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Postoperative outcomes after laparoscopic or open gastrectomy. A national cohort study of 10,343 patients.

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ABSTRACT

Background: Laparoscopy for gastric cancer has not been as popular compared with other digestive surgeries, with conflicting reports on outcomes. The aim of this study focuses on the surgical techniques comparing open and laparoscopy by assessing the morbi-mortality and long-term complications after gastrectomy.

Methods: A retrospective study (2013-2018) was performed on a prospective national cohort (PMSI). All patients undergoing resection for gastric cancer with a partial gastrectomy (PG) or total gastrectomy (TG) were included. Overall morbidity at 90 post-operative days and long-term results were the main outcomes. The groups (open and laparoscopy) were compared using a propensity score and volume activity matching after stratification on resection type (TG or PG).

Results: A total of 10,343 patients were included. The overall 90-day mortality and morbidity were 7% and 45%, with reintervention required in 9.1%. High centre volume was associated with improved outcomes. There was no difference in population characteristics between groups after matching. An overall benefit for a laparoscopic approach after PG was found for morbidity (Open=39.4% vs. Laparoscopy=32.6%, $p=0.01$), length of stay (Open=14[10-21] vs. Laparoscopy=11[8-17] days, $p<0.0001$). For TG, increased reintervention rate (Open=10.8% vs. Laparoscopy=14.5%, $p=0.04$) and increased oesophageal stricture rate (HR=2.54[1.67-3.85], $p<0.001$) were encountered after a laparoscopic approach. No benefit on mortality was found for laparoscopic approach in both type of resections after adjusted analysis.

Conclusions: Laparoscopy is feasible for PG with a substantial benefit on morbidity and length of stay, however, laparoscopic TG should be performed with caution, with of higher rates of reintervention and oesophageal stricture.

INTRODUCTION

Minimally invasive surgery has become the preferred choice in a number of specialties including colorectal, bariatric, oesophageal and hepatic surgery. [1-4] However, a laparoscopic approach for gastric cancer has not been as popular, with conflicting reports on outcomes seen in the literature. A recent randomized clinical trial (RCT) KLASS-01 [5] comparing laparoscopic and open partial gastrectomy (PG) in stage I gastric cancer reported an advantage for laparoscopy on overall morbidity rate, although, major abdominal complications were similar. Oncological outcomes were not compromised and showed the safety of the laparoscopic approach, with no difference observed in 5-year cancer specific survival rates between the open and laparoscopic group. [6] Similar results were encountered in the Klass-02 RCT [7] with a significantly reduced morbidity seen in the laparoscopic group, while the oncologic result of CLASS-01 showed no difference between laparoscopic or open resection for locally advanced cancer. [8] However, Rod *et al.* reported increased severe morbidity in terms of post-operative bleeding and reinterventions after laparoscopic gastrectomy. Conflicting reports have also been reported after laparoscopic total gastrectomy (TG). [9] A recent large retrospective study showed some benefit for the laparoscopic approach in terms of hemostasis and quicker return to normal physiological function, however, the authors did observe higher leakage and anastomotic stricture rates. [10] The latest meta-analysis of retrospective studies has reported equivalent safety to the open approach with similar five-year overall survival. [11]

Due to the conflicting reports in the literature, the present study aimed at analysing large nationwide cohort of patients undergoing gastrectomy in order to report a pragmatic real-life morbidity rate and assess the potential benefit of the laparoscopic approach. Because of the lack of

oncological staging in this database, the present study focused on results of surgical procedures by assessing postoperative complications.

PATIENTS AND METHODS

Study design and participants

A retrospective review of a prospectively maintained national database named PMSI “*programme de médicalisation des systèmes d’informations*” was realized. [12] Mandatory routine data collection on all in-hospital admissions is performed in both private and general hospitals in France. The purpose of this database is to set the financial budget of French hospitals based on the number of patients and type of procedures performed. All details regarding a patient hospitalization was recorded in individual centres. The validity of this database has been tested by cross referencing it with other cohort databases. [13-15] Information in the database includes the hospital identifier, length of stay, diagnostic codes and a national procedures classification (*Classification Commune des Actes Médicaux* [CCAM]) which describes surgical, endoscopic and radiological procedures. All patients undergoing resection for gastric cancer (C16 in ICD-10 classification) as defined by the table in appendix 1, between January 2013 to December 2018, were included.

Patients with subtotal distal gastrectomy and total gastrectomy without Billroth 1 reconstruction or atypical gastric resection were included. Two groups were created: Laparoscopic and open groups (appendix 1). Patients in the laparoscopic group who underwent a conversion to open were attached in the laparoscopic group in an intention-to-treat analysis. Patients with metastatic disease or enlarged resection for locally advanced tumour requiring combined resection of adjacent organs

(colon, hepatic, pancreatic) and those with peritoneal carcinomatosis (peritoneal resection or hyperthermic intraperitoneal chemotherapy), defined by CCAM codes from Appendix 1 were excluded. Patients undergoing simultaneous splenectomy or cholecystectomy during a gastrectomy were included in the study cohort.

Covariates

Patient characteristics and demographics extracted from the database included age, gender and hospital site. Nutritional status (malnutrition “E43 E44 E46” and obesity “E66”) and Charlson comorbidity index [16, 17] were constructed as reported in the appendix 2. Data on type of surgical resection and chemotherapy use were also collected. One chemotherapy session was defined as one hospital attendance for chemotherapy, with subsequent chemotherapy session not counted. This last variable was used as a proxy in order to take into account the lack of oncological staging.

Outcomes

Postoperative outcomes were examined. The early in-hospital mortality rate and short-term outcomes were defined as a complication or death occurring within 90 postoperative days (POD). Complications were defined as follow: leakage or deep abscess, bleeding, thrombo-embolic disease, pulmonary complications or renal insufficiency according to ICD 10 described in Appendix 3. Algorithm of complications was adapted to upper-gastro-intestinal surgery from our previous publications. [18-20] The occurrence of any one of these complications contributed to the overall morbidity at 90 POD. The impact of these complications on patients was assessed by the need for surgical reintervention as outlined in Appendix 4.

Long-term outcomes were defined as the occurrence of an incisional hernia, bowel obstruction or oesophageal stricture during follow-up. The ICD 10 codes for these complications are reported in Appendix 3. All hospital stays for each patient were recorded until December 2019.

Statistical analysis

Descriptive statistics were reported in percentage for categorical variables, with median and interquartile range for continuous variable. All analysis was stratified by type of surgery (TG or PG). Univariate analysis was performed with t-test and Chi-Square-test for respectively continuous and categorical outcomes. The impact of volume was studied with regression curves used on the main outcomes by the activity of centre per years using general linear model for binary outcomes and *linear model* for quantitative outcomes.

