DE LEESTAFEL
MAART 2020

Een Maandelijkse Selectie van Wetenschappelijke GE-nieuws

Coloproctologie

Meer pCR na chemoradiotherapy door combinatie met preoperatieve chemotherapie voor rectumcarcinoom

Total Neoadjuvant Therapy in Rectal Cancer: A Systematic Review and Meta-analysis of Treatment Outcomes. F Petrelli et al.; Annals of Surgery, March 2020 - Volume 271 - Issue 3, p440-448. Pubmed ID: 31318794.

BACKGROUND: The addition of induction chemotherapy to concomitant neoadjuvant chemoradiation in locally advanced rectal cancer could increase pathological downstaging and act on occult micrometastatic disease, leading ultimately to a better outcome. A systematic review was carried out of the existing literature on the treatment outcomes of total neoadjuvant therapy (TNT) on locally advanced rectal cancer. TNT was defined as chemotherapy using cycles of induction and/or consolidation in conjunction with standard chemoradiotherapy prior to surgery.

METHODS: A systematic search of PubMed, Embase, and the Cochrane Library was performed according to the PRISMA statement up until January 2019. The primary endpoints were complete pathologic response (pCR), disease-free survival, and overall survival rates.

RESULTS: A total of 28 studies (3 retrospective and 25 prospective for a total of 3579 patients) were included in the final analysis (n = 2688 treated with TNT and n = 891 with neoadjuvant chemoradiotherapy therapy). The pooled pCR rate was 22.4% (95% CI 19.4%-25.7%) in all patients treated with TNT (n = 27 studies with data available). In n = 10 comparative studies with data available, TNT was found to increase the odds of pCR by 39% (1.40, 95% CI 1.08-1.81, P = 0.01).

CONCLUSIONS: The addition of induction or consolidation chemotherapy to standard neoadjuvant chemoradiotherapy results in a higher pCR rate. Given that the comparative analysis was derived from few randomized publications, large confirmatory trials should be carried out before a strong recommendation is made in favor of TNT.

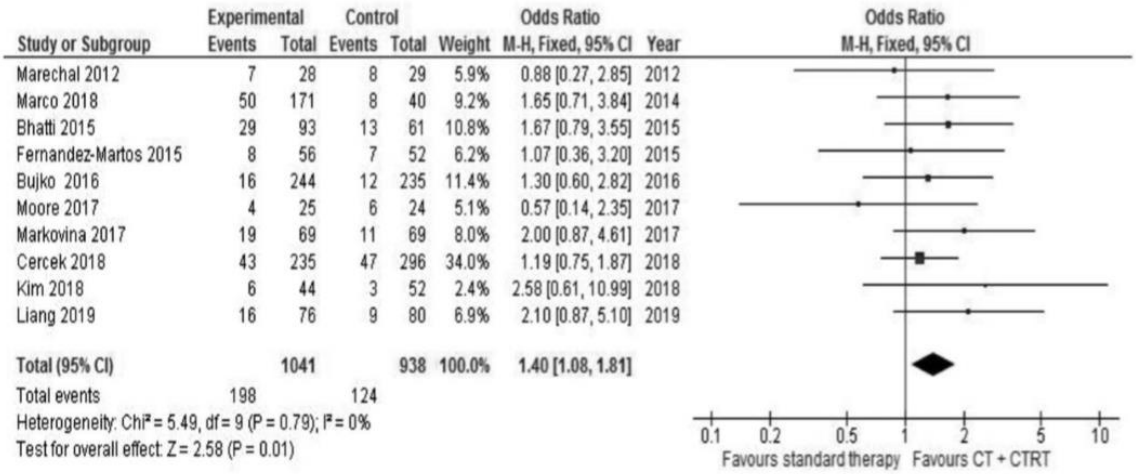


FIGURE 2. Pathologic complete response with total neoadjuvant therapy versus standard chemoradiation.

Complete mesocolic excision leidt tot verbeterde local-recurrence-free survival van het coloncarcinoom

Efficacy and Safety of Complete Mesocolic Excision in Patients With Colon Cancer: Three-year Results From a Prospective, Nonrandomized, Double-blind, Controlled Trial. Z Gao et al.; Annals of Surgery, March 2020 - Volume 271 - Issue 3, p519-526.
Pubmed ID: 30148752.

