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Perioperative outcomes in open versus minimally invasive gastrectomy for gastric cancer: a European multicenter study based on the GASTRODATA registry

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Abstract

Objective: To evaluate morbidity and mortality after minimally invasive (MIG) versus open gastrectomy (OG) for gastric cancer (GC) in a large European population, with a subgroup analysis comparing total and subtotal gastrectomy.

Summary Background Data: Real-world European studies comparing postoperative outcomes between MIG and OG are lacking.

Methods: This retrospective study included GC patients undergoing curative-intent gastrectomy between 2017 and 2021 at 24 high-volume European centers participating in the GASTRODATA registry. The primary outcome was the perioperative complication rate after MIG versus OG. Propensity score matching (PSM) was performed to adjust for potential confounders.

Results: Of 2430 patients, 1,800 (74%) underwent OG and 630 (26%) MIG. MIG was performed in patients with smaller tumors, earlier stages, and less frequently receiv~~ed~~ing neoadjuvant treatment (*P*<0.001). MIG was associated with higher R0 resection rate (96.5% vs 92.4% in OG), shorter hospital stay, lower perioperative complication rate (23.0% vs. 31.6%, *p*<0.001), and reduced 30-day and 90-day mortality rates (1.6% vs. 3.3%, [*p*=0.026] and 1.9% vs. 4.7%, [*p*=0.001], respectively). In sub-group analysis, MIG had fewer perioperative complications in subtotal (17.9% vs. 25.3%, *p*=0.005), but not total gastrectomy (31.5% vs. 36.1%, *p*=0.201). After PSM, MIG remaind significantly associated with lower perioperative complication rates compared to OG only in subtotal (OR=0.49, 95% CI, 0.30-0.80; *p*=0.005), but not in total gastrectomy (OR=1.15, 95% CI, 0.62-2.17; *p*=0.645).

Conclusions: Minimally invasive subtotal gastrectomy was associated with fewer perioperative complications than OG, while this association was not observed for total gastrectomy. Minimally invasive subtotal gastrectomy should be considered a viable option in specialized European centers.

INTRODUCTION

According to the guidelines provided by the European Society for Medical Oncology (ESMO), curative treatment for advanced gastric cancer consists of perioperative chemotherapy and a radical gastrectomy with D2 lymphadenectomy [1]. Although laparoscopy is often used in lower gastrointestinal tract surgery, its application in gastric cancer was relatively infrequent for a relatively long time. In recent years, laparoscopic gastric cancer surgery has been adopted globally, supported by trials showing outcomes comparable to open gastrectomy across cancer stages, gastrectomy types, and treatment settings.[2-14]

Randomized controlled trials (RCTs) from the East showed that laparoscopic gastrectomy is feasible and safe with similar oncological outcomes to open surgery in an Asian population.[4-9] European randomized controlled trials (the LOGICA and STOMACH trials) likewise demonstrated similar results with regard to feasibility and safety in the West.[13, 14]

However, in clinical trials, upon which guidelines are based, patients are carefully selected, and strict inclusion criteria are applied in a controlled research context. The results of minimally invasive versus open gastrectomy trials may not reflect everyday clinical practice, therefore trial results must be externally validated by extensive non-randomized cohort studies without strict selection criteria, which reproduce real-world practice.

Recently, the external validity of the LOGICA trial has been demonstrated in the Dutch setting by comparing the results of this RCT with data from laparoscopic gastrectomy performed in clinical practice at dedicated centers in the Netherlands included in the Dutch Upper Gastrointestinal Cancer Audit (DUCA) registry. Indeed, the outcomes of laparoscopic gastrectomy reported in DUCA demonstrated a progressive improvement during the course of the LOGICA trial, performing better than the open technique in the period following the completion of the randomized trial. It is important to note that the robust surgical quality assurance program of the LOGICA trial has probably been fundamental in facilitating the national dissemination of the technique. However, the Dutch experience does not necessarily reflect the reality of other European countries for which similar data are lacking.[15] Furthermore, nationwide Japanese data have fuelled concerns about increased anastomotic complication rates in minimally invasive total gastrectomy.[16, 17]

In 2015, an international consensus on gastric cancer complications was proposed by Baiocchi et al., and a list of 27 complications was accurately defined by 34 European experts.[18] Accordingly, the International Gastrectomy Complications Database (GASTRODATA) was launched using a secure online platform. The Gastrectomy Complications Consensus Group (GCCG), consisting of high-volume European referral centers for gastric cancer, records clinical, oncological, and surgical data and postoperative outcome measures at hospital discharge, and 30- and 90-day postoperatively in the GASTRODATA registry.

The GASTRODATA registry is representative of European clinical practice in dedicated centers. Its purpose is to overcome the issues of patient selection in clinical trials and to generate generalizable data after gastrectomy in the West. This study aimed to compare the short-term perioperative outcomes of minimally invasive gastrectomy (MIG) with those of open gastrectomy (OG) in a large cohort of patients with gastric cancer from Western centers.

METHODS

This European cohort study was conducted using data from the GASTRODATA web-based registry platform (www.gastrodata.org), which enable the principal investigators from each participating center to enter patient data using personal login credentials. Perioperative complications are reported in a standardized way through web-based data retrieval forms and registered in accordance with the definitions of the GCCG.[18] All data are maintained using secure coding methods and are kept anonymous to comply with international data privacy agreements, and each center has access exclusively to its own patient data. The senior advisors of the GASTRODATA working group approved this study, and twenty-four participating centres agreed to use their data for this purpose. All centers are specialized in gastric cancer surgery, performing a minimum of 20 gastrectomies annually. Each center had previously signed an agreement ensuring adherence to institutional and national ethics guidelines as well as institutional review board (IRB) requirements.

