DE LEESTAFEL

FEBRUARI 2019

Een Maandelijkse Selectie van Wetenschappelijke GE-nieuws

Coloproctologie

Verbeterde overall survival stadium 4 colon kanker na neo-adjuvante radiotherapy

Neoadjuvant radiation for clinical T4 colon cancer: A potential improvement to overall survival.
AT Hawkins et al. Surgery. February 2019 – Volume 165 – Issue 2 – p 469-475.
Pubmed ID: 30017250

BACKGROUND: Resection of T4 colon cancer remains challenging compared to lower T stages. Data on the effect of neoadjuvant radiation to improve resectability and survival are lacking. The purpose of this study is to describe the use and outcomes of neoadjuvant radiation therapy in clinical T4 colon cancer.

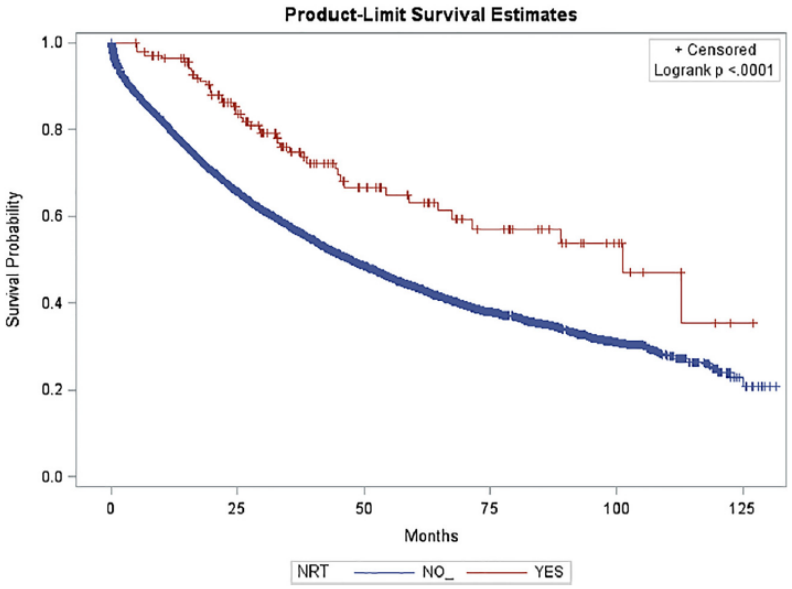


Fig. 2. Kaplan-Meier curve comparing overall survival by neoadjuvant radiation therapy for the entire cohort.

METHODS: Adults with clinical evidence of T4 locally advanced colon cancer were included from the National Cancer Database (2004-2014). Bivariate and multivariable analyses were used to examine the association between neoadjuvant radiation therapy and R0 resection rate, multivisceral resection, and overall survival.

RESULTS: Fifteen thousand two hundred and seven patients with clinical T4 disease who underwent resection were identified over the study period. One hundred ninety-five (1.3%) underwent neoadjuvant radiation therapy. Factors associated with the use of neoadjuvant radiation therapy included younger age, male sex, private insurance, lower Charlson Comorbidity Index score, and treatment at an academic research program. Neoadjuvant radiation therapy was associated with superior R0 resection rates (87.2% neoadjuvant radiation therapy vs 79.8% no neoadjuvant radiation therapy; P = .009). Five-year overall survival was increased in the neoadjuvant radiation therapy group (62.0% neoadjuvant radiation therapy vs 45.7% no neoadjuvant radiation therapy; P < .001). The benefit of neoadjuvant radiation therapy persisted in a Cox proportional hazards multivariable model containing a number of confounding variables, including comorbidity and postoperative chemotherapy (odds ratio 1.37; 95% confidence interval 1.05-1.77; P = .01). In a subgroup analysis of T4b patients, there was an even greater size effect in adjusted overall survival (odds ratio 1.71; 95% confidence interval 1.07-2.72; P = .02).

CONCLUSION: Although radiation is rarely used in locally advanced colon cancer, this National Cancer Database analysis suggests that the use of neoadjuvant radiation for clinical T4 disease may be associated with superior R0 resection rates and improved overall survival. Patients with clinical T4b disease may benefit the most from treatment. Neoadjuvant radiation therapy should be considered on a case-by-case basis in locally advanced colon cancer.

Goede lange termijn oncologische uitkomsten na chemoradiotherapie gevolgd door TEM voor rectum carcinoom

Long-term Oncological and Functional Outcomes of Chemoradiotherapy Followed by Organ-Sparing Transanal Endoscopic Microsurgery for Distal Rectal Cancer; The CARTS Study. RCH Stijns et al. JAMA Surg. 2019;154(1):47-54.

