Review Article

Surgical considerations and outcomes of minimally invasive approaches for gastric cancer resection

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Despite high mortality rates from gastric cancer, surgical management remains critical for curative potential. Optimal outcomes of gastric cancer resection depend on a multitude of variables, including the extent of resection, scope of lymphadenectomy, method of reconstruction, and potential for a minimally invasive approach. Laparoscopic gastrectomy, compared with open gastrectomy, has been analyzed in numerous randomized control trials. Generally, those trials demonstrated statistically similar postoperative complication rates, mortality, and oncologic outcomes between the two approaches. Although laparoscopic gastrectomy requires longer operative times, significant improvements in estimated blood loss, postoperative length of stay, and return of bowel function have been noted in patients who undergo laparoscopic gastrectomy. These short-term benefits, along with equivalent oncologic results, have influenced national guidelines in both Eastern and Western countries to recommend laparoscopy, especially for early stage disease. Although robotic gastrectomy has not been as widely validated in effective trials, studies have reported equivalent oncologic outcomes and similar or improved postoperative complication and recovery rates after robotic gastrectomy compared with open gastrectomy. Comparing the two minimally invasive gastrectomy approaches, robotic surgery was associated with improved estimated blood loss, incidence of pancreatic sequela, and lymph node harvests in some studies, whereas laparoscopy resulted in lower operative times and hospital costs. Ultimately, when applying outcomes from the literature to clinical patient care decisions, it is imperative to recognize these studies' range of inclusion criteria, delineating between patients originating from Eastern or Western countries, the use of neoadjuvant chemotherapy, the volume of surgeon experience, and the extent of gastrectomy, among others. ***Cancer* 2022;128:3910-3918**.

KEYWORDS: gastrectomy, laparoscopy, robotic surgical procedures, stomach neoplasms.

INTRODUCTION

Gastric cancer (GC) represents one of the leading causes of cancer-related deaths worldwide. According to the most recent estimates from the American Cancer Society, approximately 26,000 patients are diagnosed with GC annually in the United States, and greater than 10,000 will die of their disease.[1] Although the prognosis for patients with GC has improved with advances in multimodal therapy, the high mortality rate reflects aggressive disease biology, high rates of advanced disease at diagnosis, and evolving patterns of presentation.

Complete surgical resection provides the best chance for long-term survival from GC. Here, we focus on technical considerations for GC resections and compare outcomes between open versus minimally invasive approaches.

SURGICAL CONSIDERATIONS

There are numerous surgical considerations to be made in the management of GC. The approach to the oncologic resection of GCs has undergone much evolution, independent of the application of minimally invasive techniques. Most notably, considerations involve the optimal approach to the type of gastric resection, the extent of lymphadenectomy, and the method of reconstruction. Additional considerations beyond the scope of this article include the need for prophylactic cholecystectomy, the contribution of neoadjuvant chemotherapy (NAC), and the role of intraperitoneal chemotherapy.

Extent of gastrectomy

Gastrectomy is the most widely used therapeutic approach for invasive GC that cannot be endoscopically resected. Total gastrectomy (TG) is usually performed for lesions in the proximal stomach because of the lower incidence of reflux esophagitis with Roux-en-Y esophagojejunostomy and higher lymph node sampling of the perigastric nodes along the lesser curvature of

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the stomach.[2,3] However, proximal gastrectomy has gained popularity, especially in the Eastern literature, as a method to preserve gastric function and nutritional status without compromising oncologic outcomes or morbidity.[4–7] Distal subtotal gastrectomy is considered sufficient for lesions in the distal two thirds of the stomach. Randomized trials have not demonstrated an additional survival benefit for TG compared with distal gastrectomy (DG) in patients who have distal tumors with adequate margins of resection, but subtotal gastrectomy has conferred improved nutritional status and quality of life.[8,9] According to the most recent National Comprehensive Cancer Network guidelines, for T1b–T3 lesions, an adequate resection to achieve negative microscopic margins should be performed, whereas T4b lesions may require en-bloc resection of involved structures. Minimally invasive approaches can be considered for early and locally advanced disease based on Eastern and Western guidelines.[10] However, these approaches are not generally recommended for T4b or N2 disease with bulky adenopathy.