OBJECTIVE: The aim of the study was to evaluate the oncological outcomes of complete mesocolic excision (CME) in colon cancer patients.
SUMMARY BACKGROUND DATA: CME is considered a standard procedure for colon cancer patients. However, previous evidence regarding the effect of CME on prognosis has fundamental limitations that prevent it from being fully accepted.
METHODS: Patients who underwent radical resection for colon cancer were enrolled between November 2012 and March 2016. According to the principles of CME, patients were stratified into 2 groups based on intraoperative surgical fields and specimen photographs. The primary outcome was local recurrence-free survival (LRFS). The clinicopathological data and follow-up information were collected and recorded. The final follow-up date was April 2016. The trial was registered in ClinicalTrials.gov (identifier: NCT01724775).
RESULTS: There were 220 patients in the CME group and 110 patients in the noncomplete mesocolic excision (NCME) group. Baseline characteristics were well balanced. Compared with NCME, CME was associated with a greater number of total lymph nodes (24 vs 20, P = 0.002). Postoperative complications did not differ between the 2 groups. CME had a positive effect on LRFS compared with NCME (100.0% vs 90.2%, log-rank P < 0.001). Mesocolic dissection (100.0% vs 87.9%, log-rank P < 0.001) and nontumor deposits (97.2% vs 91.6%, log-rank P < 0.022) were also associated with improved LRFS.
CONCLUSIONS: Our findings demonstrate that, compared with NCME, CME improves 3-year LRFS without increasing surgical risks.

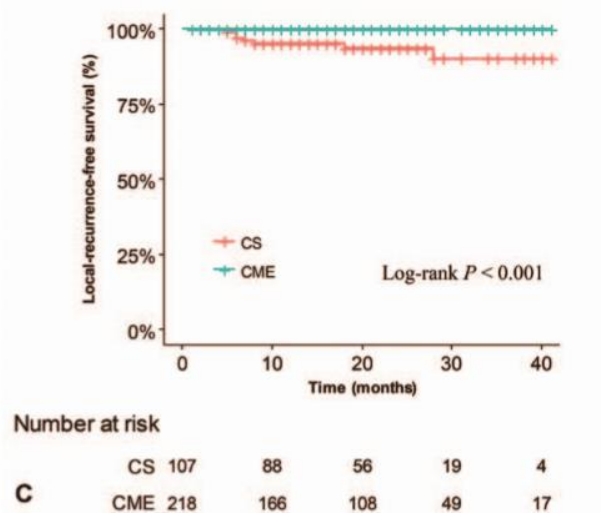


FIGURE 2. Kaplan–Meier plots of 3-year (C) local recurrence-free survival,

UPPER GI

Slechter survival met hoge mean corpuscular volume na slokdarmresectie voor oesophagus carcinoom

Clinical Importance of Mean Corpuscular Volume as a Prognostic Marker After Esophagectomy for Esophageal Cancer: A Retrospective Study. N Yoshida et al.; Annals of Surgery, March 2020 - Volume 271 - Issue 3, p494-501.
Pubmed ID: 29995687.

OBJECTIVE: To elucidate the clinical value of mean corpuscular volume (MCV) for prognostic prediction in patients with esophageal cancer who underwent radical esophagectomy.
BACKGROUND: High MCV is suggested to be relevant to the incidence and prognosis of several malignancies. However, few studies investigating the correlation between MCV and survival outcome of esophageal cancer have been conducted.
METHODS: This study included 570 patients with esophageal cancer who underwent radical esophagectomy between April, 2005 and December, 2017. Patients were divided into 2 groups according to the standard value of pretreatment MCV: normal (83-99 fL) and high (>99 fL) groups. Clinical backgrounds, short-term outcomes, and prognostic outcomes postesophagectomy were retrospectively compared between the groups.
RESULTS: Of all patients, 410 (71.9%) had normal MCV, and 160 (28.1%) had high MCV. High MCV was significantly associated with lower body mass index, higher frequency of habitual alcohol and tobacco use, and higher incidence of multiple primary malignancies other than esophageal cancer. High MCV also correlated with higher incidence of postoperative morbidity of the Clavien-Dindo classification ≥II and pulmonary morbidity. Overall survival was significantly worse in patients with high MCV. Multivariate analysis suggested that high MCV was an independent risk factor for worse survival outcome (hazard ratio 1.54, 95% confidence interval 1.098-2.151, P = 0.012).
CONCLUSIONS: Patients with high MCV have various disadvantages in clinical background that can adversely affect both short-term and long-term outcomes after esophagectomy. MCV can become a predictive marker to estimate survival outcome after esophagectomy for esophageal cancer.

