest tumor size ≤5 cm, ≤3 nodules, and R0 resection was 61.6%. In contrast, patients who had all 4 unfavorable prognostic factors (ie, alpha-fetoprotein >11 ng/mL, nodules ≥4, size >5cm, R1 resection) had a cure fraction of 15.8%. Although the probability of cure was 47.6% among Barcelona Clinic Liver Cancer-A patients, patients undergoing resection for Barcelona Clinic Liver Cancer-B hepatocellular carcinoma had a 37.6% cure fraction. Only alpha-fetoprotein levels predicted the probability of cure among Barcelona Clinic Liver Cancer-B patients.

CONCLUSION: Roughly 4 in 10 patients could be considered "cured" after liver resection for hepatocellular carcinoma. Although cure was achieved more often after resection for Barcelona Clinic Liver Cancer-A hepatocellular carcinoma, surgery still provided a reasonable probability of cure among select patients with Barcelona Clinic Liver Cancer-B hepatocellular carcinoma.

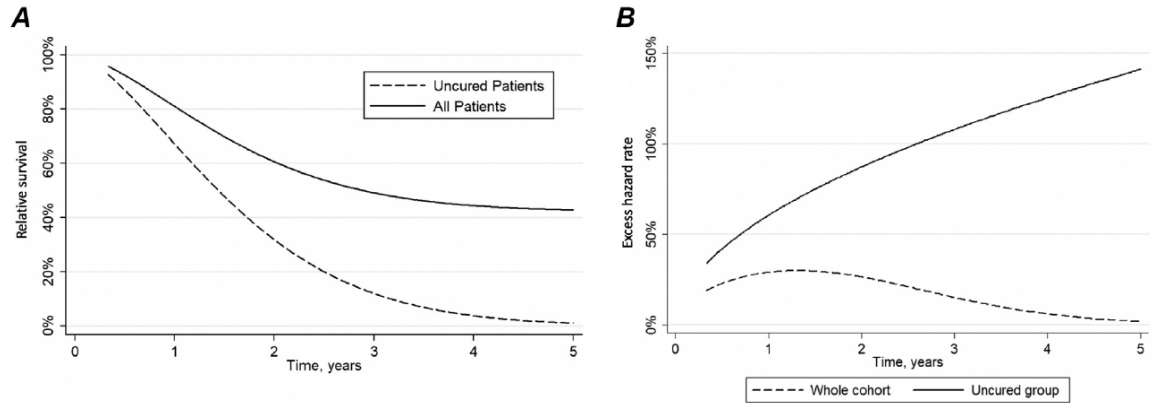


Fig 2. Cure model results depicting (*A*) the relative survival of patients in the total cohort and uncured patients. Cure model results demonstrating (*B*) the excess hazard of death of patients in the total cohort and uncured patients.

Meer resecties na chemo+radiotherapie voor irresectabele colorectale levermetastasen?

Secondary technical resectability of colorectal cancer liver metastases after chemotherapy with or without selective internal radiotherapy in the randomized SIRFLOX trial. B. Garrlipp et al. BJS, Dec 2019 – Volume 106 – Issue 13, pages 1837-1846. Pubmed ID: 31424576.

BACKGROUND: Secondary resection of initially unresectable colorectal cancer liver metastases (CRLM) can prolong survival. The added value of selective internal radiotherapy (SIRT) to downsize lesions for resection is not known. This study evaluated the change in technical resectability of CRLM with the addition of SIRT to FOLFOX-based chemotherapy.

METHODS: Baseline and follow-up hepatic imaging of patients who received modified FOLFOX (mFOLFOX6: fluorouracil, leucovorin, oxaliplatin) chemotherapy with or without bevacizumab (control arm) versus mFOLFOX6 (with or without bevacizumab) plus SIRT using yttrium-90 resin microspheres (SIRT arm) in the phase III SIRFLOX trial were reviewed by three or five (of 14) expert hepatopancreatobiliary surgeons for resectability. Reviewers were blinded to one another, treatment assignment, extrahepatic disease status, and information on clinical and scanning time points. Technical resectability was defined as at least 60 per cent of reviewers (3 of 5, or 2 of 3) assessing a patient's liver metastases as surgically removable.