Study population

Patients with primary resectable gastric adenocarcinoma clinically staged as T1-4a/x, any N who had undergone a gastrectomy between 2017 and 2021 were selected from the GASTRODATA registry. Patients who did not undergo resection because of metastatic disease or non-resectable tumors detected at the onset of gastrectomy are not included in the GASTRODATA registry. Patients with macroscopic non-radical resections (R2) and those in whom no lymphadenectomy was performed (D0) were excluded.

Study outcomes

The primary outcome was the rate of perioperative complications according to the definitions of the GCCG, consisting of 27 perioperative complications (including 3 intraoperative, 14 postoperative general, and 10 postoperative surgical complications) wich are reported until patient discharge.[18] Postoperative complications (POC) were graded according to the Clavien–Dindo classification.[19, 20] Secondary outcomes included the number of resected lymph nodes, radicality (R0 rate), length of hospital stay, rate of re-intervention, and rate of 30- and 90-day mortality.

Statistical analysis

Baseline characteristics were analyzed using descriptive statistics. Results were presented as mean (standard deviation [SD]) for normally distributed variables, median (interquartile range [IQR]) for non-normally distributed variables, and counts (percentage) for categorical variables. A preliminary unmatched multivariable analysis was performed on the whole sample using logistic regression models, in which the presence or absence of complications was the response variable and the type of surgical approach (open vs. minimally invasive surgery) the main determinant. The model was adjusted for sex, age (<65 vs. 65-75 vs. >75 years), ASA score (1-2 vs. 3-4), pT-stage (T0-T1 vs. T2-T4), pN-stage (N0-1 vs. N2-3), and type of gastrectomy (total vs. subtotal).

Propensity score matching was performed to correct for known potential confounders. Only patients from centers performing both OG and MIG were included in the propensitity score matched analyses. A propensity score was estimated for each patient using a logit model where surgical approach (OG or MIG) was the outcome and age, sex, American Society of Anesthesiologists classification (ASA score), cT-stage, cN-stage, treatment with neoadjuvant chemotherapy, and type of resection (total or subtotal gastrectomy) were the explanatory variables. To prevent poor matches, a caliper of 0.2 multiplied by the standard deviation of the logit of the propensity score was used. After assessing the strength of the common support, the nearest neighbor's 1:1 method for matching was used to create two paired groups. Subsequently to matching, the balance adequacy was assessed by the standardized mean difference (SMD), and differences >10% were considered to represent inadequate balance. The differences in outcomes between the two groups before and after matching were evaluated using Fisher’s exact or chi-square tests for nominal variables, chi-square test for trend for ordinal variables, and the Wilcoxon rank-sum test for not normally distributed continuous variables.

The main multivariable analysis to address the relation between surgical approach (OG vs MIG) and complications was accomplished on matched patients only through a conditional logistic regression model, adjusting for sex, age, ASA, pT-stage, and pN-stage. In addition, given that the complication patterns are reported to differ between subtotal and total gastrectomy, a subgroup analysis was performed by separately applying the conditional regression model on patients who underwent either subtotal or total gastrectomy.

Missing data were not imputed, and cases with a missing value on a specific variable were dropped from the analysis when calculating P-values. A two-sided $P<0.05$ was considered statistically significant for all analyses, and data were analyzed using STATA statistical software, release 18 (StataCorp, College Station, TX, USA).

RESULTS

Analysis of the unmatched series

The GASTRODATA registry included 2558 patients with primary resectable gastric cancer who underwent gastrectomy from February 2017 to August 2021. After excluding 82 cases who underwent D0 lymphadenectomy, 42 cases with non-radical - R2 resection, and 4 cases with missing data about the type of surgical approach (OG vs MIG), a total of 2430 patients were considered in the unmatched analysis of the overall series reflecting real-world practice in specialized European centres (Figure 1). In the whole group, patients were mainly male (61%) and median age was 69 years (IQR 60-77). Baseline characteristics were evaluated based on the type of surgical approach: 1800 (74%) patients underwent OG and 630 (26%) patients underwent MIG. Notably, the use of MIG was limited in the early years of the study, accounting for only 19.7% of procedures in 2017 and 17.8% in 2018, but steadily increased over time, reaching 51.7% by 2021.

The proportion of females was higher in the MIG group compared to the OG group (43.5% vs. 37.5%, p=0.009), while age did not differ between surgical approaches (p=0.554, Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/SLA/F550). Median ASA score did not differ between the two approaches (Wilcoxon-Mann-Whitney rank-sum test: P=0.315), nevertheless the OG group included a larger proportion of both I and IV ASA classes than MIG (Fisher's exact test: p=0.004). The two groups did not differ in terms of the prevalence of underweight, overweight, or obesity; weight loss >10% after tumor diagnosis; comorbidities (diabetes, peripheral vascular disease); or the Charlson Comorbidity Index. The MIG group comprised patients with smaller tumors dimensions ($p<0.001$) and earlier clinical ($p<0.001$) and pathological ($p<0.001$) stages compared to patients in the OG group. With regard to preoperative treatment, neoadjuvant chemotherapy was administered to 48.4% of patients in the OG group, compared to 35.7% of patients in the MIG group ($p<0.001$). The pattern of lymphadenectomy differed between the two surgical approaches: D2 was the preferred lymphadenectomy in both groups, being used in nearly all MIG patients (86.5%) and more than half of OG patients (63.9%). However, the latter group presented a non negligible and larger proportion of limited (D1/D1+) and extended (D2+) procedures. As a consequence, differences in lymphadenectomy were significant when using the Fisher's exact test ($p<0.001$) but not when considering the increasing extension (chi-square for trend: p=0.148), suggesting that lymphadenectomy was more standardized in MIG than OG group. The median number of retrieved lymph nodes was significantly higher in the OG group compared to the MIG group (32 [IQR 22–44] vs. 31 [IQR 21–41], p=0.030).