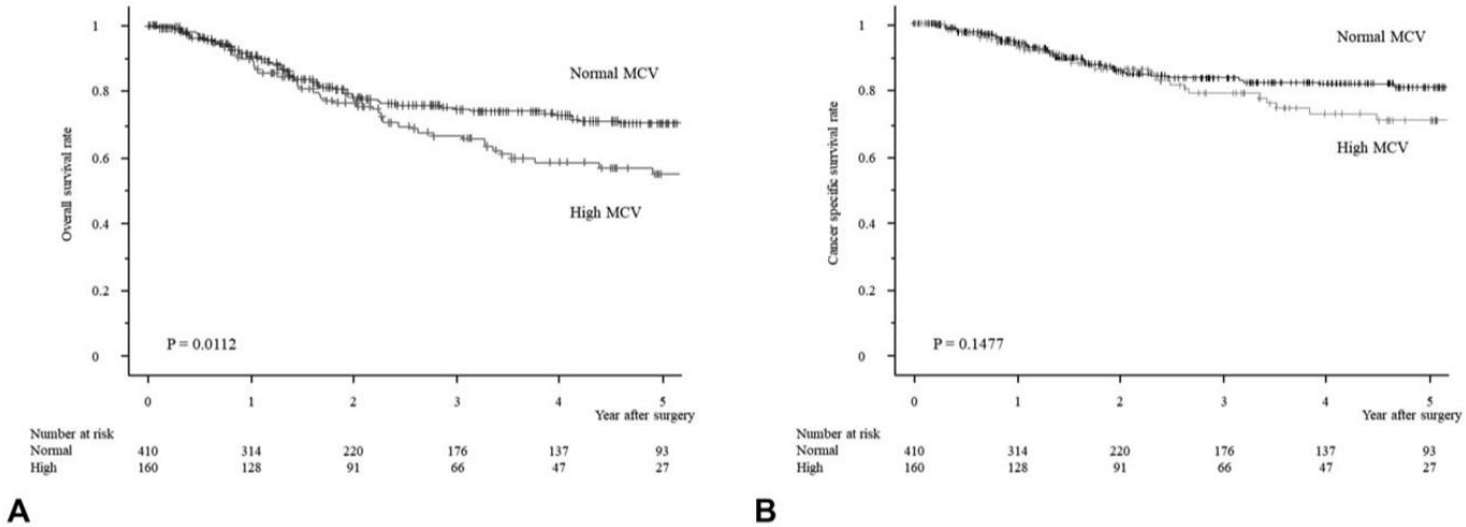


FIGURE 2. Kaplan–Meier curves of overall survival (A), cancer-specific survival (B)

HPB

Behandelstrategie op basis van (preoperatief) circulerende tumorcellen bij periampullaire tumoren?

Circulating Tumor Cells are an Independent Predictor of Shorter Survival in Patients Undergoing Resection for Pancreatic and Periampullary Adenocarcinoma. H. Hugenschmidt et al.; Annals of Surgery, March 2020 - Volume 271 - Issue 3, p549-558.
Pubmed ID: 30216219.

OBJECTIVE: We evaluated the prognostic impact of circulating tumor cells (CTCs) for patients with presumed resectable pancreatic and periampullary cancers.

SUMMARY OF BACKGROUND DATA: Initial treatment decisions for this group are currently taken without a reliable prognostic marker. The CellSearch system allows standardized CTC-testing and has shown excellent specificity and prognostic value in other applications.

METHODS: Preoperative blood samples from 242 patients between September 2009 and December 2014 were analyzed. One hundred seventy-nine patients underwent tumor resection, of whom 30 with stage-I tumors and duodenal cancer were assigned to the low-risk group, and the others to the high-risk group. Further 33 had advanced disease, 30 benign histology. Observation ended in December 2016. Cancer-specific survival (CSS) and disease-free survival (DFS) were calculated by log-rank and Cox regression.