Lymphadenectomy

The extent of lymphadenectomy had been a point of divergence between Eastern and Western recommendations, but recent literature has seen a convergence in philosophies. Gastrectomy with D2 lymphadenectomy had been the standard approach in East Asia following the Japanese experience and could involve en-bloc resection of the spleen and distal pancreas,[11,12] but more recent data have argued for de-escalation of this approach in favor of a modified D2 (D1+) lymphadenectomy.[13] In Western countries, based on randomized controlled trials (RCTs) from the Dutch group and the Medical Research Council, D2 dissection was beneficial for staging and locoregional recurrence rates but demonstrated an equivocal benefit to survival.[14–16] However, those studies have since been cited for being underpowered to demonstrate the survival advantage of D2 lymphadenectomy. The Dutch study was also criticized for its higher incidence of morbidity and questions about the quality of the D2 dissection. An update of the Dutch study demonstrated a lower rate of cancer-related death among the D2 group[14] and that, despite *noncompliance* with the standards of D2 lymphadenectomy described by the Japanese guidelines, D2 lymphadenectomy still yielded a survival advantage.[17] Similarly, the most recent Cochrane meta-analysis demonstrated a difference in disease-specific survival favoring D2 dissection.[18] Thus, modified D2 (D1+) lymphadenectomy to include perigastric, right and left gastric, common hepatic, celiac, and splenic stations with sampling of ≥16 nodes has been implemented as part of the Eastern and Western guidelines. D3 lymphadenectomy of para-aortic lymph nodes has not been shown to have a survival benefit, and most studies indicate that it is associated with greater perioperative morbidity and mortality.[19,20]

Anastomotic technique

Stapled anastomoses are common in both open and minimally invasive approaches. Linear staplers may be used to create gastrojejunostomies, esophagojejunostomies (EJs), or jejunojejunostomies. A transoral anvil device may also be used to create an end-to-end EJ anastomosis after a TG. Hand-sewn anastomoses are infrequent among laparoscopic resections, but the hand-sewn technique is facilitated by the wristed motion of the robotic approach. A randomized trial of 311 patients undergoing robotic versus open hand-sewn anastomoses demonstrated similar rates anastomotic leak, postoperative bleeding, and surgical site infection between the two approaches.[21]

Reconstruction

The three usual methods of reconstruction are Billroth I (gastroduodenostomy), Billroth II (loop gastrojejunostomy), and Roux-en-Y gastrojejunostomy. Billroth I is more common among studies performed in Eastern countries,[22,23] whereas the latter two methods are more common in the West.[24,25] This is likely reflective of more advanced disease, diffuse histology, and proximal location of primary disease seen in the West, which require more extensive resections that render the Billroth I anastomosis infeasible. Proximal gastrectomy yields the possibility of a *double-tract* reconstruction. In addition to a standard Roux-en-Y EJ reconstruction, the gastric remnant is anastomosed to the same Roux limb at a point between the EJ and the jejunojejunostomy. It has been demonstrated that this reconstruction prevents reflux esophagitis and improves quality of life without sacrificing oncologic outcomes.[26]

SURGICAL APPROACHES

When reviewing the literature on GC resections, the variability of inclusion criteria, such as extent of gastrectomy and exposure to NAC, must be considered when drawing conclusions across studies. As noted above, studies originating from East Asia versus Western countries often differ because patients in the East are diagnosed earlier, present with more distal tumors, and have a lower body mass index.[27,28]

In addition to numerous retrospective single-institution and multi-institution studies analyzing minimally invasive gastrectomy (MIG) versus open gastrectomy

(OG), a few RCTs have been completed. As surgeons become more proficient with MIG, the surgical techniques, extent of gastrectomy, and complexity of patients selected for operations have evolved.