More than 90% of the resections achieved R0 status; however, the rate of R1 resections was significantly higher in the OG group compared to the MIG group (7.6% vs. 3.5%, $p<0.001$). Compliance with ERAS protocols was greater following MIG compared to OG (47.2% vs. 58.6%, $p<0.001$).

The overall incidence of perioperative complications was significantly higher following OG compared to MIG (31.6% vs. 23.0%, $p<0.001$; Table 1). This difference was primarily driven by higher rates of postoperative surgery related complications in the OG group, including bowel perforations or necrosis (1.0% vs. 0.2%, $p=0.036$), pancreatic fistula (2.7% vs. 1.1%, $p=0.020$), and abnormal postoperative fluid collections (5.4% vs. 1.7%, $p<0.001$). Respiratory failure was less common in the MIG group compared to the OG group (1.0% vs. 2.2%, $p=0.052$), though not statistically significant. No significant differences were observed in intraoperative or non-surgical postoperative complications between the groups. While anastomotic leakage rates were comparable between OG and MIG ($p=0.690$), anastomotic leakage tended to occur later in the OG group (median postoperative day 6.5 [IQR 4–9] vs. day 4 [IQR 3–7], $p=0.035$; Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/SLA/F550).

The median length of hospital stay was significantly longer in the OG group than in the MIG group (9 days [IQR 7–14] vs. 8 days [IQR 6–11], $p<0.001$). Additionally, 30-day and 90-day mortality rates were both significantly higher following OG compared to MIG (30-day: 3.3% vs. 1.6%, $p= 0.026$; 90-day: 4.7% vs. 1.9%, $p=0.002$; Table 1).

The favorable clinical outcomes observed after MIG compared to OG in the univariable analysis were confirmed in the unmatched multivariable analysis of the entire cohort. After adjusting for sex, age, ASA score, (y)pT-stage, (y)pN-stage, and type of gastrectomy (total or subtotal), MIG was associated with a significantly lower risk of perioperative complications compared to OG (OR = 0.77, 95% CI 0.62–0.96, $p=0.023$; Table 2).

Analysis of the matched series

After applying propensity score matching with a caliper of 0.2 standard deviations,-1196 patients were matched (598 in each group). This matching achieved good balance between the two groups, with all standardized mean differences below 10% (Supplementary Figure 1, Supplemental Digital Content 1, http://links.lww.com/SLA/F550).

After matching, the clinical and demographic characteristics between the OG and MIG groups were largely comparable (Supplementary Table 3, Supplemental Digital Content 1, http://links.lww.com/SLA/F550). None of the variables included in the Propensity Score Matching remained statistically significant after matching (gender, age, ASA, cT, cN, neoadjuvant chemotherapy, type of gastrectomy). After matching, OG was more frequently performed in cT2 and cT4 cases, whereas MIG was more often chosen for cT3 tumors. Consequently, the difference between surgical approaches was statistically significant when assessed without considering the ordinal nature of cT-stage (chi-square test: $p<0.001$), but not when using a test for trend that accounts for severity ranking (p=0.319). Regarding lymphadenectomy, D2 was the preferred approach in both groups, performed in nearly all MIG patients (86.5%) and in over half of OG patients (61.5%). However, the OG group included a notable proportion of both more limited (D1/D1+) and more extended (D2+) dissections. As a result, differences in lymphadenectomy were statistically significant when assessed using Fisher's exact test ($p<0.001$), but not when evaluated as an ordered categorical variable using a test for trend ($p=0.287$).

Despite propensity score matching, patients in the OG group still had, on average, more advanced disease (pT, pM) and lower compliance with ERAS protocols during recovery. Regarding comorbidities, the prevalence of peripheral vascular disease was slightly higher in the OG group, although the overall Charlson Comorbidity Index did not differ significantly between the groups ($p=0.264$).

The OG group had a higher median number of retrieved positive lymph nodes (8 [IQR 5–14.5]) compared to the MIG group (7 [IQR 4–14], *p*=0.001). Of note, the median numbers of positive nodes differed by one lymphe node.

Overall perioperative complications remained more frequent in the OG group (27.3%) compared to the MIG group (22.7%) after matching, although the difference did not achieved statistical significance (*p*=0.071; Table 3). Two specific complications were significantly more common in the OG group: respiratory failure (3.0% vs. 1.0%, *p*= 0.021), and abnormal postoperative fluid drainage (4.5% vs. 1.8%, *p*=0.012). Multivariable analysis of the matched cohort showed lower risk of postoperative complications in the MIG group compared to the OG group (OR = 0.77, 95% CI 0.57- 1.03), which however did not achieve statistical significance (*p*=0.083; Table 2).

In the 17 centers performing both MIG and OG, the cumulative incidence of complications varied significantly across institutions for both surgical approaches—ranging from 9.5% to 52.6% for OG (median 34%, *p*<0.001) and from 5.6% to 75.0% for MIG (median 26.1%, *p*=0.005).