Pubmed ID: 30304338

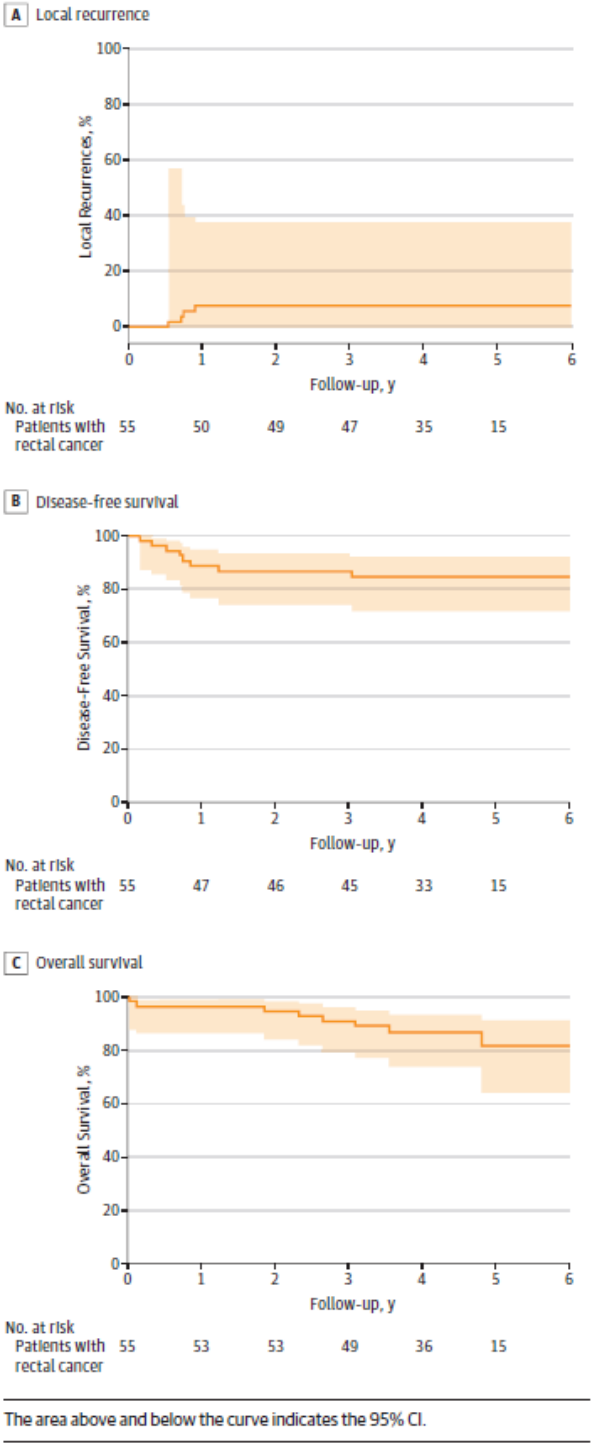
IMPORTANCE: Treatment of rectal cancer is shifting toward organ preservation aiming to reduce surgery-related morbidity. Short-term outcomes of organ-preserving strategies are promising, but long-term outcomes are scarce in the literature.

OBJECTIVE: To explore long-term oncological outcomes and health-related quality of life (HRQL) in patients with cT1-3N0M0 rectal cancer who underwent neoadjuvant chemoradiotherapy (CRT) followed by transanal endoscopic microsurgery (TEM).

DESIGN, SETTING, AND PARTICIPANTS: In this multicenter phase II feasibility study, patients with cT1- between February 2011 and September 2012 were prospectively included. These patients were to be treated with neoadjuvant CRT followed by TEM in case of good response. An intensive follow-up scheme was used to detect local recurrences and/or distant metastases. Data from validated HRQL questionnaires and low anterior resection syndrome questionnaires were collected. Data were analyzed from February 2011 to April 2017.

MAIN OUTCOMES AND MEASURES: The primary study outcome of the study was the number of ypT0-1 specimens by performing TEM. Secondary outcome parameters were locoregional recurrences and HRQL.

RESULTS: Of the 55 included patients, 30 (55%)



were male, and the mean (SD) age was 64 (39-82) years. Patients were followed up for a median (interquartile range) period of 53 (39-57) months. Two patients (4%) died during CRT, 1 (2%) stopped CRT, and 1 (2%) was lost to follow-up. Following CRT, 47 patients (85%) underwent TEM, of whom 35 (74%) were successfully treated with local excision alone. Total mesorectal excision was performed in 16 patients (4 with inadequate responses, 8 with completion after TEM, and 4 with salvage for local recurrence). The actuarial 5-year local recurrence rate was 7.7%, with 5-year disease-free and overall survival rates of 81.6% and 82.8%, respectively. Health-related quality of life during follow-up was equal to baseline, with improved emotional well-being in patients treated with local excision (mean score at baseline, 72.0; 95% CI, 67.1-80.1; mean score at follow-up, 86.9; 95% CI, 79.2-94.7; P = .001). Major, minor, and no low anterior resection syndrome was experienced in 50%, 28%, and 22%, respectively, of patients with successful organ preservation.

CONCLUSIONS AND RELEVANCE: In early-stage rectal cancer (cT1-3N0M0), CRT enables organ preservation with additional TEM surgery in approximately two-thirds of patients with good long-term oncological outcome and HRQL. This multimodality treatment triggers a certain degree of bowel dysfunction, and one-third of patients still undergo radical surgery and are overtreated by CRT.