Laparoscopic versus open surgery

Laparoscopic gastrectomy (LG) showed early promise with short-term outcomes, and the 2014 Japanese national guidelines recommended the laparoscopic approach for DG in early stage cancer.[29] More recently, long-term oncologic outcomes have also pointed toward the efficacy of the laparoscopic approach. A summary of the pertinent studies is provided in Table 1.[22,27,28,30–39]

Surgical outcomes

Certain intraoperative variables, such as operating room (OR) time and estimated blood loss (EBL), are often examined given their potential impact on postoperative recovery. Regardless of the extent of gastrectomy or whether patients have received NAC, studies have consistently demonstrated that LG results in longer OR times compared with OG, with one meta-analysis reporting an average 60-minute difference between the approaches.[40] However, laparoscopic magnification of the surgical field can assist in minimizing EBL compared with open surgery. Decreased EBL was demonstrated to be statistically significant in RCTs evaluating laparoscopic DG (LDG) and laparoscopic TG relative to their open counterparts.[30,35,39] This finding persists for locally advanced disease, in which dissection of difficult surgical planes can cause more blood loss.[32,36] Notably, those studies excluded patients who received NAC, which can obscure surgical planes and increase intraoperative bleeding. Studies incorporating NAC indeed found equivalent EBL between laparoscopic and open approaches for both DG and TG.[27,38] In summary, LG can minimize blood loss compared with OG, although this advantage may be negated by the effects of NAC.

Postoperative complication rates are statistically similar between LG and OG cohorts, although some studies have reported improvements for certain complications after LG. The Korean Laparoendoscopic Gastrointestinal Surgery Study 01 (KLASS 01; ClincalTrials.gov identifier NCT00452751)[30] evaluated LDG versus open DG (ODG) among treatment-naive patients who had early stage GC. Those investigators recorded lower rates of overall complications (13% vs. 20%; $p = .001$) and wound issues (3.1% vs. 7.7%; $p < .001$) after LDG. Numerous other trials and reviews have demonstrated similar, if not improved, rates of intra-abdominal bleeding and intra-abdominal infections in those who underwent LDG versus ODG.[27,32,35,36,39–41] This improvement in perioperative morbidity after the laparoscopic approach was preserved in one randomized trial analyzing patients with locally advanced disease who received NAC.[38]

Gastrointestinal function, including delayed gastric emptying and anastomotic stricture, was also evaluated in RCTs that revealed no significant differences between surgical approaches.[32,35,36,39] The ongoing KLASS 04 trial comparing pylorus-preserving LG with LDG may shed more light on this issue.[42] The need for reoperation and readmission to the hospital has lacked statistical difference across studies.[32,35,36]

Pancreatic complications, including pancreatitis and postoperative pancreatic fistula (POPF), also contribute to postgastrectomy morbidity and may be secondary to disruption of pancreatic blood flow, pancreatic injury from adjacent lymphadenectomy, and thermal trauma.[43] A meta-analysis by Guerra et al.[43] accumulated results from six RCTs and 14 non-RCTs in which preoperative variables known to affect pancreatic morbidity were balanced between cohorts. Those authors documented composite pancreatic morbidity in 1.24% of patients after MIG (predominantly LG) versus a 0.91% rate after OG. Although this difference was not statistically significant, LG was associated with higher rates of acute pancreatitis alone (odds ratio, 2.69; $p = .03$). Nonetheless, the incidence of pancreatic complications is limited, and laparoscopy does not cause a clinically significant increase in pancreatic morbidity.

Postoperative mortality rates are similarly low, often <1%, across RCT LG and OG cohorts. Reviews of the National Cancer Database (NCDB) reported lower rates of 30-day and 90-day mortality for patients undergoing MIG versus OG.[44,45] One of those studies[45] demonstrated a persistent mortality benefit after MIG using propensity-matching analysis. However, Farrow et al.[44] did not adjust for the overrepresentation of early stage cancer in the minimally invasive surgery group, and these results should be interpreted with caution.