In the matched cohort, the median length of hospital stay remained significantly longer by one day in the OG group (9 days [IQR 7–13] vs. 8 days [IQR 6–11], *p*<0.001). Significant differences were observed in 30-day mortality (3.7% OG vs. 1.5% MIG, *p*=0.027) or 90-day mortality rates (4.4% OG vs. 1.8% MIG, *p*=0.018) after matching.

Subgroup analysis: Total and Subtotal Gastrectomy

The association between perioperative complication rates and surgical approach (OG vs. MIG) was analyzed separately for patients who underwent total and subtotal gastrectomy. Of the 2430 patients for which the type of resection was known, 1268 patients (52.2%) underwent total gastrectomy and 1156 patients (47.6%) underwent subtotal gastrectomy, while the type of gastrectomy was unknown in 6 patients (0.2%) who were excluded from the subgroup analysis (Table 4).

MIG was more frequently used for subtotal gastrectomy (62.2%), while OG was more commonly performed for total gastrectomy (57.2%; Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/SLA/F550). The incidence of perioperative complications was significantly lower in the MIG group compared to the OG group after subtotal gastrectomy (17.9% vs. 25.3%, *p*=0.005; Table 4). However, for total gastrectomy, no statistically significant difference was observed in perioperative complication rates between MIG and OG (31.5% vs. 36.1%, *p*=0.201).When considering the 27 GCCG-defined complications separately, the incidence of postoperative abdominal collections was significantly lower after MIG compared to OG for total gastrectomy (1.3% vs 6.2%, *p*=0.001), while for subtotal gastrectomy the difference was only borderline significant (2.0% vs 4.3%, p=0.063; Table 4). Respiratory failure was significantly less common in the MIG group compared to the OG group after subtotal gastrectomy (0.3% vs. 1.7%, *p*=0.043). However, myocardial infarction occurred more frequently in the MIG group compared to the OG group after total gastrectomy (1.7% vs. 0.2%, *p*=0.013).

In the multivariable analysis, MIG was associated with a significantly lower incidence of overall perioperative complications compared to OG in the subtotal gastrectomy group, both before (OR 0.64, 95% CI 0.47–0.89, *p*=0.007) and after propensity score matching (OR 0.49, 95% CI 0.30–0.80, *p*=0.005; Table 2). In contrast, no significant association was observed in overall perioperative complications for total gastrectomy between MIG and OG, either before (OR 0.89, 95% CI 0.65–1.23, *p*=0.486) or after matching (OR 1.15, 95% CI 0.62–2.17, *p*=0.645) (Table 2).

DISCUSSION

This retrospective multicenter study assessed the short-term perioperative outcomes for minimally invasive gastrectomy versus open gastrectomy for gastric cancer across 24 high-volume centers in Europe, reflecting real-world practice. Our results indicate that MIG is associated with a significantly lower rate of overall perioperative complications compared to OG, but only after subtotal gastrectomy. The MIG approach was more frequently adopted for patients with earlier-stage gastric cancer, those planned for subtotal gastrectomy, and those who had not received preoperative chemotherapy. These findings likely highlight the cautious approach to adopting MIG in complex gastrectomy cases.

In comparing the two approaches, MIG was associated with reduction in postoperative surgery-related complications, including lower rates of pancreatic fistulas and postoperative abnormal fluid collections. Notably, respiratory failure was also less common in the MIG group both before (2.2% vs. 1.0%, p=0.052) and after matching (3.0% vs. 1.0%, p=0.021), underscoring a potential respiratory benefit of the minimally invasive approach. These findings may indicate that MIG offers benefits in reducing complications associated with surgical manipulation. However, when stratified by type of gastrectomy, the lower complication rate of MIG was only seen for subtotal gastrectomy. For total gastrectomy, the difference in perioperative complication rates between MIG and OG was less pronounced and not statistically significant, and completely disappeared in the multivariable analysis after propensity score matching, suggesting a procedure-specific safety profile for MIG that warrants further investigation.

Existing studies comparing open and minimally invasive gastrectomy have predominantly been conducted in East Asia. Notably, the KLASS-02 trial compared open and laparoscopic distal gastrectomies in patients with locally advanced tumors, showing that laparoscopy was associated with reduced estimated blood loss, shorter hospital stays, and fewer postoperative complications in both the short and long term.[8] Specifically, intra-abdominal bleeding and collections were significantly more frequent with the open approach, consistent with the findings in our study.

For total gastrectomy, two Eastern trials have supported the feasibility of the minimally invasive approach in early-stage gastric cancers (c-stage I). In the CLASS-02 trial,[9] there was no significant difference in the overall postoperative complication rate between the laparoscopic total gastrectomy group (18.1%) and the open total gastrectomy group (17.4%). The KLASS-03 trial evaluated morbidity and mortality after 160 laparoscopic total gastrectomies in patients with c-stage I gastric cancer, showing a postoperative complication rate of 20.6%, with 9.4% of complications classified as Clavien-Dindo grade III or higher. The third most common complication was anastomotic leakage, with a rate of 1.9%.[12]

No randomized Eastern trials to date have compared open and minimally invasive approach for total gastrectomy in advanced tumors. However, a Japanese retrospective study analyzed a large cohort from a nationwide database between January 2012 and December 2013, including patients undergoing total gastrectomy for both early and advanced gastric cancer. Kodera et al. examined a substantial population of stage II-IV gastric cancer patients and found similar rates of postoperative complications overall.[16] However, there was a significantly higher incidence of anastomotic leakage in patients who underwent minimally invasive gastrectomy compared to those who underwent open gastrectomy (5.7% vs. 3.6%, $p = 0.002$).