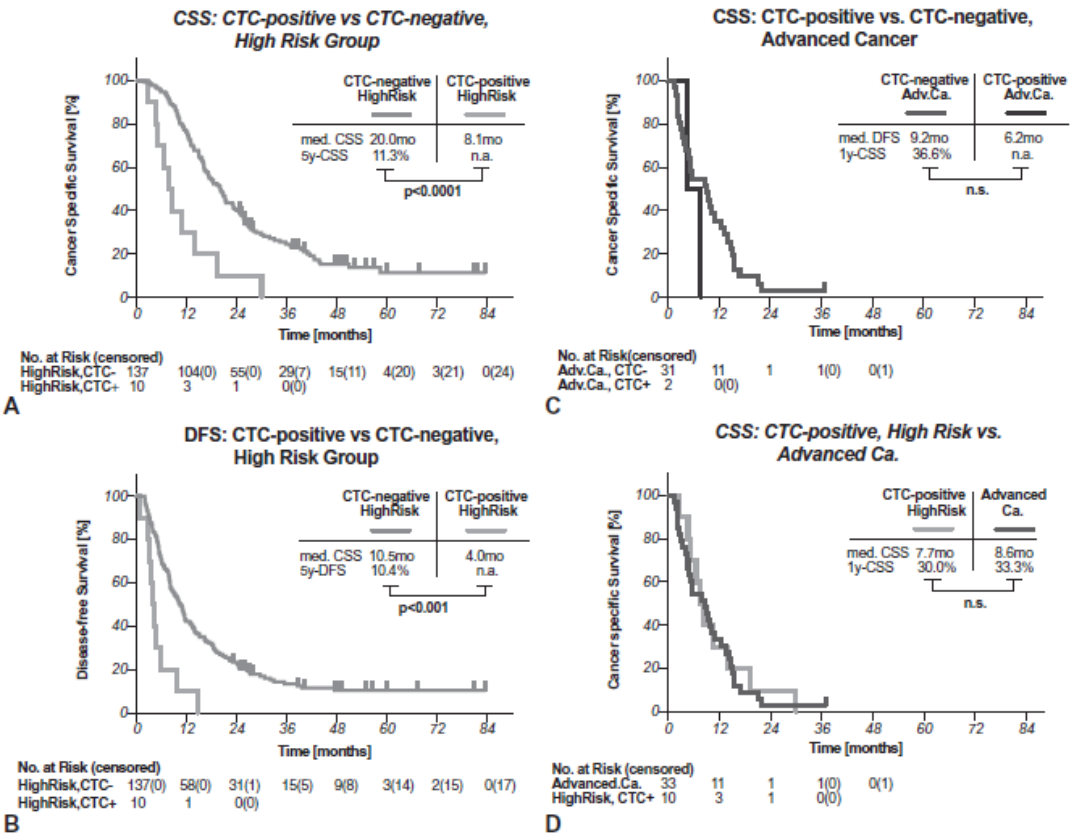


FIGURE 3. Kaplan-Meier curves, 5-year survival for resectable or 1-year survival for advanced cancers by CTC-status. A, Cancer-specific survival, high-risk group. B, Disease-free survival, high-risk group. C, Cancer-specific survival, advanced cancers. D, Comparison of cancer-specific survival for high-risk, CTC-positive versus advanced cancers. CSS indicates cancer-specific survival; DFS, disease-free survival.

RESULTS: CTCs (CTC-positive; ≥1 CTC/7.5 mL) were detected in 6.8% (10/147) of the high-risk patients and 6.2% (2/33) with advanced disease. No CTCs (CTC-negative) were detected in the low-risk patients or benign disease. In high-risk patients, median CSS for CTC-positive versus CTC-negative was 8.1

versus 20.0 months (P < 0.0001), and DFS 4.0 versus 10.5 months (P < 0.001). Median CSS in advanced disease was 7.7 months. Univariate hazard ratio (HR) of CTC-positivity was 3.4 (P < 0.001). In multivariable analysis, CTC-status remained independent (HR: 2.4, P = 0.009) when corrected for histological type (HR: 2.7, P = 0.030), nodal status (HR: 1.7, P = 0.016), and vascular infiltration (HR: 1.7, P = 0.001).

CONCLUSION: Patients testing CTC-positive preoperatively showed a detrimental outcome despite successful tumor resections. Although the low CTC-rate seems a limiting factor, results indicate high specificity. Thus, preoperative analysis of CTCs by this test may guide treatment decisions and warrants further testing in clinical trials.

Robot makkelijker dan open pancreatectomie bij de forse patiënt?

The impact of high body mass index on patients undergoing robotic pancreatectomy: A propensity matched analysis. H. Shengliang et al.; Surgery: March 2020 – Volume 167 – Issue 3 – p 556-559. Pubmed ID: 31837833.

BACKGROUND: Patients with high body mass index are associated with a higher risk of complications after open pancreatectomy. We aimed to investigate the perioperative outcome for patients with high body mass index after robotic pancreatectomy.