A propensity score on the probability of a laparoscopic approach was calculated for each patient using several variables: age, gender, Charlson comorbidity index, malnutrition, obesity, preoperative chemotherapy, cholecystectomy, preoperative laparoscopy and year of resection. A matching between open and laparoscopy using the nearest neighbour method for propensity score and the exact method on the volume of activity was performed with a ratio 1/1. The R-package (*MatchIt*) was used. [21] An univariate analysis after matching was performed for 90-day outcomes and the Kaplan Meier method, log rank test and hazard ratio with 95% confidence of cox model for long term outcomes. A p value of <0.05 was considered significant. In order to avoid bias of centre selection and learning curve, a sensitivity analysis was realized using a matching on centre identifier and propensity score with the same methods as previously explained. Analysis was done with R software. [22]

RESULTS

Characteristics of population

A total of 13,819 gastric cancer surgeries were performed in 661 centres between January 1, 2013 and December 31, 2018. The patient's flowchart is presented in appendix 5. After exclusion of metastatic patients (n=1,541) and patients with associated procedures (n=1,935), 10,343 were included in the final analysis. Characteristics of these patients are summarized in table 1. The median age was 70 [61-79] years with 3,996 (39%) females. 1,342 patients (13%) had diabetes, 1,226 patients (12%) were obese and 4,116 (40%) presented with substantial malnutrition. Preoperative chemotherapy was given to 4,309 patients (42%), with chemotherapy being more frequently administered prior to total gastrectomy (TG: 54% vs. PG: 30% p<0.001). Most patients had less than four chemotherapy sessions (≤ 4 : 68%, >4 : 32%).

TG was the most common procedure performed (5,782, 56%), including 745 (13%) laparoscopic TG. Laparoscopic PG was done for 664 (15%) patients. A concomitant cholecystectomy or splenectomy was more commonly performed in the open group (Laparoscopy: 13.6% vs. Open: 20.6%, p<0.001; Laparoscopy: 0.01% vs. Open: 3.0%, p<0.001 respectively). Laparoscopic resection rate significantly increased over the years (2013-2014: 8.2%, 2015-2016: 13.0%, 2017-2018: 20.1%; p<0.001). The table of general characteristics of the population after adjustment is given in appendix 6.

Short term outcomes

90-POD mortality and morbidity rates were 6.9% (n=714) and 45.4% (n=4,693) (Table 2). The most frequent complications were anastomotic leakage or deep abscess (22.5%, n=2,330). The

overall reintervention rate was 9.1% (n=945). The overall median length of stay was 15 [11-22] days. Tables 2 and 3 summarized the short-term outcomes before and after matching.

For TG, in univariate analysis, the mortality rate and length of stay were shorter in the laparoscopy group (Open=7.5% vs. Laparoscopy=5.2%, p=0.03; Open=15[12-23] vs. laparoscopy=14[10-21] days, p<0.0001, respectively). The laparoscopic approach was associated with increased bleeding (Open=7.6% vs. Laparoscopy=10.1%; p=0.03) and surgical reintervention rate (Open=11.5% vs. Laparoscopy=14.5%; p=0.02). After matching, a significantly higher reintervention rate was observed in the laparoscopic group (Open=10.8% vs. Laparoscopy=14.5%, p=0.04). However, a significant decrease of hospital stay was reported in the laparoscopy group (Open=14[10-21] vs. Laparoscopy=11[8-17] days, p<0.0001).

For PG, in univariate analysis, mortality rate, overall morbidity rate and length of stay were lower in the laparoscopic group (Open=7.0% vs. Laparoscopy=3.5%, p<0.001; Open=40.2% vs. Laparoscopy=32.7%, p<0.001; Open=15[11-22] vs. Laparoscopy=11[8-17] days, p<0.001, respectively). However, the surgical reintervention rate was higher in the laparoscopic group (Open=5.3% vs. Laparoscopy=7.5%, p=0.026). After matching, the benefit on morbidity and length of stay were confirmed: a laparoscopic approach significantly decreased overall morbidity rate at 90 days (Open=39.4% vs. Laparoscopy=32.6%, p=0.01) and length of stay (Open=14[10-21] vs. Laparoscopy=11[8-17] days, p<0.0001).

Long term outcomes

Long term outcomes are presented in figure 1. For TG, more oesophageal strictures were observed after a laparoscopic approach before and after adjustment (HR=2.54[1.67-3.85], p<0.001). No

differences between groups were found on incisional hernia or bowel obstruction ($p=0.08$, $p=0.33$) (Figure 1). For PG, no benefit for the laparoscopic approach were observed for incisional hernia or bowel obstruction ($p=0.37$, $p=0.09$).

Impact of center volume on outcomes

The 10,343 gastrectomies were performed in 661 centers with a median of 2 (1-3) patients per year. 86% of patients ($n=8852$) had been operated in a center with an activity < 12 gastrectomies per year. Figure 2 reported the regression curves in function of activity per year per center. All curves showed a benefit on outcomes with increased volume except for mortality and reintervention rates after laparoscopic PG.

Sensitivity analysis

After matching on center and propensity score, 346 laparoscopic TG were matched with 346 open TG and 301 laparoscopic PG with 301 open PG.

The increased prevalence of esophageal stricture ($HR=2.42[1.32-4.40]$, $p<0.001$) and reduced length of stay (Open=15[12-22] vs. Laparoscopy=14[11-22] days, $p=0.04$) was confirmed for TG after laparoscopy. The benefit of laparoscopy on overall morbidity and length of stay for PG was in line with previous results as reported in table 4 (Open=40.9% vs. Laparoscopy=32.6%, $p=0.052$ and Open=14[10-21] vs. Laparoscopy=11[8-16] days, $p<0.0001$).

DISCUSSION

This study reports the postoperative outcomes of more than 10,000 gastric cancer resections in a French nationwide cohort between 2013 and 2018. The overall 90-day morbidity was roughly 45%,

made up mainly of leakage or deep abscess (22.5%), pulmonary complications (17.4%) and bleeding (7%). After matching, a laparoscopic PG was associated with reduced morbidity rate. Significant higher oesophageal stricture and reintervention rates were observed after TG. A benefit of length of stay was reported in both groups after laparoscopy.

Patient characteristics differed significantly between the two groups in the present study. The laparoscopic group included younger patients, with less malnutrition, less preoperative chemotherapy and more frequently operated in low volume centres. This may have influenced the post-operative morbidity rate in the laparoscopic group as age [23], malnutrition [24] and centre volume [25] are recognized as independent risk factors of post-operative morbidity. Additionally, concomitant cholecystectomy or splenectomy, which were more frequently performed in the open group, could have also influenced differences observed in morbidity between groups. To limit this selection bias, an adjusted analysis using a matching on propensity score and volume of activity was performed. After adjustment, the two groups were comparable as reported in appendix 6.