Although many complications are similar between LG and OG, metrics of postoperative recovery favor the laparoscopic approach. Pain control and the time to resumption of bowel function were improved among those undergoing LDG relative to ODG,[32,35,38,40] including in the KLASS 02 trial (ClincalTrials.gov identifier NCT01283893),[36] for locally advanced disease. However, this quickened gastrointestinal recovery has not been reproduced after TG.[27,39] Finally, numerous RCTs reported that the hospital length of stay (LOS) was statistically shorter after LDG versus ODG. For example, patients in

TABLE 1. Randomized Trial Outcomes for Laparoscopic Gastrectomy

					Laparotomy/open surgery									
Reference(s)	Trial name	Type of gastrec-tomy	Clinical cancer TNM stage[a]	NAC, yes/no	No.	OR time, minutes	EBL, ml	Mortality, %	Morbidity, %[b]	POPF, %	LOS, days	ROBF, days	No. of lymph nodes	OS, %
Kim 2010,[22] 2016,[30] 2019[31]	KLASS 01	Distal	T1N0, T1N1, T2aN0	No	179/161	184/139[c]	111/191[c]	0.6/0.3	13/20[c]	0.0/0.0	7.1/7.9[c]	—	40.5/43.7[c]	94/93 (5-year)
Hu 2016,[32] Yu 2019,[33] Huang 2022[34]	CLASS 01	Distal	T2–T4a, N0–N3	No	519/520	217/186[c]	106/117[c]	0.4/0.0	15/13	0.4/0.0	10.8/11.3[c]	3.5/3.6[c]	36.1/36.9	73/76 (5-year)
Katai 2017,[35] 2020[28]	JCOG0912	Distal	T1N0, T1N1, T2N0	No[d]	457/455	278/194[c]	38/115[c]	0.0/0.0	3.3/3.7[e]	0.4/0.4	—	2.0/3.0[c]	39/39	97/95 (5-year)
Lee 2019,[36] Hyung 2020[37]	KLASS 02	Distal	T2––T4a, N0–N1	No	513/498	227/165[c]	154/230[c]	0.4/0.6	17/24[c]	1.9/0.6[f]	8.1/9.3[c]	3.5/3.7	46.6/47.4	91/90 (3-year)
Li 2019[38]	—	Distal	T2–T4a, N0–N3	Yes	45/50	225/183[c]	87/100	0.0/0.0	20/46[c]	0.0/2.0	9/9	3.3/3.2	32/33	—
Liu 2020[39]	CLASS 02	Total	T1N0, T1N1, T2N0	No	105/109	231/190[c]	92/121[c]	1.0/0.0	18/17	0.0/1.8	10.9/9.6	3.1/3.0	35/37	—
van der Wielen 2021[27]	—	Total	T1–T4, N0–N2	Yes	47/49	244/200[c]	171/200	—	34/43	—	8/8	5.0/5.0	41.7/43.4	86/90 (1-year)

Abbreviations: EBL, estimated blood loss; JCOG, Japan Clinical Oncology Group; KLASS, Korean Laparoendoscopic Gastrointestinal Surgery Study Group; LOS, length of stay; Lap, laparoscopic; NAC, neoadjuvant chemotherapy; OR, operating room; OS, overall survival; POPF, postoperative pancreatic fistula; ROBF, return of bowel function; TNM, tumor, lymph node, metastasis classification.

[a]TNM staging is the clinical staging included in the eligibility criteria or in baseline demographic data. All studies required clinical M0 classification for inclusion.

[b]Morbidity refers to overall complications as reported by each study, except where specified.

[c]These values indicate a statistically significant difference.

[d]Administration of NAC is not explicitly stated, although the assumption is that none was administered based on the clinical staging in the eligibility criteria.

[e]Rates of grade 3 and 4 nonhematologic surgical events are shown.

[f]Rates include POPF and pancreatitis.

the KLASS 01 trial experienced an LOS of 7.1 days after LDG versus 7.9 days after ODG ($p < .001$).[30] LOS results for TG have been statistically equivalent between surgical approaches.[27,39] The laparoscopic approach appears to be especially beneficial for postoperative recovery in patients undergoing DG for cancer, whereas recovery after TG is at least comparable between surgical approaches.

Oncologic outcomes

The application of LG became more widely accepted once equivalent oncologic outcomes were demonstrated. RCTs have demonstrated statistically comparable margin-negative resection rates and lymph node harvests between these surgical approaches, including among patients who underwent TG and received NAC.[27,35,36] A meta-analysis of five East Asian RCTs reviewed operations for locally advanced GC in which all patients underwent D2 lymphadenectomy.[41] Those investigators demonstrated that equivalent numbers of lymph nodes were harvested using the LG and OG approaches.

