

# DE LEESTAFEL

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### Coloproctologie

#### Laparoscopie met name kostenbesparend in de postacute fase

*An Instrumental Variable Analysis Comparing Medicare Expenditures for Laparoscopic vs Open Colectomy, K.H.Sheetz et al., JAMA surg, 2017;152(10):921-929*

*Pubmedid 28614579*

##### **Importance**

Numerous study findings suggest that the use of laparoscopy is associated with lower health care costs for many operations, including colectomy. The extent to which these differences are due to the laparoscopic approach itself or selection bias from healthier patients undergoing the less invasive procedure is unclear.

##### **Objective**

To evaluate the differences in Medicare expenditures for laparoscopic and open colectomy.

##### **Design, Setting, and Participants**

A population-based study was conducted of Medicare beneficiaries undergoing laparoscopic or open colectomy between January 1, 2010, and December 31, 2012. The dates of the analysis were November 13 to December 10, 2016. Using instrumental variable methods to account for selection bias, actual Medicare payments after each procedure were evaluated. To identify the mechanisms of potential cost savings, the frequency and amount of physician, readmission, and postacute care payments were evaluated. Several sensitivity analyses were performed restricting the study population by patient demographic or surgeon specialty.

##### **Main Outcomes and Measures**

Actual Medicare expenditures up to 1 year after the index operation.

##### **Results**

The study population included 428 799 patients (mean [SD] age, 74 [10] years; 57.0% female). When using standard methods, patients undergoing laparoscopic colectomy (vs open) had lower total Medicare expenditures (mean, -\$5547; 95% CI, -\$5408 to -\$5684;  $P < .01$ ). When using instrumental variable methods, which account for potentially unmeasured patient characteristics, patients undergoing laparoscopic colectomy (vs open) still had lower Medicare expenditures (mean, -\$3676; 95% CI, -\$2444 to -\$4907;  $P < .01$ ), although the magnitude of the association was reduced. When examining the root causes of the difference in costs between patients who underwent laparoscopic and open colectomy, the key drivers were a reduction in costs from readmissions (mean, -\$1102; 95% CI, -\$1373 to -\$831) and postacute care (mean, -\$1446; 95% CI, -\$1988 to -\$935;  $P < .01$ ).

##### **Conclusions and Relevance**

This population-based study demonstrates the influence of selection bias on cost estimates in comparative effectiveness research. While the use of laparoscopy reduced total episode payments, the source of savings is in the postacute care period, not the index hospitalization.

# Laparoscopie van invloed op maat van mesorectale excisie bij rectumcarcinoom

*Meta - analysis of the impact of surgical approach on the grade of mesorectal excision in rectal cancer, B. Creavin et al., BJS; 2017; 104: 1609-1619.*

*Pubmedid 29044484*

## **Background**

The subspecialization of colorectal surgeons, and improvements in the quality of mesorectal excision have revolutionized rectal cancer surgery. With the increasing use of minimally invasive techniques, the completeness of the mesorectal excision has been questioned. This study aimed to assess the pathological outcomes of open versus laparoscopic rectal resection.

## **Method**

A meta-analysis of RCTs was undertaken. The primary endpoint was the adequacy of the mesorectal excision. Secondary endpoints included circumferential resection margin and distance to resection margins.

## **Results**

Four studies were included, reporting on 2319 patients; 972 (41.9 per cent) had open and 1347 (58.1 per cent) had laparoscopic resections. Meta-analysis of adequacy of the mesorectal excision showed a small difference in achieving an intact mesorectum in favour of open surgery (risk ratio (RR) 1.06, 95 per cent c.i. 1.02 to 1.10;  $P = 0.001$ ). Superficial defects were more common in laparoscopic surgery (RR 0.70, 0.54 to 0.89;  $P = 0.004$ ). Deep mesorectal defects (RR 0.78, 0.51 to 1.20;  $P = 0.256$ ), circumferential margin (CRM) positivity (RR 0.85, 0.62 to 1.16;  $P = 0.310$ ), and distance to radial (mean difference (MD)  $-0.06$ , 95 per cent c.i.  $-0.10$  to  $0.23$ ;  $P = 0.443$ ) and distal (MD  $0.03$ ,  $-0.06$  to  $0.12$ ;  $P = 0.497$ ) margins were all similar. A complete resection (intact mesorectum, negative CRM and distal margin) was achieved in 350 of 478 patients (73.2 per cent) in the laparoscopic group and 372 of 457 (81.4 per cent) in the open group (risk difference (RD) 8 (95 per cent c.i. 3 to 13) per cent;  $P = 0.003$ ). However, an acceptable mesorectum (intact or superficial defects only) was present in 1254 of 1308 (95.9 per cent) and 916 of 949 (96.5 per cent) in the laparoscopic and open groups respectively (RD 1 ( $-1$  to 3) per cent;  $P = 0.263$ ).