The overall morbidity in the present study was in line with a previous French retrospective series (47-54%), [9] with similar 90-day mortality rates to previous French nationwide cohort studies (~7%) [25]. Our results are also consistent with a recent European observational study including 27 expert centers. [26, 27] Complication rate was 30% and mortality rate was 5%. [26] The morbidity reported in the present study was higher than that reported in previous studies (13-30%). [5, 7, 10, 26, 28, 29] All codes for complications including minor complications are recorded in the database in order to recover optimal funding for the hospitals. This may lead to an over-reporting of minor complications during the patient's hospital stay. Moreover, significantly higher rates of chemotherapy use (41%), malnutrition (42%) for open TG were observed in the present

study, when compared to previous reports. [6, 7, 10, 30] Most prospective studies only included PG without preoperative chemotherapy. [5, 8] The present study furthermore included both high- and low-volume centres, with some centres having little laparoscopic experience, all of which might have a detrimental impact on morbidity. [25, 31] At least, previous studies only reported 30-day morbidity, whereas the present study reported on 90-day morbidity. [5, 10, 30]

Adjusted analysis reported a benefit on morbidity and length of stay after laparoscopic PG. The results on morbidity and LOS were in line with several randomized trials on this topic. [5, 7, 30]. This may have been influenced by national guidelines stating that a laparoscopic approach should be preferentially used for early node negative gastric cancers. [32, 33] Adjusting for the volume of a centre could reduce disparity between groups, especially for mortality which has previously been demonstrated in oesophageal resections. [34] The present study again demonstrated that laparoscopic PG was safe and feasible.

The role of laparoscopic TG remains unclear. The higher surgical reintervention rate in the laparoscopic group was probably due to the increased prevalence of post-operative bleeding observed in this cohort (10.1%). Meticulous dissection and haemostasis is therefore a major issue for laparoscopic TG to reduce postoperative bleeding. [9] Oesophageal stricture was also more frequently reported after laparoscopic TG, as reported by others. [10] The performance of a laparoscopic circular anastomosis between the oesophagus and jejunum is difficult and can lead to a higher anastomotic leakage rate, which was not observed in the present study. The lack of data concerning the technique used for anastomosis in the present study limits our explanations for oesophageal stricture rate. Moreover, the lack of oncological data concerning tumour location and R-status of the oesophageal section could also bias the long-term oesophageal stricture analysis.

However, large randomized trials examining the anastomotic technique and its influence on long-term morbidity are warranted to truly improve our understanding.

The impact of centre volume on post-operative outcome is very important. As showed in the regression curves, morbi-mortality and length of stay were correlated to centre volume. In our database, the median number of procedures per centre per year was very low. The same results were observed in restorative proctocolectomy with ileal pouch anal anastomosis in France (mean: 1.65 procedure/year/center). [35] This could be explained by the low threshold in France to treat gastro-intestinal cancers (30 cancers per years). There are currently no national guidelines for a specific cut-off allowing gastric surgery for cancer. High volume centers are associated with better outcomes and with multidisciplinary team input which ultimately improves the quality of care. [36] El Amrani et al. showed that a cut-off of 16 gastrectomies per year was associated with a lower mortality. [25] This observation raises the need for centralization of gastric surgery for cancer in France to high-volume centers as already proposed by several authors. [37] In order to take into account this bias, the analysis integrates the volume per center and the sensitivity analysis used a perfect matching for center.

This database used for high-volume cohort studies is often criticized, since the mandatory input of data is collected for economical purposes and legal requirements, which may lead to over-reporting of complications. In return, the overstatement of complications is similarly reported, whatever the surgical approach used, and the strength of such studies relies on a “true-life” analysis of surgical practice and their large sample size. The lack of precise data concerning pathological reports, number of retrieved lymph nodes, tumour location, and TNM status might also bias the analysis, especially for quality of laparoscopic gastric resection. The analysis was therefore adjusted on

neoadjuvant chemotherapy and excluded patients with locally advanced or metastatic tumours. A possible imbalance between on preoperative chemotherapy response, type of lymphadenectomy could bias the analysis of morbidity after propensity score matching. Nevertheless, national guidelines actually advocate the open approach as the standard for advanced gastric cancer for total gastrectomy. [38] This recommendation could disfavour the Open group. This study was therefore only focused on surgical procedures and post-operative complications limiting risk of oncological interpretation.

Conclusion

On a national scale, including a series of over 10,000 gastrectomies, laparoscopic PG demonstrated a significant benefit on overall morbidity and length of stay. Laparoscopic TG should be performed with caution, in view of higher rates of surgical reintervention and oesophageal stricture. This is in line with national and international guidelines, emphasizing the need for randomized trials and results of long-term oncological outcomes.

Figures Legends

Figure 1. Long term outcomes for total gastrectomy and partial gastrectomy after matching.

A: risk of bowel obstruction after TG

B: risk of bowel obstruction after PG

C: risk of incisional hernia after TG

D: risk of incisional hernia after PG

E: risk of oesophageal stricture after TG

Figure 2. Regression curves of short-term outcomes by the activity per year of centre.

- A: Evolution of risk of death at 90 postoperative days
- B: Evolution of risk of overall morbidity at 90 postoperative days
- C: Evolution of risk of reintervention at 90 postoperative days
- D: Evolution of length of stay

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Table 1. Patient characteristics and 90-day post-operative outcomes (n=10,343).