UPPER GI

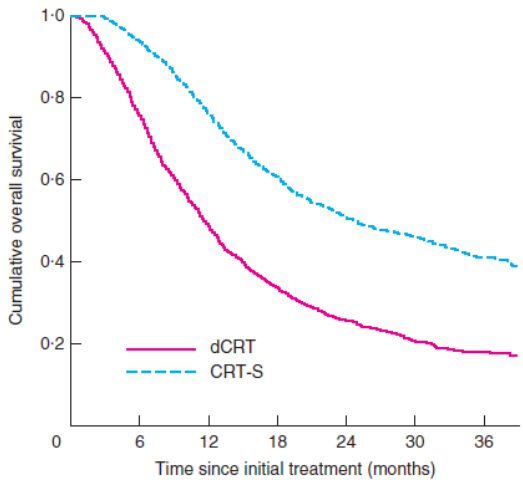
Definitieve CRT inferieur aan neo-adjuvante CRT en chirurgie voor stadium II en III oesophagus plaveiselcelcarcinoom

Survival after neoadjuvant chemoradiotherapy and oesophagectomy versus definitive chemoradiotherapy for patients with oesophageal squamous cell carcinoma. B-Y Wang et al. BJS. Feb 2019 – Volume 106 – Issue 3, pages 255-262.

Pubmed ID: 30395362

BACKGROUND: Whether there is a difference in survival after neoadjuvant chemoradiotherapy plus surgery (CRT-S) compared with definitive chemoradiotherapy (dCRT) in patients with locally advanced oesophageal squamous cell carcinoma (SCC) remains controversial.

METHODS: Patients with SCC who underwent curative treatment from 2008 to 2014 were identified from the Taiwan Cancer Registry. Propensity score matching was undertaken to balance pretreatment clinical variables. Overall survival was compared between patients undergoing CRT-S or dCRT. Univariable and multivariable analyses were performed to identify prognostic factors for overall survival.



RESULTS: A total of 5832 patients with clinical stage II and III oesophageal SCC receiving CRT-S (1754) or dCRT (4078) were included. After propensity score matching, each group included 1661 patients. The 3-year overall survival rate for patients treated with CRT-S was 41·1 per cent compared with 17·9 per cent for those who had dCRT (P < 0·001). In multivariable analysis, treatment modality was an independent prognostic factor in the overall cohort before propensity score matching: hazard ratio 0·45 (95 per cent c.i. 0·40 to 0·51) for CRT-S versus dCRT (P < 0·001). In separate analyses of patients with clinical stage II and those with stage III disease, CRT-S was

associated with significantly better overall survival than dCRT.
CONCLUSIONS: Neoadjuvant chemoradiotherapy and oesophagectomy is associated with better overall survival than dCRT in patients with stage II and III oesophageal SCC.

Wereldwijde gestandaardiseerde complicatie registratie voor slokdarmresectie

Benchmarking Complications Associated with Esophagectomy. DE Low et al. Ann Surg: 2019;269(2):291–298
Pubmed ID: 29206677

OBJECTIVE: Utilizing a standardized dataset with specific definitions to prospectively collect international data to provide a benchmark for complications and outcomes associated with esophagectomy.
SUMMARY OF BACKGROUND DATA: Outcome reporting in oncologic surgery has suffered from the lack of a standardized system for reporting operative results particularly complications. This is particularly the case for esophagectomy affecting the accuracy and relevance of international outcome assessments, clinical trial results, and quality improvement projects.
METHODS: The Esophageal Complications Consensus Group (ECCG) involving 24 high-volume esophageal surgical centers in 14 countries developed a standardized platform for recording complications and quality measures associated with esophagectomy. Using a secure online database (ESODATA.org), ECCG centers prospectively recorded data on all resections according to the ECCG platform from these centers over a 2-year period.
RESULTS: Between January 2015 and December 2016, 2704 resections were entered into the database. All demographic and follow-up data fields were 100% complete. The majority of operations were for cancer (95.6%) and typically located in the distal esophagus (56.2%). Some 1192 patients received neoadjuvant chemoradiation (46.1%) and 763 neoadjuvant chemotherapy (29.5%). Surgical approach involved open procedures in 52.1% and minimally invasive operations in 47.9%. Chest anastomoses were done most commonly (60.7%) and R0 resections were accomplished in 93.4% of patients. The overall incidence of complications was 59% with the most common individual complications being pneumonia (14.6%) and atrial dysrhythmia (14.5%). Anastomotic leak, conduit necrosis, chyle leaks, recurrent nerve injury occurred in 11.4%, 1.3%, 4.7%, and 4.2% of cases, respectively. Clavien-Dindo complications ≥ IIIb occurred in 17.2% of patients. Readmissions occurred in 11.2% of cases and 30- and 90-day mortality was 2.4% and 4.5%, respectively.
CONCLUSIONS: Standardized methods provide contemporary international benchmarks for reporting outcomes after esophagectomy.