## **Conclusion**

Small differences in mesorectal quality were evident between open and laparoscopic rectal resections. This may be attributable to use of laparoscopic instruments; however, to date minor defects have not affected oncological outcomes.

## UPPER GI

# Neoadjuvante behandeling geeft significant overlevingsvoordeel in T3N0M0 oesofaguscarcinoom

*Survival Benefit of Neoadjuvant Treatment in Clinical T3N0M0 Esophageal Cancer: Results From a Retrospective Multicenter European Study, S. Mantziari et al., Annals of Surgery; November 2017 – Volume 266 – Issue 5 – p 805-813*

*Pubmedid 28742698*

## **Background**

Based on current guidelines, clinical T3N0M0 esophageal tumors may or may not receive neoadjuvant treatment, according to their perception as locally advanced (cT3) or early-stage tumors (stage II). The study aim was to assess the impact of neoadjuvant treatment upon survival for cT3N0M0 esophageal cancer patients, with subgroup analyses by histological type (squamous cell carcinoma vs adenocarcinoma) and type of neoadjuvant treatment (chemotherapy vs radiochemotherapy).

## **Methods**

Data from patients operated on for esophageal cancer in 30 European centers were collected. Among the 382 of 2944 patients with clinical T3N0M0 stage at initial diagnosis (13.0%), we compared those treated with primary surgery (S,  $n = 193$ ) versus with neoadjuvant treatment plus surgery (NS,  $n = 189$ ).

## **Results**

The S and NS groups were similar regarding their demographic and surgical characteristics. In-hospital postoperative morbidity and mortality rates were comparable between groups. Patients were found to be pN+ in 64.2% versus 42.9% in the S and NS groups respectively ( $P < 0.001$ ), pN2/N3 in 35.2% versus 21.2% ( $P < 0.001$ ), stage 0 in 0% versus 16.4% ( $P < 0.001$ ), and R0 in 81.3% versus 89.4% of cases ( $P = 0.026$ ). Median overall and disease-free survivals were significantly better in the NS group, 38.4 versus 27.9 months ( $P = 0.007$ ) and 31.6 versus 27.5 months ( $P = 0.040$ ), respectively, and this difference remained for both histological types. Radiotherapy did not offer a benefit compared with chemotherapy alone ( $P = 0.687$ ). In multivariable analysis, neoadjuvant treatment was an independent favorable prognostic factor (HR 0.76, 95% CI 0.58–0.99,  $P = 0.044$ ).

#### **Conclusion**

Neoadjuvant treatment offers a significant survival benefit for clinical T3N0M0 esophageal cancer.

## **Sarcopenie als risicofactor voor postoperatieve complicaties in patiënten met locally advanced oesofaguscarcinoom**

*Sarcopenia: Prevalence, and Impact on Operative and Oncologic Outcomes in the Multimodal Management of Locally Advanced Esophageal Cancer, J. Elliott et al., Annals of Surgery; November 2017 – Volume 266 – Issue 5 – p 822-830*

*Pubmedid 28796017*

*Pubmedid 28796017*

#### **Objective**

The aim of this article was to study the prevalence and significance of sarcopenia in the multimodal management of locally advanced esophageal cancer (LAEC), and to assess its independent impact on operative and oncologic outcomes.

#### **Summary of Background Data**

Sarcopenia in cancer may confer negative outcomes, but its prevalence and impact on modern multimodal regimens for LAEC have not been systematically studied.