Characteristics	Total gastrectomy n= 5,782			Partial gastrectomy n=4,561		
	Open (n=5,037)	Laparoscopy (n=745)	P	Open (n=3,897)	Laparoscopy (n=664)	P
Age	68 [58-76]	64 [54-74]	< 0.0001	75 [65-82]	73 [63-81]	0.0001
Female	1784 (35.4%)	283 (38.0%)	0.185	1652 (42.4%)	277 (41.7%)	0.777
Charlson score categorization	2 3-4 5-6 ≥7	2,885 (57.3%) 437 (58.7%) 215 (28.9%) 34 (4.6%) 59 (7.9%)	0.094	2,099 (53.9%) 1195 (30.7%) 267 (6.9%) 336 (8.6%)	376 (56.6%) 194 (29.2%) 38 (5.7%) 56 (8.4%)	0.513
Diabetes	626 (12.4%)	85 (11.4%)	0.465	557 (14.3%)	74 (11.1%)	0.035
Severe diabetes	149 (3.0%)	21 (2.8%)	0.925	148 (3.8%)	21 (3.2%)	0.490
Congestive heart failure	152 (3.0%)	18 (2.4%)	0.429	201 (5.2%)	34 (5.1%)	1.0
Myocardial infarction	229 (4.5%)	28 (3.8%)	0.380	229 (5.9%)	41 (6.2%)	0.832
Distal vascular disease	253 (5.0%)	22 (3.0%)	0.017	213 (5.5%)	34 (5.1%)	0.787
Cerebral vascular disease	250 (5.0%)	42 (5.6%)	0.487	244 (6.3%)	38 (5.7%)	0.656
Obesity	584 (11.6%)	97 (13.0%)	0.286	467 (12.0%)	78 (11.7%)	0.913
Malnutrition	2115 (42.0%)	282 (37.9%)	0.0358	1557 (40.0%)	212 (31.9%)	0.0001
Enteral nutrition prior surgery	209 (4.1%)	20 (2.7%)	0.0699	59 (1.5%)	4 (0.6%)	0.093
Laparoscopic exploration prior surgery	469 (9.3%)	87 (11.7%)	0.0478	157 (4.0%)	42 (6.3%)	0.010
Hospitalization for chemotherapy before surgery	0 1-3 4 5-8 ≥9	2,455 (48.7%) 855 (17.0%) 888 (17.6%) 757 (15.0%) 82 (1.6%)	0.0002	2,783 (71.4%) 402 (10.3%) 363 (9.3%) 314 (8.1%) 35 (0.9%)	460 (69.3%) 51 (7.7%) 82 (12.3%) 66 (9.9%) 5 (0.8%)	0.016
Cholecystectomy	1192 (23.7%)	124 (16.6%)	< 0.0001	647 (16.6%)	67 (10.1%)	< 0.0001
Splenectomy	243 (4.8%)	12 (1.6%)	< 0.0001	28 (0.7%)	2 (0.3%)	0.332
Volume of surgical centre	<3 3-5 6-12 13-18 19-24 >24	1,669 (33.1%) 1229 (24.4%) 1314 (26.1%) 563 (11.2%) 163 (3.2%) 99 (2.0%)	< 0.0001	1,745 (44.8%) 894 (22.9%) 818 (21.0%) 315 (8.1%) 65 (1.7%) 60 (1.5%)	225 (33.9%) 162 (24.4%) 186 (28.0%) 75 (11.3%) 6 (0.9%) 10 (1.5%)	< 0.0001
Teaching Centre	1671 (33.2%)	210 (28.2%)	0.0076	1019 (26.1%)	195 (29.4%)	0.092
Years of resection	2013 2014 2015 2016 2017 2018	942 (18.7%) 859 (17.1%) 851 (16.9%) 854 (17.0%) 771 (15.3%) 760 (15.1%)	< 0.0001	758 (19.5%) 719 (18.5%) 671 (17.2%) 613 (15.7%) 599 (15.4%) 537 (13.8%)	66 (9.9%) 87 (13.1%) 105 (15.8%) 116 (17.5%) 128 (19.3%) 162 (24.4%)	< 0.0001

Continuous variables are represented as median and interquartile range.

Table 2. Univariate analysis of short-term outcomes.

Outcomes	Total gastrectomy n= 5,782			Partial gastrectomy n=4,561		
	Open (n=5,037)	Laparoscopy (n=745)	P	Open (n=3,897)	Laparoscopy (n=664)	P
Death at 90 POD	379 (7.5%)	39 (5.2%)	0.030	273 (7.0%)	23 (3.5%)	0.0008
Global morbidity at 90 POD	2541 (50.4%)	367 (49.3%)	0.572	1568 (40.2%)	217 (32.7%)	0.0003
Leakage	1377 (27.3%)	212 (28.5%)	0.552	649 (16.7%)	92 (13.9%)	0.080
Bleeding	385 (7.6%)	75 (10.1%)	0.027	218 (5.6%)	48 (7.2%)	0.116
Thromboembolic disease	285 (5.7%)	33 (4.4%)	0.198	184 (4.7%)	27 (4.1%)	0.520
Pulmonary complication	1045 (20.7%)	171 (23.0%)	0.183	520 (13.3%)	65 (9.8%)	0.013
Renal insufficiency	469 (9.3%)	75 (10.1%)	0.553	281 (7.2%)	34 (5.1%)	0.060
Surgical reintervention	581 (11.5%)	108 (14.5%)	0.023	206 (5.3%)	50 (7.5%)	0.026
Length of stay	15 [12-23]	14 [10-21]	< 0.0001	15 [11-22]	11 [8-17]	<0.0001
Length of stay > 15 days	2784 (55.3%)	342 (45.9%)	< 0.0001	1942 (49.8%)	451 (67.9%)	<0.0001

POD: Post-operative days; continuous variables are represented as median and interquartile range.

Table 3. Adjusted analysis of peri-operative outcomes at 90 post-operative days for total and partial gastrectomy after matching on propensity score and volume activity

Outcomes	TG			PG		
	Open n=743	Laparoscopy n=743	p	Open n=662	Laparoscopy n=662	p
Death at 90 POD	38 (5.1%)	39 (5.2%)	1.00	30 (4.5%)	23 (3.5%)	0.40
Global morbidity at 90 POD	340 (45.8%)	365 (49.1%)	0.21	261 (39.4%)	216 (32.6%)	0.01
Surgical reintervention	80 (10.8%)	108 (14.5%)	0.04	33 (5.0%)	50 (7.6%)	0.07
Length of stay median [iqr]	15 [12, 22]	14 [10, 21]	<0.0001	14 [10, 21]	11 [8.0, 16.8]	<0.0001

POD: Post-operative days; ICU: intensive care unit; OR: Odd ratio; 95% CI: 95% confidence interval

Table 4. Sensitive analysis with matching on propensity score and centers

Outcomes	TG			PG		
	Open n=346	Laparoscopy n=346	p	Open n=301	Laparoscopy n=301	p
Death at 90 POD	27 (7.8%)	20 (5.8%)	0.36	19 (6.3%)	11 (3.7%)	0.19
Global morbidity at 90 POD	185 (53.5%)	170 (49.1%)	0.29	123 (40.9%)	99 (32.9%)	0.052
Surgical reintervention	39 (11.3%)	53 (15.3%)	0.15	21 (7.0%)	27 (9.0%)	0.45
Length of stay median [iqr]	15 [12, 22]	14 [11, 22]	0.04	14 [10, 21]	11 [8, 16]	<0.0001

POD: Post-operative days; continuous variables are represented as median and interquartile range.