HPB

Onderstadiering van pancreascarcinoom

Understaging of clinical stage I pancreatic cancer and the impact of multimodality therapy. KA Baugh et al; Surgery 2019; 165 (2); 307-314.
Pubmed ID: 30243481

BACKGROUND AND OBJECTIVE: Although current guidelines recommend multimodal therapy for all patients with pancreatic ductal adenocarcinoma, it is unclear the extent to which clinical stage I patients are accurately staged and how this may affect management.
METHODS: In this retrospective cohort study of 4,404 patients aged 18–79 years with clinical stage 1 (ie, T1N0 or T2N0) pancreatic ductal adenocarcinoma treated with upfront resection in the National Cancer Database (2004–2014), understaging was ascertained by comparing pretreatment clinical stage with pathologic stage. The association between adjuvant treatment and overall risk of death among true stage I and understaged patients was evaluated using multivariable Cox regression.

RESULTS: Upstaging was identified in 72.6% of patients (62.8% T3/4, 53.9% N1) of whom 69.7% received adjuvant therapy compared with 47.0% with true stage I disease. Overall survival at 5 years among those with true stage I disease was significantly higher than those who had been clinically understaged (42.9% vs 16.6%; log-rank, $p < 0.001$). For true stage I patients, adjuvant therapy was not associated with risk of death (hazard ratio: 1.07, 95% confidence interval: 0.89–1.29). For understaged patients, adjuvant therapy significantly decreased risk of death (hazard ratio: 0.64, 95% confidence interval: 0.55–0.74).
CONCLUSION: The majority of clinical stage I pancreatic ductal adenocarcinoma patients actually have higher-stage disease and benefit from multimodal therapy; however, one third of understaged patients do not receive any adjuvant treatment. Clinicians should discuss all potential treatment strategies with patients (in the context of the acknowledged risks and benefits), including the utilization of neoadjuvant approaches in those presenting with potentially resectable disease.

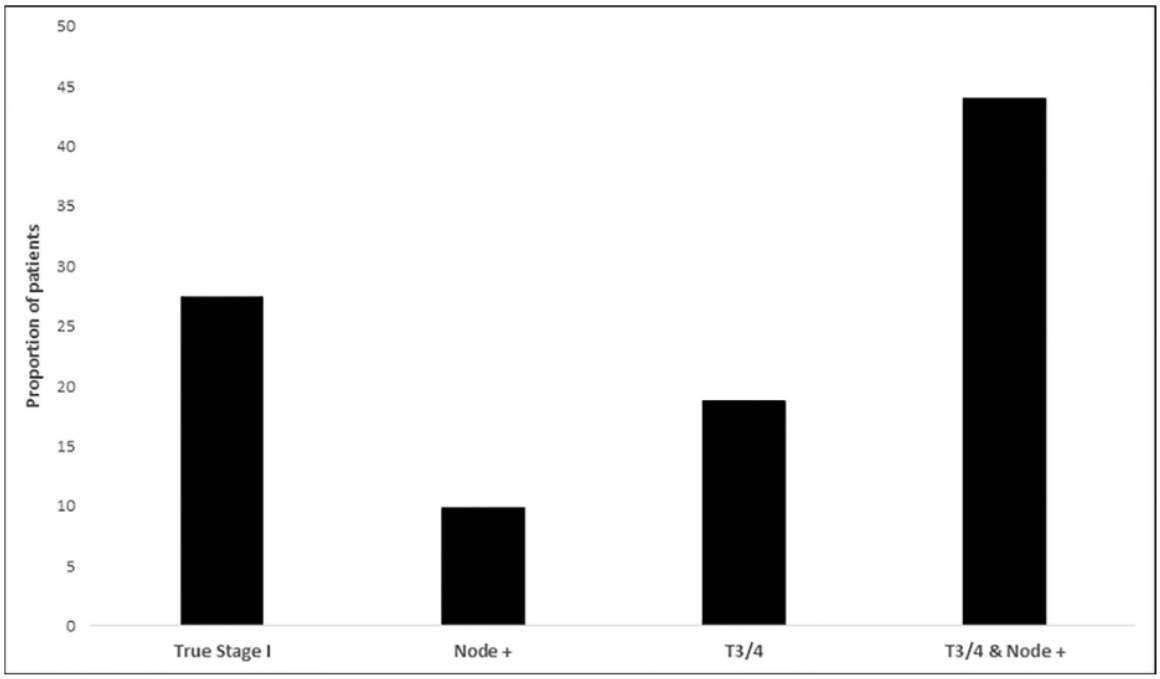


Fig. 2. Final pathologic stage among clinical stage I patients.

Uitkomsten van het LAELAPS-2 trainingsprogramma

Outcomes of a Multicenter Training Program in Laparoscopic Pancreatoduodenectomy (LAELAPS-2). T De Rooij et al; Ann Surg 2019; 269 (2); 344-350.
Pubmed ID: 29099400

OBJECTIVE: The aim of the study was to assess feasibility and outcomes of a multicenter training program in laparoscopic pancreatoduodenectomy (LPD).
BACKGROUND: Whereas expert centers have reported promising outcomes of LPD, nationwide analyses have raised concerns on its safety, especially during the learning curve. Multicenter, structured LPD training programs reporting outcomes including the first procedures are lacking. No LPD had been performed in the Netherlands before this study.
METHODS: During 2014–2016, 8 surgeons from 4 high-volume centers completed the Longitudinal Assessment and Realization of Laparoscopic Pancreatic Surgery (LAELAPS-2) training program in LPD, including detailed technique description, video training, and proctoring. In all centers, LPD was performed by 2 surgeons with extensive experience in pancreatic and laparoscopic surgery. Outcomes of all LPDs were prospectively collected.