#### **Methods**

Two hundred fifty-two consecutive patients were studied. Lean body mass (LBM), skeletal muscle index (SMI), and fat mass (FM) were determined pre-treatment, preoperatively, and 1 year postoperatively. Sarcopenia was defined by computed tomography (CT) at L3 as  $SMI < 52.4 \text{ cm}^2/\text{m}^2$  for males and  $SMI < 38.5 \text{ cm}^2/\text{m}^2$  for females. All complications were recorded prospectively, including comprehensive complications index (CCI), Clavien-Dindo complication (CDC), and pulmonary complications (PPCs). Multivariable linear, logistic, and Cox regression analysis was performed.

#### **Results**

In-hospital mortality was 1%, and CCI was  $21 \pm 19$ . Sarcopenia increased ( $P = 0.02$ ) from 16% at diagnosis to 31% post-neoadjuvant therapy, with loss of LBM ( $-3.0 \pm 5.4 \text{ kg}$ ,  $P < 0.0001$ ), but not FM ( $-0.3 \pm 2.7 \text{ kg}$ ,  $P = 0.31$ ) during treatment. On multivariable analysis, preoperative sarcopenia was associated with CCI ( $P = 0.043$ ), and  $CDC \geq IIIb$  ( $P = 0.003$ ). PPCs occurred in 36% nonsarcopenic versus 55% sarcopenic patients ( $P = 0.01$ ). Sarcopenia did not impact disease-specific ( $P = 0.14$ ) or overall survival ( $P = 0.11$ ) after resection. At 1 year, 35% had sarcopenia, significantly associated with pre-treatment BMI ( $P = 0.013$ ) but not complications ( $P = 0.20$ ).

#### **Conclusions**

Sarcopenia increases through multimodal therapy, is associated with an increased risk of major postoperative complications, and is prevalent in survivorship. These data highlight a potentially modifiable marker of risk that should be assessed and targeted in modern multimodal care pathways.

## **Minimaal invasieve gastrectomy geeft minder wondinfecties en kortere ziekenhuisopname**

*Postoperative Outcomes of Minimally Invasive Gastrectomy Versus Open Gastrectomy During the Early Introduction of Minimally Invasive Gastrectomy in the Netherlands: A Population-based Cohort Study, H. Brenkman et al., Annals of Surgery; November 2017 – Volume 266 – Issue 5 – p 831-838*

*Pubmedid 28742708*

### **Objective**

To compare postoperative outcomes of minimally invasive gastrectomy (MIG) to open gastrectomy (OG) for cancer during the introduction of MIG in the Netherlands.

### **Background**

Between 2011 and 2015, the use of MIG increased from 4% to 53% in the Netherlands.

### **Methods**

This population-based cohort study included all patients with curable gastric adenocarcinoma that underwent gastrectomy between 2011 and 2015, registered in the Dutch Upper GI Cancer Audit. Patients with missing preoperative data, and patients in whom no lymphadenectomy or reconstruction was performed were excluded. Propensity score matching was applied to create comparable groups between patients receiving MIG or OG, using year of surgery and other potential confounders. Morbidity, mortality, and hospital stay were evaluated.

### **Results**

Of the 1697 eligible patients, 813 were discarded after propensity score matching; 442 and 442 patients who underwent MIG and OG, respectively, remained. Conversions occurred in 10% of the patients during MIG. Although the overall postoperative morbidity (37% vs 40%,  $P = 0.489$ ) and mortality rates (6% vs 4%,  $P = 0.214$ ) were comparable between the 2 groups, patients who underwent MIG experienced less wound complications (2% vs 5%,  $P = 0.006$ ). Anastomotic leakage occurred in 8% of the patients after MIG, and in 7% after OG ( $P = 0.525$ ). The median hospital stay declined over the years for both procedures (11 to 8 days,  $P < 0.001$ ). Overall, hospital stay was shorter after MIG compared with OG (8 vs 10 days,  $P < 0.001$ ).