Appendix 1. Inclusion criteria defined by ICD-10 and CCAM codes

Inclusion criteria	Gastric cancer	C16.0	Malignant neoplasm of cardia
		C16.1	Malignant neoplasm of fundus of stomach
		C16.2	Malignant neoplasm of body of stomach
		C16.3	Malignant neoplasm of pyloric antrum
		C16.4	Malignant neoplasm of pylorus
		C16.5	Malignant neoplasm of lesser curvature of stomach, unspecified
		C16.6	Malignant neoplasm of greater curvature of stomach, unspecified
		C16.8	Malignant neoplasm of overlapping sites of stomach
		C16.9	Malignant neoplasm of stomach, unspecified
	Type of gastrectomy	HFFA002	Subtotal gastrectomy, open approach
		HFFA006	Total gastrectomy, open approach
		HFFC002	Subtotal gastrectomy, laparoscopic approach
HFFC017		Total gastrectomy, laparoscopic approach	
Exclusion criteria	Associated resection the same day of gastric resection	HHFA008 HHFA009 HHFA026 HHFC296 HHFA023 HHFA018 HHFA002 HHFA010 HHFA006 HHFA017 HHFA014 HHFA021 HHFA024	Colic resection
		HLFA003 HLFA009 HLFA011 HLFA019 HLFA020 HLFC004 HLFC003 HLFC002 HLFC027 HLFA004 HLFA005 HLFA006 HLFA007 HLFA010 HLFA017 HLFA018 HLFC801 HLFC032 HLFC037	Hepatic resection
		HNFA007 HNFA001 HNFA002 HNFA010 HNFA004 HNFA005 HNFA006 HNFA008 HNFA011 HNFA013 HNFC002 HNFC028	Pancreatic resection
		HPBA001 HPFA003 HPFA004 HPFC001 HPFC002 HPFA001 HPFC007	Peritoneal resection
		HPLB003	Hipec
		Metastatic cancer	C77, C770, C771, C772, C773, C774, C775, C778, C779, C78, C780, C781, C782, C783, C784, C785, C786, C787, C788, C79, C790, C791, C792, C793, C794, C795, C796, C797, C798, C799, C80, C80+0, C800, C809

Appendix 2. Charlson comorbidity score calculation

Variable	Coef	ICD codes
Congestive heart failure	1	I110, I130, I132, I50, I500, I501, I509
Myocardial infarction	1	I21, I2,2 I252, I255
Peripheral vascular disease	1	I70, I700, I701, I702, I708, I709, I71, I710, I711, I712, I713, I714, I715, I716, I718, I719, I731, I738, I739, I771, I790, I792, K551, K558, K559, Z958, Z959
Cerebrovascular disease	1	G45, G450, G451, G452, G453, G454, G458, G459, G46, G460, G461, G462, G463, G464, G465, G466, G467, G468, H340, I60, I600, I601, I602, I603, I604, I605, I606, I607, I608, I609, I61, I610, I611, I612, I613, I614, I615, I616, I618, I619, I621, 620, I621, I629, I63, I630, I631, I632, I633, I634, I635, I636, I638, I639, I64, I65, I650, I651, I652, I653, I658, I659, I66, I660, I661, I662, I663, I664, I668, I669, I67, I670, I671, I672, I673, I674, I675, I676, I677, I678, I679, I68, I680, I681, I682, I688, I69, I690, I691, I692, I693, I694, I698
Dementia	1	F00, F000, F0000, F00000, F00001, F00002, F0001, F00010, F00011, F00012, F0002, F00020, F00021, F00022, F0003, F00030, F00031, F00032, F0004, F00040, F00041, F00042, F001, F0010, F00100, F00101, F00102, F0011, F00110, F00111, F00112, F0012, F00120, F00121, F00122, F0013, F00130, F00131, F00132, F0014, F00140, F00141, F00142, F002, F0020, F00200, F00201, F00202, F0021, F00210, F00211, F00212, F0022, F00220, F00221, F00222, F0023, F00230, F00231, F00232, F0024, F00240, F00241, F00242, F009, F0090, F00900, F00901, F00902, F0091, F00910, F00911, F00912, F0092, F00920, F00921, F00922, F0093, F00930, F00931, F00932, F0094, F00940, F00941, F00942, F01, F010, F0100, F01000, F01001, F01002, F0101, F01010, F01011, F01012, F0102, F01020, F01021, F01022, F0103, F01030, F01031, F01032, F0104, F01040, F01041, F01042, F011, F0110, F01100, F01101, F01102, F0111, F01110, F01111, F01112, F0112, F01120, F01121, F01122, F0113, F01130, F01131, F01132, F0114, F01140, F01141, F01142, F012, F0120, F01200, F01201, F01202, F0121, F01210, F01211, F01212, F0122, F01220, F01221, F01222, F0123, F01230, F01231, F01232, F0124, F01240, F01241, F01242, F013, F0130, F01300, F01301, F01302, F0131, F01310, F01311, F01312, F0132, F01320, F01321, F01322, F0133, F01330, F01331, F01332, F0134, F01340, F01341, F01342, F018, F0180, F01800, F01801, F01802, F0181, F01810, F01811, F01812, F0182, F01820, F01821, F01822, F0183, F01830, F01831, F01832, F0184, F01840, F01841, F01842, F019, F0190, F01900, F01901, F01902, F0191, F01910, F01911, F01912, F0192, F01920, F01921, F01922, F0193, F01930, F01931, F01932, F0194, F01940, F01941, F01942, F02, F020, F0200, F02000, F02001, F02002, F0201, F02010, F02011, F02012, F0202, F02020, F02021, F02022, F0203, F02030, F02031, F02032, F0204, F02040, F02041, F02042, F021, F0210, F02100, F02101, F02102, F0211, F02110, F02111, F02112, F0212, F02120, F02121, F02122, F0213, F02130, F02131, F02132, F0214, F02140, F02141, F02142, F022, F0220, F02200, F02201, F02202, F0221, F02210, F02211, F02212, F0222, F02220, F02221, F02222, F0223, F02230, F02231, F02232, F0224, F02240, F02241, F02242, F023, F0230, F02300, F02301, F02302, F0231, F02310, F02311, F02312, F0232, F02320, F02321, F02322, F0233, F02330, F02331, F02332, F0234, F02340, F02341, F02342, F024, F0240, F02400, F02401, F02402, F0241, F02410, F02411, F02412, F0242, F02420, F02421, F02422, F0243, F02430, F02431, F02432, F0244, F02440, F02441, F02442, F028, F0280, F02800, F02801, F02802, F0281, F02810, F02811, F02812, F0282, F02820, F02821, F02822, F0283, F02830, F02831, F02832, F0284, F02840, F02841, F02842, F03, F03+0, F03+00, F03+01, F03+02, F03+1, F03+10, F03+11, F03+12, F03+2, F03+20, F03+21, F03+22, F03+3, F03+30, F03+31, F03+32, F03+4,