RESULTS: Some 472 patients were evaluable (SIRT, 244; control, 228). There was no significant baseline difference in the proportion of technically resectable liver metastases between SIRT (29, 11·9 per cent) and control (25, 11·0 per cent) arms (P = 0·775). At follow-up, significantly more patients in both arms were deemed technically resectable compared with baseline: 159 of 472 (33·7 per cent) versus 54 of 472 (11·4 per cent) respectively (P = 0·001). More patients were resectable in the SIRT than in the control arm: 93 of 244 (38·1 per cent) versus 66 of 228 (28·9 per cent) respectively (P < 0·001).

CONCLUSION: Adding SIRT to chemotherapy may improve the resectability of unresectable CRLM.

BARIATRISCHE CHIRURGIE

Wachttijden voor bariatrische chirurgie lopen op in USA

Factors Associated With Long Wait Times for Bariatric Surgery. R. Alvarez et al. Annals of Surgery, December 2019, Volume 270, Issue 6, p1103-1109.
Pubmed ID: 29794842.

BACKGROUND: Despite its proven safety and efficacy, bariatric surgery is an underutilized therapy for severe obesity. Wait times for surgery are largely unexplored in the United States and may impact access to care.

OBJECTIVE: To determine the amount of time between initial bariatric surgery clinic visit and operative date and identify factors associated with longer wait times.

METHODS: A statewide clinical data registry was queried from 2006 to 2016 and 60,791 patients undergoing primary bariatric surgery were identified. Demographics, comorbidities, 30-day complications, and 1-year patient-reported outcomes were compared between shortest and longest wait time quartiles. Analyses were performed using Chi-square, t-test, and logistic regression.

RESULTS: Median wait times for bariatric surgery increased from 86 to 159 days during the study period. Median wait times were ≤67 days for the shortest wait time quartile and ≥204 days for the longest wait time quartile. Factors independently associated with longer wait times included Medicaid insurance [odds ratio (OR) 3.02; 95% confidence interval (CI): 2.58-3.53], sleep apnea (OR 1.49; 95% CI: 1.41-1.58), psychological disorder (OR 1.25; 95% CI: 1.18-1.32), hyperlipidemia (OR 1.21; 95% CI:

1.14-1.28), smoking history (OR 1.11; 95% CI: 1.05-1.17), and white race (OR 0.665; 95% CI: 0.614-0.720). Preoperative weight loss, risk adjusted complication rates, postoperative self-reported weight loss, and comorbidity remission were similar between groups.

CONCLUSIONS: Over the past decade, eligible patients are experiencing longer wait times when pursuing bariatric surgery. Complex patients with Medicaid insurance are experiencing the longest delay despite similar outcomes and preoperative weight loss. Policies that delay surgery should be re-examined.

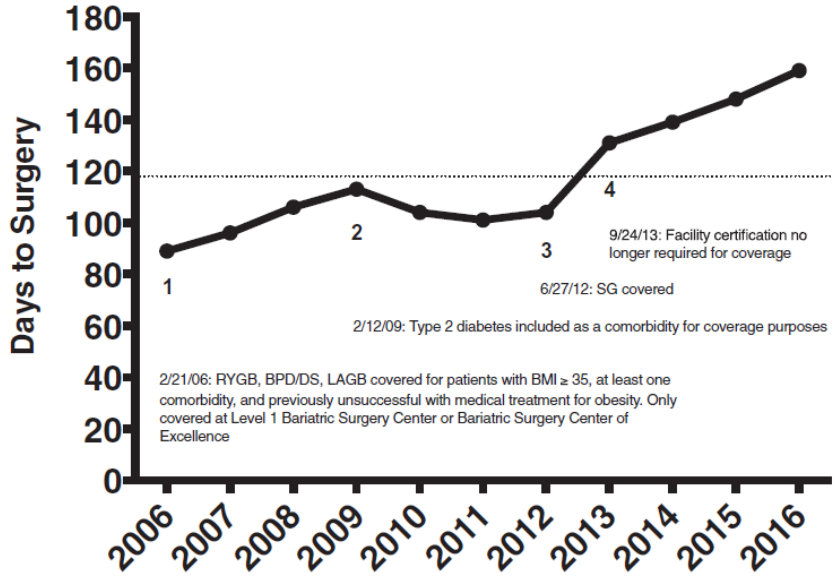


FIGURE 1. Evolution of patient wait time for bariatric surgery from 2006 to 2016 including chronology of major changes to the National Coverage Determination for Bariatric Surgery for Treatment of Co-Morbid Conditions Related to Morbid Obesity by the Centers for Medicare and Medicaid Services. Dotted line represents the median number of days for the entire study period.

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