METHODS: This is a retrospective, propensity-score matched cohort analysis. From our prospectively maintained database, we identified consecutive patients with body mass index >25 who underwent robotic pancreatectomy between January 2016 and December 2018. Propensity score matching with open pancreatectomy was applied in 1:2 fashion based on age, gender, American Society of Anesthesiologists classification, surgery type, histology, neoadjuvant therapy, and body mass index during the same study period.

RESULTS: A total of 127 patients were included. The mean age for all patients was 61.7 ± 12.8 years and 65 (51.2%) were male. Median body mass index was 29.9 (interquartile range, 27.0-31.8) for both groups. Propensity score matching provided equally distributed general demographic and clinicopathological factors. Robotic pancreatectomy was associated with decreased blood loss (100 mL vs 300 mL, P < .001) and shorter hospital stay (7 vs 9 days, P = .019).

Table II
Postoperative complications between robotic and open pancreatectomy

	Robotic ($n = 44$)	Open ($n = 83$)	*P* value
Estimated blood loss, mL, median (IQR)	100 (75–200)	300 (200–600)	**< .001**
Intraoperative blood transfusion, no. (%)	0 (0.0)	5 (6.0)	.160
Delayed gastric emptying, no. (%)	1 (2.3)	10 (12.1)	.056
Postoperative pancreatic fistula, no. (%)	5 (11.4)	8 (9.6)	.770
Postoperative hemorrhage, no. (%)	0 (0.0)	5 (6.0)	.237
Chyle leak, no. (%)	3 (6.8)	5 (6.0)	.99
Wound complication, no. (%)	0 (0.0)	6 (7.2)	.165
Bile leakage, no. (%)	0 (0.0)	1 (1.2)	.99
90-day readmission, no. (%)	6 (13.6)	19 (22.9)	.311
90-day mortality, no. (%)	0 (0.0)	0 (0.0)	-
Median hospital stay ± standard deviation	6.9 ± 3.0	9.2 ± 5.6	**.019**

Bold indicates statistically significant *P* value.

CONCLUSION: Robotic pancreatectomy is associated with decreased blood loss and shorter length of hospital stay in overweight patients. Robotic approach may help alleviate morbidity in overweight patients undergoing pancreatectomy.

LEVERCHIRURGIE

Subtotale cholecystectomie bij acute cholecystitis?

Nationwide trends in the use of subtotal cholecystectomy for acute cholecystitis. A.F. Sabour et al.; Surgery: March 2020 – Volume 167 – Issue 3 – p 569-574.
Pubmed ID: 31879089.

BACKGROUND: Subtotal cholecystectomy is a viable alternative approach to the proverbial "difficult" gallbladder. To date, only a few studies have observed the establishment of those bail-out procedures as an increasingly common surgical practice. The purpose of this study is to assess nationwide trends of subtotal cholecystectomy through evaluation of operative variables and patient- and institution-level characteristics in procedure preference.

METHODS: Data were obtained from the National Inpatient Sample for the years between 2003 and 2014. Patients with acute cholecystitis were categorized based on the ninth revision International Classification of Disease Clinical Modification procedure codes for open total, laparoscopic total, open subtotal, or laparoscopic subtotal cholecystectomy. Any patient younger than 18 years of age or with a preoperative stay >1 week was excluded. Logistic regression analysis was performed to evaluate significant patient- and institution-level characteristics associated with the performance of subtotal cholecystectomy.

RESULTS: A total of 290,855 patients were evaluated. During the study period, the rate of open and laparoscopic subtotal cholecystectomy sharply increased (0.10% of all cholecystectomy procedures to 0.52% and 0.12% to 0.28%, respectively). The conversion rate from laparoscopic to open total cholecystectomy decreased from 10.5% to 7.6%. Subtotal cholecystectomies were performed at significantly higher rates in men (odds ratio: 1.95, P < .001), Asian Americans (odds ratio: 2.21, P = .037), and patients with alcohol abuse (odds ratio: 2.23, P < .001). Teaching hospitals (odds ratio: 2.41, P < .001) and those in rural areas (odds ratio: 2.26, P < .001) were more likely to perform subtotal cholecystectomies.

CONCLUSION: Growing trends in the use of subtotal cholecystectomy suggest evolving surgical practices for acute cholecystitis. Our data suggests that several patient- and hospital-level characteristics might play a deciding role in procedure preference.