		F03+40, F03+41, F03+42, F051, G30, G300, G301, G308, G309, G311
Chronic pulmonary disease	1	(I278, I279, J40, J41, J410, J411, J418, J42, J43, J430, J431, J432, J438, J439, J44, J440, J441, J448, J449, J45, J450, J451, J458, J459, J46, J47, J60, J61, J62, J620, J628, J63, J630, J631, J632, J633, J634, J635, J638, J64, J65, J66, J660, J661, J662, J668, J67, J670, J671, J672, J673, J674, J675, J676, J677, J678, J679, J684, J701, J703
Connective tissue disease	1	M05, M050, M0500, M0501, M0502, M0503, M0504, M0505, M0506, M0507, M0508, M0509, M051, M0510, M0511, M0512, M0513, M0514, M0515, M0516, M0517, M0518, M0519, M052, M0520, M0521, M0522, M0523, M0524, M0525, M0526, M0527, M0528, M0529, M053, M0530, M0531, M0532, M0533, M0534, M0535, M0536, M0537, M0538, M0539, M058, M0580, M0581, M0582, M0583, M0584, M0585, M0586, M0587, M0588, M0589, M059, M0590, M0591, M0592, M0593, M0594, M0595, M0596, M0597, M0598, M0599, M06, M060, M0600, M0601, M0602, M0603, M0604, M0605, M0606, M0607, M0608, M0609, M061, M0610, M0611, M0612, M0613, M0614, M0615, M0616, M0617, M0618, M0619, M062, M0620, M0621, M0622, M0623, M0624, M0625, M0626, M0627, M0628, M0629, M063, M0630, M0631, M0632, M0633, M0634, M0635, M0636, M0637, M0638, M0639, M064, M0640, M0641, M0642, M0643, M0644, M0645, M0646, M0647, M0648, M0649, M068, M0680, M0681, M0682, M0683, M0684, M0685, M0686, M0687, M0688, M0689, M069, M0690, M0691, M0692, M0693, M0694, M0695, M0696, M0697, M0698, M0699, M315, M32, M320, M321, M328, M329, M33, M330, M331, M332, M339, M34, M340, M341, M342, M348, M349, M351, M353, M360
Ulcer disease	1	K25, K250, K251, K252, K253, K254, K255, K256, K257, K259, K26, K260, K261, K262, K263, K264, K265, K266, K267, K269, K27, K270, K271, K272, K273, K274, K275, K276, K277, K279, K28, K280, K281, K282, K283, K284, K285, K286, K287, K289
Mild liver disease	1	B18, B180, B181, B182, B188, B189, K70, K700, K701, K702, K703, K704, K709, K713, K714, K715, K717, K73, K730, K731, K732, K738, K739, K74, K740, K741, K742, K743, K744, K745, K746, K760, K762, K763, K764, K768, K769, Z944
Diabetes	1	E100, E101, E106, E108, E109, E110, E111, E116, E118, E119, E120, E121, E126, E128, E129, E130, E131, E136, E138, E139, E140, E141, E146, E148, E149
Hemiplegia	2	G041, G114, G801, G802, G81, G810, G8100, G8101, G8108, G811, G819, G82, G820, G821, G822, G823, G824, G825, G830, G831, G832, G833, G834, G839
Moderate or severe renal disease	2	I120, I131, N032, N033, N0330, N0339, N034, N035, N036, N037, N052, N053, N054, N055, N056, N057, N18, N180, N181, N182, N183, N184, N185, N188, N189, N19, N250, Z490, Z491, Z492, Z940, Z992, Z992+0, Z992+1, Z992+8
Diabetes with end organ damage	2	E102, E103, E104, E105, E107, E112, E1120, E1128, E113, E1130, E1138, E114, E1140, E1148, E115, E117, E122, E123, E124, E125, E127, E132, E133, E134, E135, E137, E142, E143, E144, E145, E147
Cancer	2	C00, C000, C001, C002, C003, C004, C005, C006, C008, C009, C01, C02, C020, C021, C022, C023, C024, C028, C029, C03, C030, C031, C039, C04, C040, C041, C048, C049, C05, C050, C051, C052, C058, C059, C06, C060, C061, C062, C068, C069, C07, C08, C080, C081, C088, C089, C09, C090, C091, C098, C099, C10, C100, C101, C102, C103, C104, C108, C109, C11, C110, C111, C112, C113, C118, C119, C12, C13, C130, C131, C132, C138, C139, C14, C140, C142, C148, C15, C150, C151, C152, C153, C154, C155, C158, C159, C16, C160, C161, C162, C163, C164, C165, C166, C168, C169, C169+0, C169+8, C17, C170, C171, C172, C173, C178, C179, C18, C180, C181, C182, C183, C184, C185, C186, C187, C188, C189, C189+0, C189+8, C19, C20, C21, C210, C211, C212, C218, C22, C220, C221, C222, C223, C224, C227, C229, C23, C24, C240, C241, C248, C249, C25, C250, C251, C252, C253, C254, C254+0, C254+8, C257, C258, C259, C259+0, C259+8, C26, C260, C261, C268, C269, C30, C300, C301, C31, C310, C311, C312, C313, C318, C319, C32, C320, C321, C322, C323, C328, C329, C33, C34, C340, C341, C342, C343, C348, C349, C37, C38, C380, C381, C382, C383, C384, C388, C39, C390, C398, C399, C40, C400, C401, C402, C403, C408, C409,

		C41, C410, C411, C412, C413, C414, C418, C419, C43, C430, C431, C432, C433, C434, C435, C436, C437, C438, C439, C45, C450, C451, C452, C457, C459, C46, C460, C461, C462, C463, C467, C4670, C4671, C4672, C4678, C468, C469, C47, C470, C471, C472, C473, C474, C475, C476, C478, C479, C48, C480, C481, C482, C488, C49, C490, C491, C492, C493, C4930, C4938, C494, C4940, C4948, C495, C4950, C4958, C496, C498, C499, C50, C500, C501, C502, C503, C504, C505, C506, C508, C509, C51, C510, C511, C512, C518, C519, C52, C53, C530, C531, C538, C539, C54, C540, C541, C542, C543, C548, C549, C55, C56, C57, C570, C571, C572, C573, C574, C577, C578, C579, C58, C60, C600, C601, C602, C608, C609, C61, C62, C620, C621, C629, C63, C630, C631, C632, C637, C638, C639, C64, C65, C66, C67, C670, C671, C672, C673, C674, C675, C676, C677, C678, C679, C68, C680, C681, C688, C689, C69, C690, C691, C692, C693, C694, C695, C696, C698, C699, C70, C700, C701, C709, C71, C710, C711, C712, C713, C714, C715, C716, C717, C718, C719, C72, C720, C721, C722, C723, C724, C725, C728, C729, C73, C74, C740, C741, C749, C75, C750, C751, C752, C753, C754, C755, C758, C759, C76, C760, C761, C762, C763, C764, C765, C767, C768, C81, C810, C811, C812, C813, C814, C817, C819, C82, C820, C821, C822, C823, C824, C825, C826, C827, C829, C83, C830, C831, C832, C833, C834, C835, C836, C837, C838, C839, C84, C840, C841, C842, C843, C844, C845, C846, C847, C848, C849, C85, C850, C851, C852, C857, C859, C88, C880, C881, C882, C883, C884, C887, C889, C90, C900, C901, C902, C903, C91, C910, C911, C912, C913, C914, C915, C916, C917, C918, C919, C92, C920, C921, C922, C923, C924, C925, C926, C927, C928, C929, C93, C930, C931, C932, C933, C937, C939, C94, C940, C941, C942, C943, C944, C945, C946, C947, C95, C950, C951, C952, C957, C959, C96, C960, C961, C962, C963, C964, C965, C966, C967, C968, C969, C97
Moderate or severe liver disease	3	I850, I859, I864, I982, K704, K711, K721, K729, K765, K766, K767
Metastatic cancer	6	C77, C770, C771, C772, C773, C774, C775, C778, C779, C78, C780, C781, C782, C783, C784, C785, C786, C787, C788, C79, C790, C791, C792, C793, C794, C795, C796, C797, C798, C799, C80, C80+0, C800, C809
AIDS	6	B20, B200, B201, B202, B203, B204, B205, B206, B207, B208, B209, B21, B210, B211, B212, B213, B217, B218, B21, B22, B220, B221, B222, B227, B24, B24+0, B24+1, B24+9, Z21