In Western settings, only a few studies are available. The LOGICA trial compared patients with locally advanced tumors treated at 10 high-volume Dutch centers: 115 patients underwent a laparoscopic approach, and 112 patients an open approach. Both groups included a similar distribution of total and subtotal gastrectomies (total gastrectomies: 42% in the MIG group and 39% in the OG group; subtotal: 51% in the MIG and 58% in the OG). Postoperative complications occurred in 50 patients (44%) in the laparoscopic group and 46 patients (42%) in the open group, with 19.5% classified as severe (Clavien-Dindo grade >3a) in both groups (13). The incidence of anastomotic leakage did not significantly differ between the groups (8.7% in MIG vs. 10% in OG). In subgroup analysis, all anastomotic leaks in the MIG group occurred after total gastrectomy, whereas in the open group, 8 patients had anastomotic leakage following total gastrectomy and 3 patients following subtotal gastrectomy.[13]

The STOMACH trial, a randomized study involving six European centers, compared total gastrectomies using open and minimally invasive approaches after neoadjuvant chemotherapy. No significant difference was found in postoperative complications between the OG and MIG groups (42.9% in OG vs. 34.0% in MIG). Further assessment of specific complications, such as postoperative bleeding, abscesses, anastomotic leaks, and wound dehiscence, showed no statistically significant differences between the two approaches.[14]

Our findings, derived from populations outside of clinical trials, demonstrate that after subtotal gastrectomy, the incidence of perioperative complications is comparable to that reported in Eastern randomized trials, particularly KLASS-02.[8] The incidence of postoperative intra-abdominal collections is also consistent with that shown in randomized trials, with a similar difference favoring the minimally invasive approach. This specific complication may be closely related to the surgical approach itself, as the MIG technique involves limited manipulation of the intestinal loops. However, for total gastrectomy, the overall perioperative complication rate observed in our study was higher than that reported in Eastern randomized trials and observational studies, though comparable to rates in Western studies.[13, 14] Although the difference in postoperative abdominal collections favoring MIG remains significant, no overall benefit in perioperative complication rate was observed.

The anastomotic leakage rate after total gastrectomy in our series aligns with the rate reported in the STOMACH trial. Although minimally invasive cases in our study were more selectively chosen, the anastomotic leakage rate (9.7%) for MIG after total gastrectomy underscores the need for enhanced surgical training for European surgeons, to support skill development before performing such complex procedures. A study based on the DUCA dataset showed that no clear learning curve effect could be identified for anastomotic leakage as the primary outcome.[21] However, an initial increase in anastomotic leakage rates was observed, plateauing at 10% after approximately 36 cases.

Recently, Markar et al. have re-analyzed the DUCA registry (2012–2021) to evaluate the impact of the LOGICA trial on laparoscopic gastrectomy practice and outcomes in the Netherlands.[15] The analysis showed a significant increase in the rate of laparoscopic gastrectomy, from 6% in 2012 to 82% in 2021, with reductions in both overall and severe complications. Improvements in postoperative outcomes became apparent only after the trial period, once surgeons had advanced along their learning curve, particularly for complex procedures such as total gastrectomy.

This study has limitations. Its retrospective design and the inclusion of only high-volume centers may introduce selection bias. Additionally, the study reports experiences during a period when MIG was newly introduced in Europe, and some participating centers may have been in an early phase of the learning curve for minimally invasive total gastrectomy, potentially impacting results. Also, due to sample heterogeneity across centers, it was not feasible to include the centers in the propensity score matching, which may limit the ability to account for institutional variations. Of note, centers performing only open gastrectomy were excluded from propensity score matching and final analyses. While propensity score matching was used to adjust for observed confounders, it cannot account for unmeasured variables that influence surgical decision-making. As a result, confounding may persist despite statistical adjustment. Although this is one of the largest European studies providing real-world data on gastrectomy, the findings should be interpreted considering the inherent limitations of its observational nature.

In conclusion, this large European series shows that minimally invasive subtotal gastrectomy is associated with a lower rate of perioperative complications compared to open subtotal gastrectomy, supporting its use in this population. However, the benefit of MIG for total gastrectomy was not apparent, with complication rates comparable to OG. These findings suggest that minimally invasive subtotal gastrectomy should become a viable option in dedicated centers across Europe, while further training and evaluation of MIG for total gastrectomy are warranted to support the safe and effective integration of this approach.

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Conflict of Interest

MIvanBH declares consultancies for Johnson and Johnson, Stryker, Boston Scientific, Intuitive and Medtronic. All fees paid to institution. The remaining authors have no conflicts of interest to declare.

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Figure 1. Flowchart of patients who underwent gastrectomy between 2017-2021 of 24 European expert centers, from the GASTRODATA registry