RESULTS: In total, 114 patients underwent LPD. Median pancreatic duct diameter was 3 mm [interquartile range (IQR = 2–4)] and pancreatic texture was soft in 74% of patients. The conversion rate was 11% (n = 12), median blood loss 350 mL (IQR = 200–700), and operative time 375 minutes (IQR = 320–431). Grade B/C postoperative pancreatic fistula occurred in 34% of patients, requiring catheter drainage in 22% and re-operation in 2%. A Clavien-Dindo grade ≥ III complication occurred in 43% of patients. Median length of hospital stay was 15 days (IQR = 9–25). Overall, 30-day and 90-day mortality were both 3.5%. Outcomes were similar for the first and second part of procedures.
CONCLUSION: This LPD training program was feasible and ensured acceptable outcomes during the learning curve in all centers. Future studies should determine whether such a training program is applicable in other settings and assess the added value of LPD.

LEVERCHIRURGIE

Wereldwijde variatie in pijn- en vochtbeleid bij leverchirurgie

Fluid and pain management in liver surgery (MILESTONE): A worldwide study among surgeons and anesthesiologists. TM Mungroop et al; Surgery 2019; 165 (2); 337-344.
Pubmed ID: 30314727

BACKGROUND AND OBJECTIVE: Fluid and pain management during liver surgery (eg, low central venous pressure) is a classic topic of controversy between anesthesiologists and surgeons. Little is known about practices worldwide. The aim of this study was to assess perioperative practices in liver surgery among and between surgeons and anesthesiologists worldwide that could guide the design of future international studies.
METHODS: An online questionnaire was sent to 22 societies, including 4 international hepatopancreatobiliary societies, the American Society of Anesthesiologists, and 17 other (inter-)national societies.
RESULTS: A total of 913 participants (495 surgeons and 418 anesthesiologists) from 66 countries were surveyed. A large heterogeneity in fluid management practices was identified, with 66% using low central venous pressure, 22% goal-directed fluid therapy, and 6% normovolemia. In addition, large heterogeneity was found regarding pain management practices, with 49% using epidural analgesia, 25% patient-controlled analgesia with opioids, and 12% regional techniques. Most participants assume that there is a relation between perioperative pain management and morbidity and mortality (78% of surgeons vs 89% of anesthesiologists; $P < .001$). Both surgeons and anesthesiologists have the highest expectations for minimally invasive surgery and enhanced recovery pathways for improving outcomes in liver surgery. No clear differences between continents were found.
CONCLUSION: Worldwide there is a large heterogeneity in fluid and pain management practices in liver surgery. This survey identified several areas of interest for future international studies aiming to improve outcomes in liver surgery.

Verlies van spiermassa tijdens preoperatieve chemotherapie geassocieerd met kortere recurrence-free survival bij colorectale levermetastasen

Loss of muscle mass during preoperative chemotherapy as a prognosticator for poor survival in patients with colorectal liver metastases. M Okuno et al.; Surgery 2019; 165 (2); 329-336.

Pubmed ID: 30197278

BACKGROUND AND OBJECTIVE: The survival impact of specific body composition changes during preoperative chemotherapy in patients with colorectal liver metastases undergoing curative-intent surgery remains unclear. This study aimed to determine the impact of changes in body weight and muscle mass during preoperative chemotherapy on survival after hepatectomy in patients with colorectal liver metastases.

METHODS: Consecutive patients with colorectal liver metastases undergoing preoperative chemotherapy and curative hepatectomy during 2009–2013 were retrospectively analyzed. Recurrence-free and overall survival were examined according to body compositions, including muscle mass, as measured by skeletal muscle index (area of muscle [cm2]/square of height [m2]), and body weight before and after preoperative chemotherapy.

RESULTS: The median follow-up duration in overall 169 patients was 47 months. Skeletal muscle index and body weight changed significantly during chemotherapy (skeletal muscle index: –0.52 cm2/m2, P = .03; body weight: +1.1 kg, P = .002). Patients with major muscle mass loss (≥7%) had significantly shorter median RFS than patients with no or minor muscle mass loss (<7%) (9.6 months vs 15.9 months; P = .02). Although major muscle mass loss was associated with poor outcome, skeletal muscle index before or after preoperative chemotherapy was not associated with recurrence-free or overall survival. On multivariate analysis, major muscle mass loss was independently associated with poorer recurrence-free survival (hazard ratio, 1.76; P = .045).