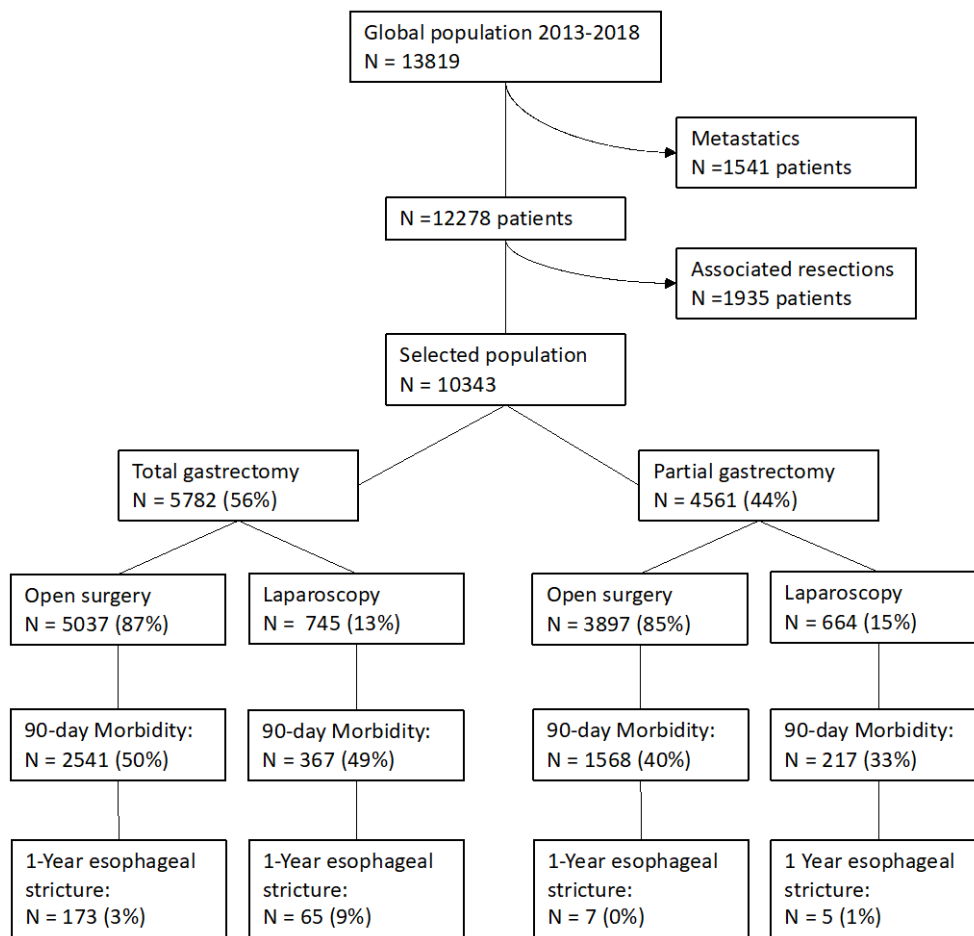
Appendix 3. Definition of complications as per ICD classification

Short term outcomes	Leakage or deep abscess	K223	Perforation of oesophagus
		K281	Gastrojejunal ulcer: acute with perforation
		K282	Gastrojejunal ulcer: acute with both haemorrhage and perforation
		K316	Fistula of stomach and duodenum
		K631	Perforation of intestine (nontraumatic)
		K632	Fistula of intestine
		K65	Peritonitis
		K823	Fistula of gallbladder
		K833	Fistula of bile duct
		K630	Abscess of intestine
		K750	Abscess of liver
		T814	Infection following a procedure, not elsewhere classified
	Bleeding	K280	Gastrojejunal ulcer acute with haemorrhage
		K661	Haemoperitoneum
		R58	Haemorrhage, not elsewhere classified
		T810	Haemorrhage and haematoma complicating a procedure, not elsewhere classified
	Thrombo-embolic diseases	I26	Pulmonary embolism
		I80	Phlebitis and thrombophlebitis
		I81	Portal vein thrombosis
	Respiratory complications	J80	Adult respiratory distress syndrome
		J952	Acute pulmonary insufficiency following nonthoracic surgery
		J960	Acute respiratory failure
		J969	Respiratory failure, unspecified
		J981	Pulmonary collapse
		J12	Viral pneumonia, not elsewhere classified
		J13	Pneumonia due to <i>Streptococcus pneumoniae</i>
		J14	Pneumonia due to <i>Haemophilus influenzae</i>
		J15	Bacterial pneumonia, not elsewhere classified
		J16	Pneumonia due to other infectious organisms, not elsewhere classified
		J17	Pneumonia in diseases classified elsewhere
		J18	Pneumonia, organism unspecified
		J69	Pneumonitis due to solids and liquids
		J690	Pneumonitis due to food and vomit
		J85	Abscess of lung and mediastinum
		J850	Gangrene and necrosis of lung
		J851	Abscess of lung with pneumonia
		J852	Abscess of lung without pneumonia
		J853	Abscess of mediastinum
		J86	Pyothorax
	J860	Pyothorax with fistula	
	J869	Pyothorax without fistula	
	J954	Mendelson syndrome	
Renal failure	N17	Acute renal failure	
	N170	Acute renal failure with tubular necrosis	
	N171	Acute renal failure with acute cortical necrosis	
	N172	Acute renal failure with medullary necrosis	
	N178	Other acute renal failure	
	N179	Acute renal failure, unspecified	
	N19	Unspecified kidney failure	
	N990	Postprocedural renal failure	
R34	Anuria and oliguria		
Long term outcomes	Post operative wound hernia	K43	Incisional hernia
	Esophageal stricture	K222	Esophageal obstruction
	Occlusion	K565	Intestinal adhesions [bands] with obstruction

Appendix 4. Definition of complications from CCAM classification

Outcomes	CCAM codes
Surgical reintervention	ZCQA001 ZCQC002 QZJA011 ZCJA004 ZCJA002 ZCJA005 ZCJC001 GGJA002 GGJA001 GGJC001 GGJC002 HGCC026 HGCA008 HGLA001 HGCA004 HGCA001 HGCA005 HGCC003 HFCA004 HMFA007 HMFC004 HMFC003 HMFA005 HFFA008 HGFA003 HGFA004 HGCA007 HGCC003 HFCC001 HFCA003 HGFA005

Appendix 5. Flowchart of the study.