Given its association with improved survival rates, receipt of adjuvant chemotherapy after adequate oncologic resection has become a metric by which to judge surgical appropriateness.[46,47] In large RCTs from Korea (KLASS 01 and KLASS 02)[31,37] and China (CLASS-01; ClinicalTrials.gov identifier NCT01609309),[34] the proportion of patients receiving adjuvant chemotherapy was statistically similar between the LG and OG cohorts. Although only 10% of patients in the KLASS 01 trial[31] received adjuvant chemotherapy across both surgical cohorts, this reflected early stage disease in the study population. Adjuvant treatment rates rose to 60% for each cohort in the KLASS 02 trial[37] for locally advanced disease. From a Western perspective, the review of the NCDB by Farrow et al.[44] demonstrated no difference in the receipt of adjuvant chemotherapy for patients who underwent MIG versus OG (odds ratio, 1.03; $p = .50$). Importantly, although some studies reported no impact of surgical approach on the time from surgery to adjuvant chemotherapy induction,[31,38] Li et al.,[38] whose patients had received NAC, observed that those who underwent LG were able to complete more cycles of adjuvant chemotherapy (odds ratio, 4.39; $p = .003$) and had improved tolerance of the regimen (22% vs. 42% termination; $p = .04$) compared with those who underwent OG.

In the KLASS 01 trial,[31] disease recurrence rates were similar between the two cohorts (LDG vs. ODG, 5.6% vs. 4.8%; $p = .49$), a finding also reflected in the CLASS-01[33] trial (LDG vs. ODG, 18.3% vs. 16.3%; $p = .35$) and the KLASS 02[37] trial (LDG vs. ODG, 15.4% vs. 14.9%; $p = .78$) for locally advanced cancer. Furthermore, LG was not inferior to OG in terms of recurrence-free survival or disease-free survival (DFS) at 3 years and 5 years postoperatively. This was corroborated by a meta-analysis combining 5-year DFS results from RCTs for DG (hazard ratio, 0.99).[40]

Similarly, overall survival (OS) was consistently noninferior in patients who underwent LG versus OG. In the Japan Clinical Oncology Group (JCOG) 0912 trial,[28] which evaluated DG for early stage GC, 5-year OS rate was as high as 97% in the LDG group (vs. 95.2% in the OG group); whereas, in the CLASS-01 trial for locally advanced GC, the rate dropped to 73% in the LDG group (vs. 76.3% the OG group).[34] Because the RCTs that included patients who underwent TG and received NAC are more recent, significant long-term data are sparse. In the Western experience, a propensity-matched NCDB review demonstrated a slight improvement in the 5-year OS rate for patients who underwent MIG compared with OG (51.9% vs. 47.7%; $p < .001$).[45] However, an RCT of TG from the Netherlands, in which all patients received NAC, reported 1-year OS rates that were statistically equivalent between the LG and OG groups (86% vs. 90%, respectively; $p = .70$).[27]

Robotic versus open surgery

The robotic experience in foregut surgery is nascent relative to the laparoscopic experience. Therefore, availability and quality of data are more limited.

Surgical outcomes

Intraoperative results from robotic GC resections echo those from other surgical disciplines that report longer OR times and decreased EBL for robotic gastrectomy (RG) cases compared with OG cases.[48] In a meta-analysis of 11 RG versus OG retrospective studies, Chen et al.[49] demonstrated a mean difference that was 83 minutes longer for RG compared with OG ($p = .01$). A Chinese RCT,[21] which included both DG and TG, likewise reported longer OR times in the robotic cohort (243 vs. 192 minutes; $p = .002$). Multiple studies reported significantly lower EBL for robotic cases, although none of those studies included patients who had received NAC.[21,40,49,50]

Postoperative complication rates have demonstrated statistical equivalence or have favored robotic operations. Although the RCT by Wang et al.[21] and the meta-analysis by Caruso et al.[50] showed no statistical difference in overall morbidity, another meta-analysis reported a lower likelihood with RG (odds ratio, 0.57; $p = .025$).[49] Conflicting results were also demonstrated in two Western single-institution studies that included patients who had previously received NAC.[51,52]

Results are similarly mixed for postoperative mortality; however, overall, RG appears to be noninferior to OG.[49,50] Authors of national database analyses concluded that MIG was associated with improved rates of 30-day[53] and 90-day mortality,[44] but the proportion of MIG cases that were performed robotically is unclear.