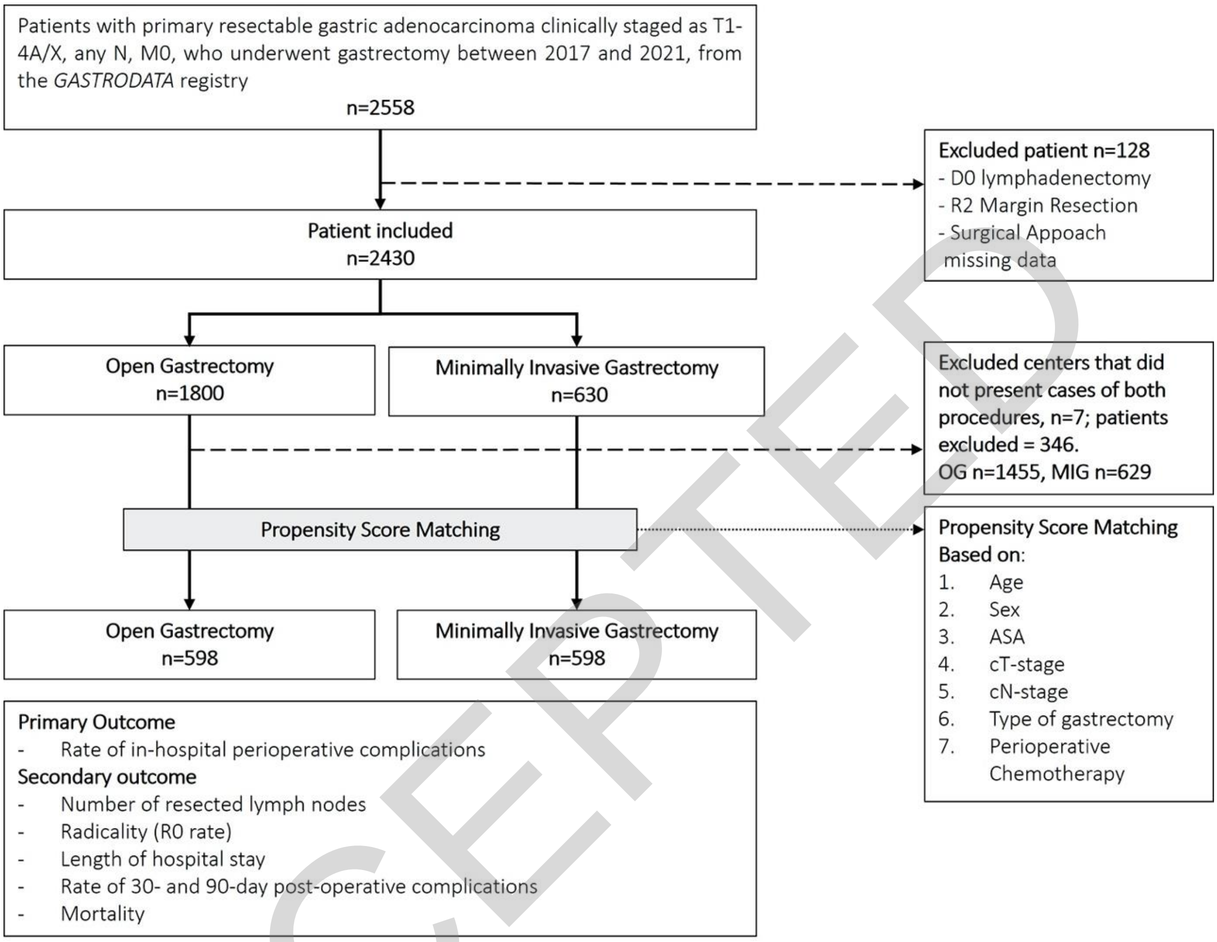

Table 1. Perioperative complications and postoperative outcomes in patients who underwent open vs. minimally invasive gastrectomy, of the overall series, per GCCG Definitions.

	OG (n=1800)	MIG (n=630)	*p*-value
Total Perioperative Complication	568 (31.6%)	145 (23.0%)	**<0.001**
Intraoperative Complications			
1. Intraoperative damage to major vessels	10 (0.6%)	3 (0.5%)	1.000
2. Intraoperative bleeding	6 (0.3%)	2 (0.3%)	1.000
3. Unexpected medical conditions interrupting or changing the planned procedure	1 (0.1%)	0 (0.0%)	1.000
Postoperative General Complications			
4. Stroke	3 (0.2%)	0 (0.0%)	0.573
5. Need for CPR	7 (0.4%)	3 (0.5%)	0.725
6. Myocardial infarction	3 (0.2%)	4 (0.6%)	0.079
7. Cardiac dysrhythmia	6 (0.3%)	2 (0.3%)	1.000
8. Acute myocardial failure	5 (0.3%)	0 (0.0%)	0.336
9. Pulmonary embolism	11 (0.6%)	4 (0.6%)	1.000
10. Need for prolonged intubation	20 (1.1%)	5 (0.8%)	0.497
11. Respiratory failure	39 (2.2%)	6 (1.0%)	0.052
12. Need for tracheostomy	11 (0.6%)	3 (0.5%)	1.000
13. Pleural effusion	65 (3.6%)	16 (2.5%)	0.197
14. Pneumothorax	12 (0.7%)	1 (0.2%)	0.204
15. Acute liver dysfunction	4 (0.2%)	0 (0.0%)	0.578
16. Acute renal insufficiency	25 (1.4%)	4 (0.6%)	0.134
17. Non-surgical related infections	182 (10.1%)	47 (7.5%)	**0.050**
Postoperative Surgical Complications			
18. Postoperative bleeding	63 (3.5%)	15 (2.4%)	0.170
19. Postoperative bowel obstruction	41 (2.3%)	9 (1.4%)	0.196
20. Postoperative bowel perforation	18 (1.0%)	1 (0.2%)	**0.036**
21. Duodenal leak	47 (2.6%)	12 (1.9%)	0.322
22. Anastomotic leak	93 (5.2%)	30 (4.8%)	0.690
23. Postoperative pancreatic fistula	49 (2.7%)	7 (1.1%)	**0.020**
24. Postoperative pancreatitis	13 (0.7%)	2 (0.3%)	0.380
25. Other postoperative abnormal fluid from drainage	97 (5.4%)	11 (1.7%)	**<0.001**
26. Delayed gastric emptying	15 (0.8%)	8 (1.3%)	0.330
27. Other major complications	46 (2.6%)	13 (2.1%)	0.490
Other outcomes			
30-day Mortality	60 (3.3%)	10 (1.6%)	**0.026**
Post-operative Chemotherapy at 30 days	476 (26.4%)	131 (20.8%)	**<0.001**
Post-operative Radiotherapy at 30 days	32 (1.8%)	1 (0.2%)	**<0.001**
Re-interventions at 30 days	57 (3.2%)	29 (4.6%)	0.103
90-day Mortality	85 (4.7%)	12 (1.9%)	**<0.001**
Post-operative Chemotherapy at 90 days	525	87	**<0.001**