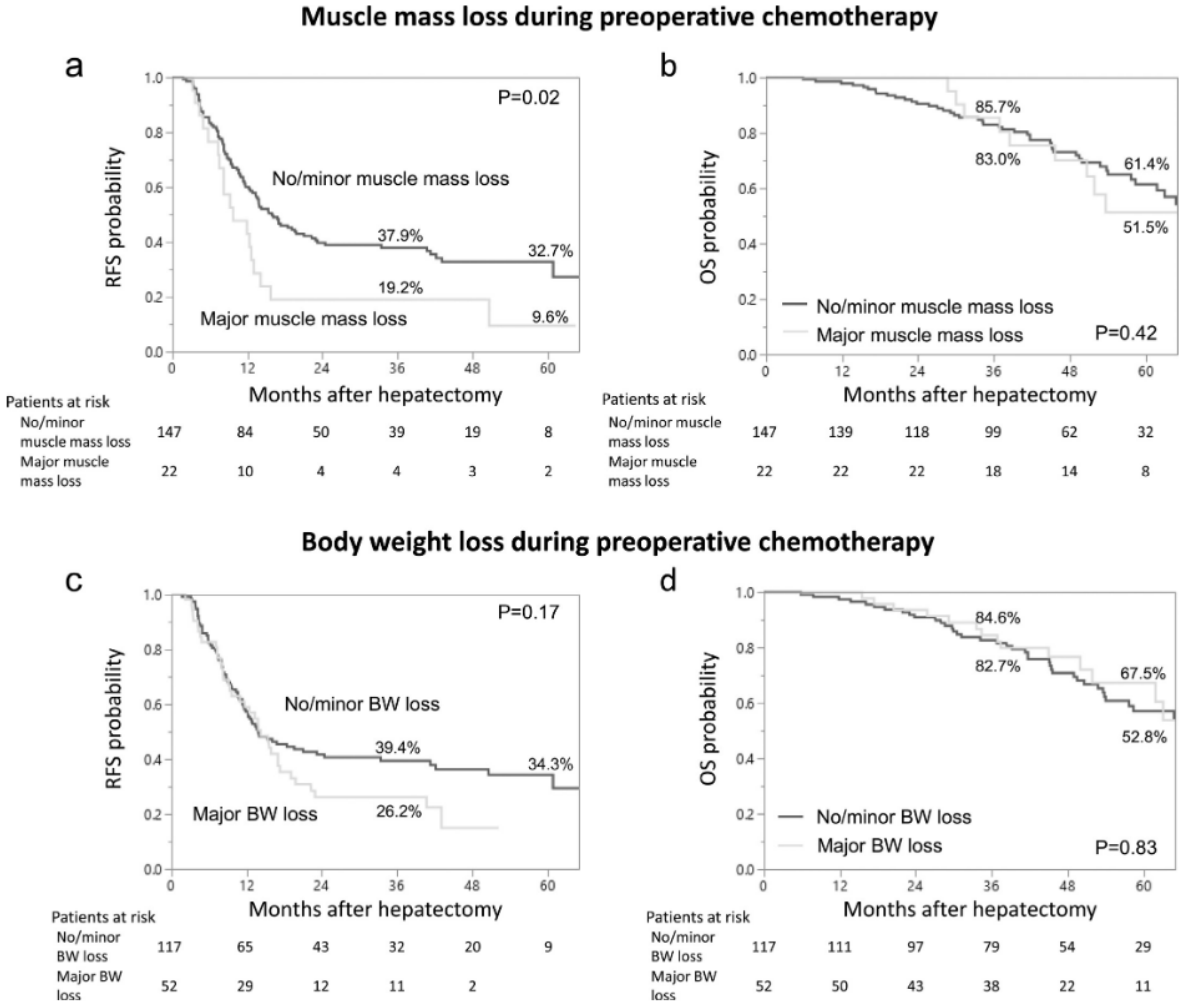


Fig. 3. (A) Recurrence-free survival (RFS) and (B) overall survival (OS) in patients with major muscle mass loss and no or minor muscle mass loss during preoperative chemotherapy; (C) RFS and (D) OS in patients with major body weight (BW) loss and no or minor BW loss during preoperative chemotherapy.

CONCLUSIONS: Major loss of muscle mass but not body weight loss during preoperative

chemotherapy is significantly associated with poor recurrence-free survival after hepatectomy in patients with colorectal liver metastases. The mechanisms mediating this association may inform future trials on maintaining muscle mass with dedicated nutrition and exercise programs to improve outcomes.

BARIATRISCHE CHIRURGIE

Sleeve gastrectomy of Roux-Y gastric bypass tijdens heroperatie na falen gastric banding?

Safety of Revision Sleeve Gastrectomy Compared to Roux-Y Gastric Bypass After Failed Gastric Banding: Analysis of the MBSAQIP. MR Janik et al. Annals of Surgery: 2019;269(2):299–303. Pubmed ID: 29095195

OBJECTIVE: The aim of this study was to assess the safety of revisional surgery to laparoscopic sleeve gastrectomy (LSG) compared to laparoscopic Roux-Y gastric bypass (LRYGB) after failed laparoscopic adjustable gastric banding (LAGB).

BACKGROUND: The number of reoperations after failed gastric banding rapidly increased in the United States during the last several years. A common approach is band removal with conversion to another weight loss procedure such as gastric bypass or sleeve gastrectomy in a single procedure. The safety profile of those procedures remains controversial.