RG has routinely been associated with quicker postoperative recovery. Although the propensity-matched study from Solaini et al.[51] reported statistically similar rates of recovery, Wang et al.[21] reported faster times to first flatus (RG vs. OG, 2.6 vs. 3.1 days; $p = .03$) and shorter LOS (RG vs. OG, 5.7 vs. 6.5 days; $p = .02$) for the robotic group. These findings were corroborated in meta-analyses.[49,50]

Oncologic outcomes

It has been demonstrated that the limited data available on oncologic outcomes from RGs are statistically comparable to the data from OGs. Lymph node harvests were similar between RG and OG in multiple studies,[49–51] including the RCT by Wang et al.,[21] who separately analyzed DG and TG.

Recurrence rates are infrequently reported, but a propensity-matched Western study demonstrated similar 5-year DFS rates as well as comparable 1-year (RG vs. OG, 96% vs. 97%), 3-year (RG vs. OG, 80% vs. 87%), and 5-year (RG vs. OG, 73% vs. 78%) OS rates ($p = .70$).[51] These rates were echoed by another Western institutional review.[52] Although margin-negative resection rates were rarely reported, this outcome was associated with surgical approach in the meta-analysis by Chen et al.,[49] who noted that negative margins were six times more likely with RG compared with OG (odds ratio, 6.26; $p = .00$).

Robotic versus laparoscopic surgery

As minimally invasive surgery becomes more commonplace, randomized studies evaluating RG frequently use LG as a benchmark comparison because benefits have already been demonstrated with MIG over OG. Although many meta-analyses and reviews have been performed, the RCTs completed are still small and are restricted to one or two surgical centers, indicating a need for more high-impact trials.

Surgical outcomes

Studies of various types have found that RG is associated with longer OR time compared with LG.[52,54–58] In a single-center RCT evaluating patients who underwent only DG for early stage and locally advanced cancer, Lu et al.[54] reported longer OR times for the RG cohort (201 vs. 182 minutes; $p < .001$). This difference persisted in another RCT by Ojima et al.,[55] who analyzed patients from two institutions undergoing either TG or DG (RG vs. LG, 297 vs. 245 minutes; $p = .001$). The robotic approach was also associated with smaller volumes of EBL,[54,57] but some studies that included robotic TG indicated that EBL was statistically equivalent between the two approaches.[55,56]

A heterogenous pattern of postoperative morbidity rates has been depicted among these studies, but the robotic approach was noninferior compared with laparoscopy. Lu et al.[54] recorded significantly lower rates of overall complications for RG (9.2% vs. 17.6%; $p = .04$), which were attributed specifically to the lower incidence of postoperative pneumonia in the robotic cohort. Ojima et al.[55] documented lower rates of 90-day severe complications for their robotic group (RG vs. LG, 5.3% vs. 16.2%; $p = .01$) but noted that the rates of intra-abdominal infections from anastomotic leak or abscess were equivalent between the groups. The meta-analysis by Guerrini et al.[57] indicated similar overall complication rates but reported a lower likelihood of severe surgical complications with RG compared with LG (odds ratio, 0.66; $p = .005$).

RG has also been associated with favorable rates of pancreatic sequela in some studies. In their RCT, Ojima et al.[55] found similarly low rates of POPF in both the RG and LG cohorts (0% vs. 1.7%, respectively; $p = .50$). Conversely, a meta-analysis by Jin et al.,[56] who analyzed pooled results from 30 comparative studies, and the RCT from Lu et al.[54] reported a correlation between RG and lower incidence of pancreatic morbidity (odds ratio, 0.376; $p = .03$). Guerra et al.,[59] focusing on pancreatic complications as the primary outcome, found statistically similar rates of overall pancreas-related complications, acute pancreatitis, and POPF between the RG and LG groups. But those authors emphasized that, even with equivalent rates, the robotic approach may prove advantageous in minimizing postoperative pancreatic pathology because patients in their robotic cohort had a significantly higher body mass index and underwent more extensive lymph node dissection, both of which are risk factors for developing POPF that could have increased the relative incidence of complications among patients in the robotic cohort.