	(29.2%)*	(13.8%)	
Post-operative Radiotherapy at 90 days	21 (1.2%)*	0 (0.0%)	<**0.001**
Re-interventions at 90 days	39 (2.2%)	14 (2.2%)	1.000
Total Length of Postoperative Hospitalization, days, (median, IQR)	9 (7-14)	8 (6-11)	<**0.001**

Results are represented as number (%). *16 patients had received both chemotherapy and radiotherapy within 90 days. OG indicates Open gastrectomy; MIG, Minimally invasive gastrectomy; IQR, Inter quartile range

Table 2. Multivariable analysis of perioperative complications in patients who underwent open vs. minimally invasive gastrectomy: unadjusted of the overall series, adjusted of the overall series, and Propensity Score matched models for total and subtotal gastrectomy groups.

	MIG vs. OG	**OR**	**CI 95%**	***p*-value**
	ALL DATA	0.65	0.52-0.80	<0.001
Unadjusted*	Total gastrectomy	0.81	0.60-1.10	0.181
	Subtotal Gastrectomy	0.64	0.47-0.87	0.005
	ALL DATA	0.77	0.62-0.96	0.023
Adjusted Pre-matching†	Total gastrectomy	0.89	0.65-1.23	0.486
	Subtotal Gastrectomy	0.64	0.47-0.89	0.007
	ALL DATA	0.77	0.57-1.03	0.083
Matched#	Total gastrectomy	1.15	0.62-2.17	0.645
	Subtotal Gastrectomy	0.49	0.30-0.80	0.005

* Crude without adjustment for confounder.

† Logistic regression adjusted for Surgical Approach, sex, age, ASA, pT-stage, and pN-stage (and type of gastrectomy in ALL DATA analysis)

Conditional Logistic Regression adjusted for Surgical Approach, sex, age, ASA, pT-stage, and pN-stage (and type of gastrectomy in ALL DATA analysis).

MIG indicated Minimally invasive gastrectomy; OG, Open gastrectomy; OR, Odds ratio; CI, Confidence interval.

Table 3. Perioperative complications and postoperative outcomes in patients who underwent open vs. minimally invasive Gastrectomy, after Propensity Score matching, per GCCG definitions.

	OG (n=598)	**MIG (n=598)**	***p*-value**
Total perioperative Complications	163 (27.3%)	136 (22.7%)	0.071
Intraoperative Complications			
1. intraoperative damage to major vessels	2 (0.3%)	3 (0.5%)	1.000
2.Intraoperative bleeding	2 (0.3%)	2 (0.3%)	1.000
3. Unexpected medical conditions interrupting or changing the planned procedure	1 (0.2%)	0 (0.0%)	1.000
Postoperative General Complications			
4. Stroke	0 (0.0%)	0 (0.0)	---
5. Need for CPR	3 (0.5%)	3 (0.5%)	1.000
6. Myocardial infarction	2 (0.3%)	4 (0.7%)	0.687
7. Cardiac dysrhythmia	3 (0.5%)	2 (0.3%)	1.000
8. Acute myocardial failure	1 (0.2%)	0 (0.0%)	1.000
9. Pulmonary embolism	3 (0.5%)	4 (0.7%)	1.000
10. Need for prolonged intubation	6 (1.0%)	4 (0.7%)	0.753
11. Respiratory failure	18 (3.0%)	6 (1.0%)	0.021
12. Need for tracheostomy	5 (0.8%)	3 (0.5%)	0.726
13. Pleural effusion	17 (2.8%)	15 (2.5%)	0.858
14. Pneumothorax	1 (0.2%)	1 (0.2%)	1.000
15. Acute liver dysfunction	2 (0.3%)	0 (0.0%)	0.500
16. Acute renal insufficiency	7 (1.2%)	4 (0.7%)	0.547
17. Non-surgical related infections	49 (8.2%)	42 (7.0%)	0.513
Postoperative Surgical Complications			
18. Postoperative bleeding	23 (3.8%)	15 (2.5%)	0.124
19. Postoperative bowel obstruction	16 (2.7%)	9 (1.5%)	0.225
20. Postoperative bowel perforation	7 (1.2%)	1 (0.2%)	0.069
21. Duodenal leak	10 (1.7%)	11 (1.8%)	1.000
22. Anastomotic leak	28 (4.7%)	29 (4.8%)	1.000
23. Postoperative pancreatic fistula	12 (2.0%)	6 (1.0%)	0.234
24. Postoperative pancreatitis	2 (0.3%)	2 (0.3%)	1.000
25. Other postoperative abnormal fluid	27 (4.5%)	11 (1.8%)	0.012
26. Delayed gastric emptying	6 (1.0%)	8 (1.3%)	0.789
27. Other major complications	9 (1.5%)	13 (2.2%)	0.520
Other outcomes			