### **Conclusions**

MIG was safely introduced in the Netherlands, with overall morbidity and mortality comparable with OG, less wound complications and shorter hospitalization

## **HPB**

## **Definitieve behandeling na biliare pancreatitis als kwaliteitsindicator**

*Early definitive treatment rate as a quality indicator of care in acute gallstone pancreatitis, R. Green, BJS 2017; 104: 1686-1694.*

*Pubmedid 28792589*

### **Background**

Early definitive treatment (cholecystectomy or endoscopic sphincterotomy in the same admission or within 2 weeks after discharge) of gallstone disease after a biliary attack of acute pancreatitis is standard of care. This study investigated whether compliance with early definitive treatment for acute gallstone pancreatitis can be used as a care quality indicator for the condition.

### **Method**

A retrospective cohort study was conducted using the Hospital Episode Statistics database. All emergency admissions to National Health Service hospitals in England with a first time diagnosis of acute gallstone pancreatitis in the financial years 2008, 2009 and 2010 were examined. Trends in early definitive treatment between hospital trusts were examined and patient morbidity outcomes were determined.

### **Results**

During the study interval there were 19 510 patients with an overall rate of early definitive treatment at 34.7 (range 9.4–84.7) per cent. In the 1-year follow-up period, 4661 patients (23.9 per cent) had one or more emergency readmissions for complications related to gallstone pancreatitis. Of these, 2692 (57.8 per cent) were readmissions for acute pancreatitis; 911 (33.8 per cent) were within the first 2 weeks of discharge, with the remaining 1781 (66.2 per cent) occurring after the point at which

definitive treatment should have been received. Early definitive treatment resulted in a 39 per cent reduction in readmission risk (adjusted risk ratio (RR) 0·61, 95 per cent c.i. 0·58 to 0·65). The risk was further reduced for acute pancreatitis readmissions to 54 per cent in the early definitive treatment group (adjusted RR 0·46, 0·42 to 0·51).

#### **Conclusion**

In acute gallstone pancreatitis, compliance with recommended early definitive treatment varied considerably, with associated variation in outcomes. Compliance should be used as a quality indicator to improve care.

## **Patientselectie en verbeteringen in techniek van ALPPS verminderd mortaliteit en postoperatieve morbiditeit**

*Risk Adjustment in ALPPS Is Associated With a Dramatic Decrease in Early Mortality and Morbidity, M. Linecker et al, Annals of Surgery; November 2017 – Volume 266 – Issue 5 – p 779-786*

*Pubmedid 28806301*

#### **Objective**

To longitudinally assess whether risk adjustment in Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS) occurred over time and is associated with postoperative outcome.

#### **Background**

ALPPS is a novel 2-stage hepatectomy enabling resection of extensive hepatic tumors. ALPPS has been criticized for its high mortality, which is reported beyond accepted standards in liver surgery. Therefore, adjustments in patient selection and technique have been performed but have not yet been studied over time in relation to outcome.

#### **Methods**

ALPPS centers of the International ALPPS Registry having performed  $\geq 10$  cases over a period of  $\geq 3$  years were assessed for 90-day mortality and major interstage complications ( $\geq 3b$ ) of the longitudinal study period from 2009 to 2015. The predicted prestage 1 and 2 mortality risks were calculated for each patient. In addition, questionnaires were sent to all centers exploring center-specific risk adjustment strategies.

#### **Results**

Among 437 patients from 16 centers, a shift in indications toward colorectal liver metastases from 53% to 77% and a reverse trend in biliary tumors from 24% to 9% were observed. Over time, 90-day mortality decreased from initially 17% to 4% in 2015 ( $P = 0.002$ ). Similarly, major interstage complications decreased from 10% to 3% ( $P = 0.011$ ). The reduction of 90-day mortality was independently associated with a risk adjustment in patient selection ( $P < 0.001$ ; OR: 1.62; 95% CI: 1.36–1.93) and using less invasive techniques in stage-1 surgery ( $P = 0.019$ ; OR: 0.39; 95% CI: 0.18–0.86). A survey indicated risk adjustment of patient selection in all centers and ALPPS technique in the majority (80%) of centers.

#### **Conclusions**

Risk adjustment of patient selection and technique in ALPPS resulted in a continuous drop of early mortality and major postoperative morbidity, which has meanwhile reached standard outcome measures accepted for major liver surgery.