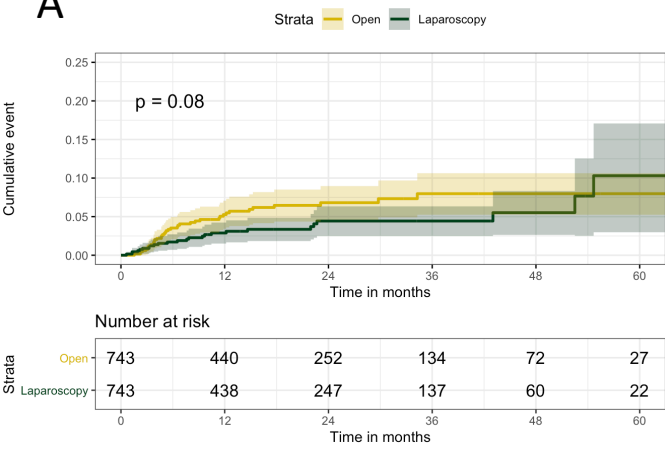


Appendix 6. Characteristics for population after matching stratified on type of gastrectomy

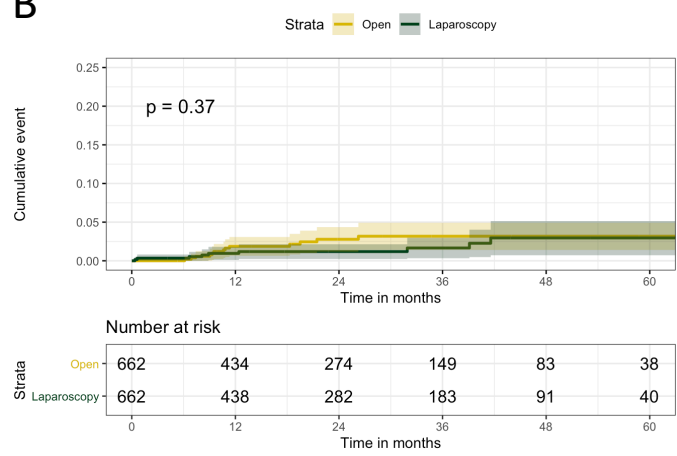
Characteristics	Level	TG			PG		
		Open (n=743)	Laparoscopy (n=743)	P	Open (n=662)	Laparoscopy (n=662)	P
Age (mean±sd)		62.4 ± 14	62.7 ± 14.4	0.61	70.4 ± 13	70.8 ± 13	0.51
Female		33.5 (n=249)	38.0 (n=282)	0.08	44.9 (n=297)	41.7 (n=276)	0.27
Charlson score	2	61.5 (n=457)	58.8 (n=437)	0.51	55.7 (n=369)	56.5 (n=374)	0.80
	3-4	28.1 (n=209)	28.7 (n=213)		29.9 (n=198)	29.3 (n=194)	
	5-6	3.4 (n=25)	4.6 (n=34)		6.8 (n=45)	5.7 (n=38)	
	>6	7.0 (n=52)	7.9 (n=59)		7.6 (n=50)	8.5 (n=56)	
Obesity		11.8 (n=88)	13.1 (n=97)	0.53	14.8 (n=98)	11.6 (n=77)	0.10
Denutrition		38.0 (n=282)	37.8 (n=281)	1	32.0 (n=212)	31.9 (n=211)	1
Years	2013-2015	33.4 (n=248)	31.8 (n=236)	0.54	38.5 (n=255)	39.0 (n=258)	0.91
	2016-2018	66.6 (n=495)	68.2 (n=507)		61.5 (n=407)	61.0 (n=404)	
Cholecystectomy		14.8 (n=110)	16.6 (n=123)	0.39	11.5 (n=76)	10.1 (n=67)	0.48
Preoperative laparoscopic exploration		12.7 (n=94)	11.7 (n=87)	0.63	6.8 (n=45)	6.3 (n=42)	0.82
Preoperative chemotherapy		56.9 (n=423)	57.6 (n=428)	0.83	27.6 (n=183)	31.7 (n=210)	0.12
Propensity score (mean ± sd)		0.2 ± 0.1	0.2 ± 0.1	0.86	0.2 ± 0.1	0.2 ± 0.1	0.98
Volume of surgical center	<3	25.7 (n=191)	25.7 (n=191)	1.00	34.0 (n=225)	34.0 (n=225)	1.00
	3-5	25.4 (n=189)	25.4 (n=189)		24.5 (n=162)	24.5 (n=162)	
	6-12	30.7 (n=228)	30.7 (n=228)		27.8 (n=184)	27.8 (n=184)	
	13-18	17.1 (n=127)	17.1 (n=127)		12.2 (n=81)	12.2 (n=81)	
	19-24	1.1 (n=8)	1.1 (n=8)		1.5 (n=10)	1.5 (n=10)	

A

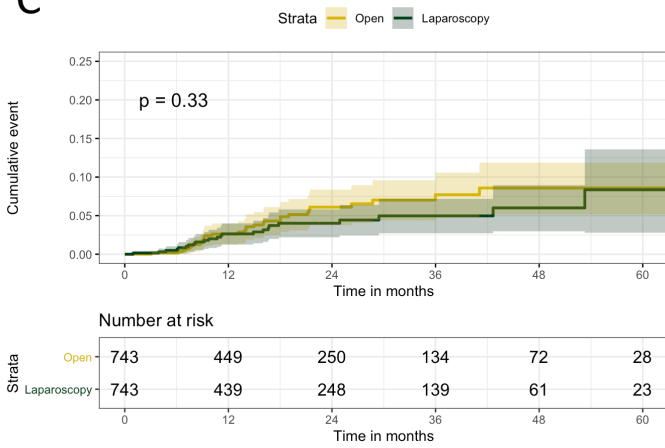
Risk of bowel obstruction after TG

**B**

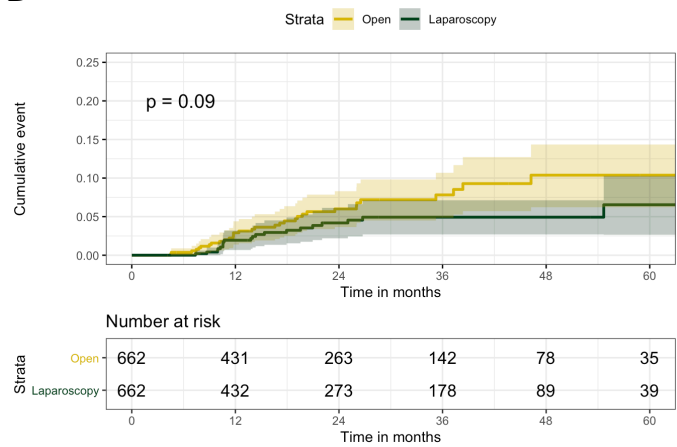
Risk of bowel obstruction after PG

**C**

Risk of incisional hernia after TG

**D**

Risk of incisional hernia after PG

**E**

Risk of esophageal stricture after TG