METHODS: Preoperative characteristics and 30-day outcomes from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program Participant Use Files 2015 were selected for all patients who underwent a 1-stage conversion of LAGB to LSG (conv-LSG) or LRYGB (conv-LRYGB). Conv-LSG cases were matched (1:1) with conv-LRYGB patients by age (±1 year), body mass index (±1 kg/m), sex, and comorbidities including diabetes, hypertension, hyperlipidemia, venous stasis, and sleep apnea.

RESULTS: A total of 2708 patients (1354 matched pairs) were included in the study. The groups were closely matched as intended. The mean operative time in conv-LRYGB was significantly longer in comparison to conv-LSG patients (151 ± 58 vs 113 ± 45 minutes, P < 0.001). No mortality was observed in either group. Patients after conv-LRYGB had a clinically increased anastomotic leakage rate (2.07% vs 1.18%, P = 0.070) and significantly increased bleed rate (2.66% vs 0.44%, P < 0.001). Thirty-day readmission rate was significantly higher in conv-LRYGB patients (7.46% vs 3.69%, P < 0.001), as was 30-day reoperation rate (3.25% vs 1.26%, P < 0.001). The length of hospital stay was longer in conv-LRYGB.

TABLE 2. Comparison of Primary Outcomes

	Conv-LSG N = 1345	Conv-LRYGB N = 1354		
Outcome	%		***P***	**Definition**
Mortality	0%	0%	—	Death
Leak/anastomotic leakage rate	1.18%	2.07%	0.070	One of following: drain present >30 days, organ space surgical site infection, leak-related 30-day readmission, or leak-related 30-day reoperation or intervention.
Bleeding event	0.44%	2.66%	<0.001	One of following: bleed-related 30-day readmission, bleed-related 30-day reoperation, or requiring a transfusion within 72 hours postoperatively.
30-day readmission	3.69%	7.46%	<0.001	Any readmission to an acute care bed (eg, OBS, in-patient) or 23-hour observation within 30 days following the bariatric or metabolic surgery procedure.
30-day reoperation	1.26%	3.25%	<0.001	Return to the operating room within 30 days following the bariatric or metabolic surgery procedure.

OBS indicates observation.

CONCLUSIONS: A single-stage conversion of failed LAGB leads to greater morbidity and higher complication rates when converted to LRYGB versus LSG in the first 30 days postoperatively. These differences are particularly notable with regards to bleed events, 30-day reoperation, 30-day readmission, operative time, and hospital stay.

In de keuze voor bariatrische chirurgie zijn kosten, gewichtsverlies en verdwijnen comorbiditeiten de belangrijkste factoren voor patiënten

Patient Preferences for Bariatric Surgery: Findings From a Survey Using Discrete Choice Experiment Methodology. JR Rozier et al. JAMA Surg: 2019;154(1):e184375.
Pubmed ID: 30484820

IMPORTANCE: Surgical options for weight loss vary considerably in risks and benefits, but the relative importance of procedure-associated characteristics in patient decision making is largely unknown.

OBJECTIVE: To identify patient preferences for risks, benefits, and other attributes of treatment options available to individuals who are candidates for bariatric surgery.