## **LEVERCHIRURGIE**

## **Resterende lever ischemie als maat voor kankerspecifieke overleving na resectie colorectale levermetastasen**

*Remnant Liver Ischemia as a Prognostic Factor for Cancer-Specific Survival After Resection of Colorectal Liver Metastases, JAMA surg, S. Yamashita, 2017;152(10):e172986*

*Pubmedid 28854316*

#### **Importance**

Ischemia-reperfusion injury during hepatic resection has been shown to accelerate progression of liver cancer. However, the prognostic relevance of remnant liver ischemia (RLI) after resection of colorectal liver metastases (CLMs) is unknown to date.

### **Objectives**

To assess the prognostic influence of RLI after resection of CLMs and to identify correlates of greater extent of RLI.

### **Design, Setting, and Participants**

This study was a retrospective analysis at The University of Texas MD Anderson Cancer Center based on prospectively collected data. The study identified 202 patients who underwent curative resection of CLMs between January 1, 2008, and December 31, 2014, and had enhanced computed tomographic images obtained within 30 days after surgery.

### **Main Outcomes and Measures**

Remnant liver ischemia was defined as reduced or absent contrast enhancement during the portal phase. Postoperative RLI was classified as grade 0 (none), 1 (marginal), 2 (partial), 3 (segmental), or 4 (necrotic) as previously defined. Experienced members of the surgical team retrospectively performed imaging assessments. Team members were masked to the postoperative outcomes. Survival after resection was stratified by RLI grade. Predictors of RLI grade 2 or higher and survival were identified.

### **Results**

Among 202 patients (median [range] age, 56 [27-87] years; 84 female), the RLI grades were as follows: grade 0 (105 patients), grade 1 (47 patients), grade 2 (45 patients), grade 3 (5 patients), and grade 4 (0 patients). Recurrence-free survival (RFS) and cancer-specific survival (CSS) rates after hepatic resection were worse in patients with RLI grade 2 or higher vs grade 1 or lower (RFS at 3 years, 6.4% [3 of 50] vs 39.2% [60 of 152];  $P < .001$  and CSS at 5 years, 20.7% [10 of 50] vs 63.7% [97 of 152];  $P < .001$ ). A largest metastasis at least 3 cm (OR, 2.74; 95% CI, 1.35-5.70;  $P = .005$ ), multiple CLMs (OR, 2.51; 95% CI, 1.25-5.24;  $P = .009$ ), and nonanatomic resection (odds ratio [OR], 3.29; 95% CI, 1.52-7.63;  $P = .002$ ) were associated with RLI grade 2 or higher. A largest metastasis at least 3 cm (hazard ratio [HR], 1.70; 95% CI, 1.01-2.88;  $P = .045$ ), mutant RAS (HR, 2.15; 95% CI, 1.27-3.64;  $P = .005$ ), and RLI grade 2 or higher (HR, 2.90; 95% CI, 1.69-4.84;  $P < .001$ ) were associated with worse CSS.

### **Conclusions and Relevance**

In this study, remnant liver ischemia grade 2 or higher was associated with worse CSS after resection of CLMs. High-quality anatomic surgery to minimize RLI after resection is essential.

## **Patiënten met hepatocellulair adenoom dienen een langere periode te worden geëvalueerd voor overgegaan wordt tot interventies**

*Retrospective study on timing of resection of hepatocellular adenoma, A.J. Klompenhouwer et al., BJS 2017; 104: 1695-1703.*

*Pubmedid 28857134*

### **Background**

Hepatocellular adenoma (HCA) is a benign liver tumour that may be complicated by bleeding or malignant transformation. Present guidelines advise cessation of oral contraceptives and surgical resection if the lesion is still larger than 5 cm at 6 months after diagnosis. The aim of this study was to evaluate whether this 6-month interval is sufficient to expect regression of a large HCA to 5 cm or smaller.

### **Method**

This retrospective cohort study included all patients with an HCA larger than 5 cm diagnosed between 1999 and 2015 with follow-up of at least 6 months. Medical records were reviewed for patient characteristics, clinical presentation, lesion characteristics, management and complications. Differences in characteristics were assessed between patients kept under surveillance and those who underwent treatment for an HCA larger than 5 cm.