Table II
Comparative analysis of patient demographics, outcomes, and hospital characteristics between conversion to an open total or subtotal cholecystectomy and laparoscopic subtotal cholecystectomy

Variables	Converted to open total or subtotal cholecystectomy ($n = 24,750$)	Laparoscopic subtotal cholecystectomy ($n = 554$)	*P* value	Adjusted OR*	*P* value
Outcome variables					
Mortality	297 (1.20%)	4 (0.79%)	1.000	-	-
Length of stay	7.21 ± 0.07	6.20 ± 0.56	< .001	-	-
Total charge (U.S. dollars)	60,727 ± 880	55,076 ± 5,020	.055	-	-

* Laparoscopic subtotal cholecystectomy is the dependent variable in the multinomial logistic regression.

Galwegletsel na laparoscopische cholecystectomie: vroeg verwijzen en laat behandelen?

Early Versus Delayed Surgical Repair and Referral for Patients With Bile Duct Injury: A Systematic Review and Meta-analysis. W. Wang et al.; Annals of Surgery, March 2020 - Volume 271 - Issue 3, p449-459.
Pubmed ID: 32106173.

OBJECTIVE: The aim of the study was to systematically review and meta-analyze the available evidence regarding the association between timing of repair or referral and clinical outcomes in bile duct injury (BDI).

BACKGROUND: Surgical repair is recommended for patients with complex BDI following laparoscopic cholecystectomy. However, consensus on the timing of surgery or referral to a specialist is lacking.
METHODS: We searched PubMed, Embase, Cochrane Library, and Scopus for eligible studies. The coprimary outcomes were repair failure in follow-up and postoperative complications. We pooled odds ratios (ORs) using random-effects models.
RESULTS: We included 32 studies. The rate of repair failure was significantly higher for early versus delayed repair [OR 1.65, 95% confidence interval (CI) 1.14-2.37, P= 0.007], lower for early versus delayed referral (OR 0.28, 95% CI 0.17-0.45, P < 0.001), but did not differ substantially for on-table versus postcholecystectomy repair (OR 2.06, 95% CI 0.89-4.73, P = 0.09). Regarding postoperative complications, early referral outperformed delayed referral (OR 0.24, 95% CI 0.09-0.68, P= 0.007); however, we found no significant differences between early and delayed repair (OR 1.34, 95% CI 0.96-1.87, P= 0.08), or between on-table and postcholecystectomy repair (OR 1.13, 95% CI 0.42-3.07, P= 0.81). At the cutoff time point of 6 weeks, early repair was associated with increased rates of repair failure (OR 4.03; P < 0.001), postoperative complications (OR 2.18; P < 0.001), and biliary stricture (OR 6.23; P < 0.001).
CONCLUSIONS: Among patients with BDI, early referral and delayed repair appear to confer favorable outcomes.

TABLE 4. Summary of Findings and Strength of Evidence Assessed by Grading of Recommendations Assessment, Development, and Evaluation System

Outcome	No. Studies	No. Patients (Group A)	No. Patients (Group B)	Odds Ratio (95% CI)	*P*	I^2, %	$P_{heterogeneity}$	Strength of Evidence
Early (group A) versus delayed (group B) repair								
Repair failure	27	438/1374 (31.9%)	298/1743 (17.1%)	1.65 (1.14–2.37)	**0.007**	57.2	**<0.001**	Very low
Postoperative complications	12	153/674 (22.7%)	180/1105 (16.3%)	1.34 (0.96–1.87)	0.08	24.8	0.20	Very low
Biliary stricture	16	128/557 (23.0%)	115/944 (12.2%)	1.64 (0.94–2.84)	0.08	50.1	**0.012**	Very low
Bile leak	7	24/229 (10.5%)	30/620 (4.8%)	2.27 (1.22–4.25)	**0.01**	0	0.71	Very low
Revision surgery	4	105/439 (23.9%)	25/632 (4.0%)	3.72 (1.64–8.43)	**0.002**	46.4	0.11	Very low
On-table (group A) versus postoperative (group B) repair								
Repair failure	9	210/350 (60.0%)	273/800 (34.1%)	2.06 (0.89–4.73)	0.09	73.8	**<0.001**	Very low
Postoperative complications	4	84/234 (35.9%)	106/437 (24.3%)	1.13 (0.42–3.07)	0.81	58.6	**0.06**	Very low
Biliary stricture	7	31/96 (32.3%)	56/211 (26.5%)	1.39 (0.79–2.47)	0.26	0	0.66	Very low
Bile leak	4	8/52 (15.4%)	6/99 (6.1%)	2.21 (0.51–9.57)	0.29	19.1	0.30	Very low
Early (group A) versus delayed (group B) referral								
Repair failure*	6	40/276 (14.5%)	89/347 (25.6%)	0.28 (0.17–0.47)	**<0.001**	0	0.82	Very low
Postoperative complications	5	28/125 (22.4%)	142/262 (54.2%)	0.24 (0.09–0.68)	**0.007**	64.6	**0.02**	Very low
Biliary stricture	5	27/228 (11.8%)	67/264 (25.4%)	0.28 (0.17–0.47)	**<0.001**	0	0.71	Very low