30-day Mortality	22 (3.7%)	9 (1.5%)	0.027
Post-operative Chemotherapy at 30 days	126 (21.1%)	126 (21.7%)	0.887
Post-operative Radiotherapy at 30 days	7 (1.2%)	1 (0.2%)	0.038
Re-interventions at 30 days	18 (3.0%)	28 (4.7%)	0.175
90-day Mortality	26 (4.4%)	11 (1.8%)	0.018
Post-operative Chemotherapy at 90 days	166 (27.8%)	85 (14.2%)	<0.001
Post-operative Radiotherapy at 90 days	6 (1.0%)	0 (0.0%)	0.015
Re-interventions at 90 days	9 (1.5%)	14 (2.3%)	0.400
Total Length of Postoperative Hospitalization, days, (median, IQR)	9 (7-13)	8 (6-11)	<0.001

OG indicates Open gastrectomy; MIG, Minimally invasive gastrectomy; IQR, Interquartile range.

Table 4. Perioperative complications per GCCG definitions, in patients who underwent total vs. subtotal gastrectomy by surgical approach (open vs. minimally Invasive).

	Total Gastrectomy (n=1268)			**Subtotal Gastrectomy (n=1156)**		
	OG (n=1030)	**MIG (n=238)**	***p*-value**	**OG (n=764)**	**MIG (n=392)**	***p*-value**
Total Perioperative Complication	372 (36.1%)	75 (31.5%)	0.201	193 (25.3%)	70 (17.9%)	**0.005**
Intraoperative Complications						
1. Intraoperative damage to major vessels	9 (0.9%)	3 (1.3%)	0.579	1 (0.1%)	0 (0.0%)	0.474
2. Intraoperative bleeding	4 (0.4%)	2 (0.8%)	0.360	2 (0.3%)	0 (0.0%)	0.311
3. Interrupting or changing the planned procedure	0 (0.0%)	0 (0.0%)	0.788	1 (0.1%)	0 (0.0%)	0.474
Postoperative General Complications						
4. Stroke	1 (0.1%)	0 (0.0%)	0.631	2 (0.3%)	0 (0.0%)	0.311
5. Need for CPR	5 (0.5%)	2 (0.8%)	0.505	2 (0.3%)	1 (0.3%)	0.983
6. Myocardial infarction	2 (0.2%)	4 (1.7%)	0.013	1 (0.1%)	0 (0.0%)	0.474
7. Cardiac dysrhythmia	3 (0.3%)	2 (0.8%)	0.223	3 (0.4%)	0 (0.0%)	0.214
8. Acute myocardial failure	4 (0.4%)	0 (0.0%)	0.336	1 (0.1%)	0 (0.0%)	0.474
9. Pulmonary embolism	9 (0.9%)	2 (0.8%)	0.960	2 (0.3%)	2 (0.5%)	0.496
10. Need for prolonged intubation	14 (1.4%)	4 (1.7%)	0.706	6 (0.8%)	1 (0.3%)	0.271
11. Respiratory failure	26 (2.5%)	5 (2.1%)	0.703	13 (1.7%)	1 (0.3%)	0.043
12. Need for tracheostomy	6 (0.6%)	3 (1.3%)	0.261	5 (0.7%)	0 (0.0%)	0.108
13. Pleural effusion	58 (5.6%)	14 (5.9%)	0.880	6 (0.8%)	2 (0.5%)	0.593
14. Pneumothorax	11 (1.1%)	1 (0.4%)	0.352	---	---	---
15. Acute liver dysfunction	3 (0.3%)	0 (0.0%)	0.405	1 (0.1%)	0 (0.0%)	0.474
16. Acute renal insufficiency	18 (1.7%)	4 (1.7%)	0.943	6 (0.8%)	0 (0.0%)	0.079
17. Non-surgical related infections	117 (11.4%)	22 (9.2%)	0.346	63 (8.2%)	25 (6.4%)	0.257
Postoperative Surgical Complications						
18. Postoperative bleeding	38 (3.7%)	7 (2.9%)	0.574	25 (3.3%)	8 (2.0%)	0.234
19. Postoperative bowel obstruction	26 (2.5%)	4 (1.7%)	0.440	15 (2.0%)	5 (1.3%)	0.396
20. Postoperative bowel perforation	10 (1.0%)	0 (0.0%)	0.127	8 (1.0%)	1 (0.3%)	0.147
21. Duodenal leak	28 (2.7%)	4 (1.7%)	0.358	19 (2.5%)	8 (2.0%)	0.634
22. Anastomotic leak	78	23	0.288	15	7 (1.8%)	0.834

	(7.6%)	(9.7%)		(2.0%)		
23. Postoperative pancreatic fistula	33 (3.2%)	4 (1.7%)	0.208	16 (2.1%)	3 (0.8%)	0.093
24. Postoperative pancreatitis	9 (0.9%)	1 (0.4%)	0.476	4 (0.5%)	1 (0.3%)	0.510
25. Other postoperative abnormal fluid from drainage	64 (6.2%)	3 (1.3%)	0.001	33 (4.3%)	8 (2.0%)	0.063
26. Delayed gastric emptying	3 (0.3%)	1 (0.4%)	0.749	12 (1.6%)	7 (1.8%)	0.785
27. Other major complications	34 (3.3%)	10 (4.2%)	0.494	11 (1.4%)	3 (0.8%)	0.321

Results are represented as number (%). OG indicates Open gastrectomy; MIG, Minimally invasive gastrectomy; CPR, Cardiopulmonary resuscitation.