### **Results**

Some 194 patients were included, of whom 192 were women. Eighty-six patients were kept under surveillance and 108 underwent HCA treatment. Patients in the surveillance group had a significantly

higher BMI ( $P = 0.029$ ), smaller baseline HCA diameter ( $P < 0.001$ ), more centrally located lesions ( $P < 0.001$ ) and were more likely to have multiple lesions ( $P = 0.001$ ) than those in the treatment group. There were no significant differences in sex, age at diagnosis, symptoms, complication rates and HCA subtype distribution. Time-to-event analysis in patients managed conservatively and those still undergoing treatment more than 6 months after diagnosis showed that 69 of 118 HCAs (58.5 per cent) regressed to 5 cm or smaller after a median of 104 (95 per cent c.i. 80–128) weeks. Larger HCAs took longer to regress ( $P < 0.001$ ). No complications were documented during follow-up.

### Conclusion

This study suggests that a 6-month cut-off point for assessment of regression of HCA larger than 5 cm to no more than 5 cm is too early. As no complications were documented during follow-up, the cut-off point in women with typical, non- $\beta$ -catenin-activated HCA could be prolonged to 12 months, irrespective of baseline diameter.

## BARIATRISCHE CHIRURGIE

### Patiënten met preoperatief leverfunctiestoornissen hebben meer baat bij gastric sleeve dan RYGB

*Liver Function in Patients With Nonalcoholic Fatty Liver Disease Randomized to Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy: A Secondary Analysis of a Randomized Clinical Trial, P. Kalinowski et al., Annals of Surgery; November 2017 – Volume 266 – Issue 5 – p 738-745*

*Pubmedid 28767558*

#### Objectives

The aim of the study was to compare the influence of sleeve gastrectomy (SG) versus Roux-en-Y gastric bypass (RYGB) on liver function in bariatric patients with non-alcoholic fatty liver disease (NAFLD) in a randomized clinical trial (NCT01806506).

#### Background

Rapid weight loss and malabsorption after bariatric surgery in patients with NAFLD or steatohepatitis (NASH) may impair liver function.

#### Methods

Sixty-six morbidly obese patients randomized to SG or RYGB were included in a secondary outcome analysis. Intraoperative liver biopsies were categorized with NAFLD Activity Score (NAS) and liver function tests were done before surgery and after 1, 6 and 12 months.

#### Results

NASH was present in 54.5% RYGB and 51.5% SG patients ( $P > 0.05$ ). At 12 months excess weight loss was  $68.7 \pm 19.7\%$  after SG and  $62.8 \pm 18.5\%$  after RYGB ( $P > 0.05$ ). At 1 month international normalized ratio (INR) increased after RYGB ( $0.98 \pm 0.05$  vs  $1.14 \pm 0.11$ ;  $P < 0.05$ ) and SG ( $0.99 \pm 0.06$  vs  $1.04 \pm 0.06$ ;  $P < 0.05$ ), RYGB induced significantly greater increase in INR in the whole group and NASH patients than SG. After RYGB albumin decreased at 1 month ( $41.2 \pm 2.7$  vs  $39.0 \pm 3.2$  g/L;  $P < 0.05$ ). At 12 months, INR and albumin returned to baseline. At 12 months in NASH group, SG induced significant improvement in aspartate aminotransferase ( $32.4 \pm 17.4$  vs  $21.5 \pm 6.9$  U/L), alanine aminotransferase ( $39.9 \pm 28.6$  U/L vs  $23.8 \pm 14.1$  U/L), gamma-glutamyl transpeptidase ( $34.3 \pm 16.6$  vs  $24.5 \pm 16.8$  U/L), and lactate dehydrogenase ( $510.8 \pm 33$  vs  $292.4 \pm 29$ ). Variables predictive of INR change after 1 month included operation type,  $NAS \geq 5$ , bilirubin, body mass index, hemoglobin A1C, and dyslipidemia.

#### Conclusions

Patients with NASH undergoing RYGB are more susceptible to early transient deterioration of liver function than after SG.