Significant *P* values are shown in bold ($P < 0.05$ for outcomes; $P < 0.1$ for heterogeneity).
*The study by Wudel et al was not included, which accounted for high heterogeneity.

BARIATRISCHE CHIRURGIE

Bariatrische chirurgie en CVRM?

Impact of bariatric surgery on cardiovascular outcomes and mortality: a population ‐based cohort study. P. Singh et al. BJS, March 2020 – Volume 107 – Issue 4, pages 432-442.
Pubmed ID: 31965568.

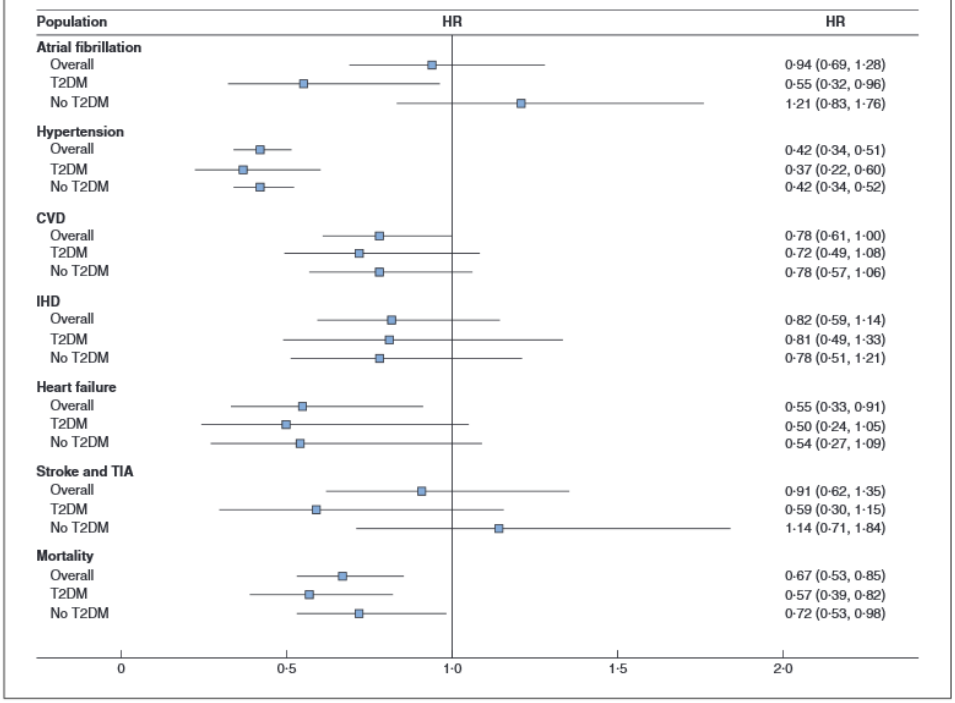
BACKGROUND: Cohort studies have shown that bariatric surgery may reduce the incidence of and mortality from cardiovascular disease (CVD), but studies using real-world data are limited. This study examined the impact of bariatric surgery on incident CVD, hypertension and atrial fibrillation, and all-cause mortality.

METHODS: A retrospective, matched, controlled cohort study of The Health Improvement Network primary care database (from 1 January 1990 to 31 January 2018) was performed (approximately 6 per cent of the UK population). Adults with a BMI of 30 kg/m^2 or above who did not have gastric cancer were included as the exposed group. Each exposed patient, who had undergone bariatric surgery, was matched for age, sex, BMI and presence of type 2 diabetes mellitus (T2DM) with two controls who had not had bariatric surgery.