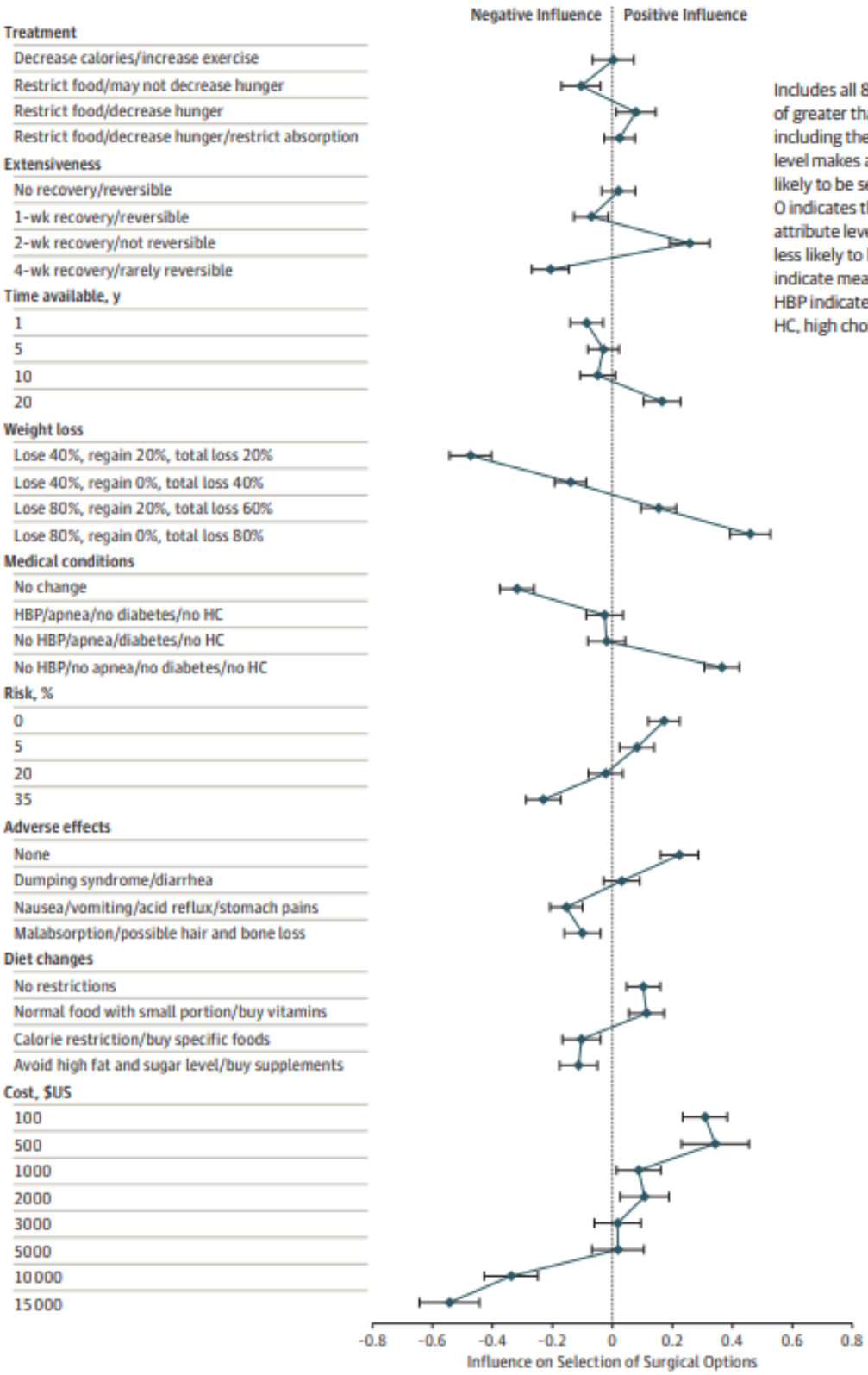
DESIGN, SETTING, AND PARTICIPANTS: This discrete choice experiment of weight loss procedures was performed as an internet-based survey administered to patients recruited from bariatric surgery information sessions in the State of Michigan. Each procedure was described by the following set of attributes: (1) treatment method, (2) recovery and reversibility, (3) time that treatment has been available, (4) expected weight loss, (5) effect on other medical conditions, (6) risk of complication, (7) adverse effects, (8) changes to diet, and (9) out-of-pocket costs. Participants chose between surgical profiles by comparing attributes. Survey data were collected from May 1, 2015, through January 30, 2016, and analyzed from February 1 to June 30, 2016.

MAIN OUTCOMES AND MEASURES: Estimated relative value of risks and benefits for leading weight-loss surgical options and marginal willingness to pay for procedure attributes. A latent class analysis identified respondent subgroups.

RESULTS: Among the 815 respondents (79.9% women; mean [SD] age, 44.5 [12.0] years), profiles of hypothetical procedures that included resolution of medical conditions (coefficient for full resolution, 0.229 [95% CI, 0.177 to 0.280; P < .001]; coefficient for no resolution, −0.207 [95% CI, −0.254 to −0.159; P < .001]), higher total weight loss (coefficient for each additional 20% loss, 0.185 [95% CI, 0.166 to 0.205; P < .001]), and lower out-of-pocket costs (coefficient for each additional $1000, −0.034 [95% CI, −0.042 to −0.025; P < .001]) were most likely to be selected. Younger respondents were more likely than older respondents to choose treatments with higher weight loss (coefficient for loss of 80% excess weight 0.543 [95% CI, 0.435-0.651] vs 0.397 [95% CI, 0.315-0.482]) and were more sensitive to out-of-pocket costs (coefficient for $100 out-of-pocket costs, 0.346 [95% CI, 0.221-0.470] vs 0.262 [95% CI, 0.174 to 0.350]; coefficient for $15 000 in out-of-pocket costs, −0.768 [95% CI, −0.938 to −0.598] vs −0.384 [95% CI, −0.500 to −0.268]). Marginal willingness to pay indicated respondents would pay $5470 for losing each additional 20% of excess body weight and $12 843 for resolution of existing medical conditions, the most desired procedure attributes. Latent class analysis identified the following 3 unobserved subgroups: cost-sensitive (most concerned with costs); benefit-focused (most concerned with excess weight loss and resolution of medical conditions); and procedure-focused (most concerned with how the treatment itself worked, including recovery and reversibility).

CONCLUSIONS AND RELEVANCE: Candidates for bariatric surgery identified costs, expected weight loss, and resolution of medical conditions as the most important characteristics of weight loss surgery decisions. Other information, such as risk of complications and adverse effects, were important to patients but less so.

Figure 2. Attribute Variables From Discrete Choice Experiment



Includes all 815 respondents. A value of greater than 0 indicates that including the associated attribute level makes a surgical profile more likely to be selected. A value less than 0 indicates that the associated attribute level makes a surgical profile less likely to be selected. Data points indicate mean; error bars, SD. HBP indicates high blood pressure; HC, high cholesterol levels.