RESULTS: A total of 5170 exposed and 9995 control participants were included; their mean(s.d.) age was 45·3(10·5) years and 21·5 per cent (3265 of 15 165 participants) had T2DM. Median follow-up was 3·9 (i.q.r. 1·8-6·4) years. Mean(s.d.) percentage weight loss was 20·0(13·2) and 0·8(9·5) per cent in exposed and control groups respectively. Overall, bariatric surgery was not associated with a significantly lower CVD risk (adjusted hazard ratio (HR) 0·80; 95 per cent c.i. 0·62 to 1·02; P = 0·074). Only in the gastric bypass group was a significant impact on CVD observed (HR 0·53, 0·34 to 0·81; P = 0·003). Bariatric surgery was associated with significant reduction in all-cause mortality (adjusted HR 0·70, 0·55 to 0·89; P = 0·004), hypertension (adjusted HR 0·41, 0·34 to 0·50; P < 0·001) and heart failure (adjusted HR 0·57, 0·34 to 0·96; P = 0·033). Outcomes were similar in patients with and those without T2DM (exposed versus controls), except for incident atrial fibrillation, which was reduced in the T2DM group.

CONCLUSION: Bariatric surgery is associated with a reduced risk of hypertension, heart failure and mortality, compared with routine care. Gastric bypass was associated with reduced risk of CVD compared to routine care.

Fig. 2 Forest plot of cardiovascular disease outcomes and mortality in all patients, and those with and without type 2 diabetes mellitus



Unadjusted hazard ratios (HRs) are shown with 95 per cent confidence intervals. CVD, cardiovascular disease; IHD, ischaemic heart disease; TIA, transient ischaemic attack.

Minder colorectale carcinoom na bariatrische chirurgie?

Role of bariatric surgery in reducing the risk of colorectal cancer: a meta‐analysis. S. Almazeedi et al.; BJS, March 2020 – Volume 107 – Issue 4, pages 348-354.
Pubmed ID: 31976551.

BACKGROUND: Obesity increases the risk of multiple co-morbidities such as type 2 diabetes, cardiovascular disease and most cancers, including colorectal cancer. Currently, the literature presents conflicting results regarding the protective effects of bariatric surgery on the incidence of colorectal cancer. This meta-analysis was conducted to investigate the effect of bariatric surgery on the risk of developing colorectal cancer in obese individuals.
METHODS: Ovid Embase, Ovid MEDLINE, Cochrane CENTRAL and Web of Science were searched for relevant articles. Articles published by the end of December 2018 were retrieved; data were extracted according to evidence-based PICO (population, intervention, control, outcome) model and analysed using a random-effects model to estimate the pooled relative risk (RR) and its 95 per cent confidence interval. The heterogeneity of studies was tested and quantified using Cochran's Q and I^2 statistics. Meta-regression was used to investigate the association of year of study, region, mean length of follow-up and sample size with RR.
RESULTS: Seven articles, involving a total of 1 213 727 patients, were included in the meta-analysis. The pooled estimate of the RR was 0·64 (95 per cent c.i. 0·42 to 0·98). The test of asymmetry found no significant publication bias. Meta-regression showed that sample size was a statistically significant factor (P = 0·037), but year of publication, region and mean duration of follow-up were not significant.
CONCLUSION: Patients who underwent bariatric surgery had a greater than 35 per cent reduction in the risk of developing colorectal cancer compared with obese individuals who had no surgery.

Fig. 2 Forest plot of colorectal cancer in patients who had bariatric surgery and those who did not

Reference	Colorectal cancer: Surgery	Colorectal cancer: No surgery	Relative risk	Relative risk	Weight (%)
Adams *et al.*[26]	25 of 6596	52 of 9442		0·69 (0·43, 1·11)	16·6
Aravani *et al.*[27]	43 of 39 747	3237 of 962 860		0·32 (0·24, 0·43)	19·1
Christou *et al.*[28]	2 of 1035	35 of 5746		0·32 (0·08, 1·32)	6·2
Derogar *et al.*[29]	70 of 15 095	373 of 62 016		0·77 (0·60, 0·99)	19·6
Mackenzie *et al.*[30]	35 of 8794	16 of 8794		2·19 (1·21, 3·95)	14·9
Schauer *et al.*[31]	105 of 22 198	533 of 66 427		0·59 (0·48, 0·73)	20·1
McCawley *et al.*[32]	1 of 1482	11 of 3495		0·21 (0·03, 1·66)	3·5
Random-effects model	281 of 94 947	4257 of 1 118 780		0·64 (0·42, 0·98)	100·0
Heterogeneity: I^2 = 85%, τ^2 = 0.2177, P < 0·01			0·1 0·5 1 2 10		

Sizes of markers indicate weight for each study according to sample size, and the diamond represents the overall pooled estimate of the relative risk (RR). An inverse-variance random-effects model was used for meta-analysis. RR values are shown with 95 per cent confidence intervals.

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