Statistically similar rates of delayed gastric emptying, anastomotic stricture, reoperation, and readmission have been reported after RG and LG in a few studies.[54,56,58] Likewise, mortality rates after the operations were similar throughout many studies.[54–57,60]

One meaningful benefit demonstrated of both RG and LG over OG is the quicker recovery time, but no appreciable gap between the two minimally invasive approaches has been shown. Patients undergoing RG tended to have statistically quicker bowel function after surgery,[55,56] but the clinical impact of this difference, which was only 0.3 days in the RCT from Lu et al.,[54] is likely negligible. Postoperative LOS was equivalent for both approaches throughout a multitude of studies.[54–58,60]

Oncologic outcomes

Rates of both margin-negative resection and receipt of adjuvant therapy have been statistically similar.[54,55,58,60] Lymph node harvest is used as an outcome in many studies because the three-dimensional visualization and wristed articulation with the robotic approach should allow for easier dissection of anatomically challenging nodal basins compared with laparoscopy.[21] Although two meta-analyses did portray a larger nodal yield as significantly associated with RG, the mean difference was only two more lymph nodes after RG versus LG.[56,57] Other studies, including RCTs, showed equivalent lymph node yields between groups.[54,55] However, focusing on certain lymph node regions, Lu et al.[54] noted a higher number of dissected extraperigastric nodes for the robotic cohort (17.6 vs. 15.8 lymph nodes; $p = .02$), whereas a propensity-matched study recorded more suprapancreatic lymph nodes harvested after RG (12.4 vs. 11.7 lymph nodes; $p = .048$).[58]

Greater lymph node harvest has not yet translated into improved long-term outcomes for RG compared with LG. Recurrence rates, recurrence-free survival, and OS have been shown to be statistically equivalent in meta-analyses from Guerrini et al.[57] and Jin et al.[56] as well as in the propensity-matched study from Shin et al.[58] Notably, the NCDB review by Hendriksen et al.,[45] which demonstrated improved 5-year OS rates for MIG compared with OG, found no OS difference on propensity matching of the robotic and laparoscopic techniques.

Conversion rates

Conversion of minimally invasive to open surgery is a key variable to evaluate when considering the selection of LG or RG. Cases requiring conversion have been shown in surgical fields, including gastrectomy, to be associated with worse outcomes.[61–63] For example, LOS was significantly longer for patients who had LG converted to OG compared with those who remained laparoscopic (8.7 vs. 7.6 days; $p = .02$).[62] Whereas meta-analyses have quoted similar conversion rates between robotic and laparoscopic cohorts,[56,57] single-institution reviews have reported that RG was associated with significantly lower conversion rates.[52,58] Overall, the available data hint that the robotic approach may curb conversion rates, but more convincing results are required.

Notably, the actual conversion rates of these two retrospective studies varied drastically. Shin et al.,[58] who analyzed early stage cancers, documented rates of 0% (RG) and 0.2% (LG), whereas Nakauchi et al.,[52] who included Western patients who had received NAC, reported conversions in 26% and 40% of RG and LG cases, respectively ($p = .01$). Conversion rates from the large laparoscopic RCTs performed for early stage cancer were often below 4%.[30,35] Evidently, this clinically meaningful variation in the conversion rate between the studies themselves highlights the importance of patient selection as well as surgeon experience when considering MIG.

Cost analysis

Perioperative costs are partially attributable to operative times and surgical equipment, leading to a higher cost attributed to minimally invasive approaches. A national database review from Park et al.[53] reported a $4700 higher hospital cost for MIG compared with OG, whereas other studies have indicated that cost increases are more likely associated with RG compared with LG. For example, Lu et al.[54] documented total hospital costs of $13,423 for RG compared with $10,165 for LG ($p < .001$); but Jin et al.[56] calculated a mean difference of $19,141 in perioperative costs between RG and LG. However, as surgeon experience with minimally invasive approaches increases (discussed below), coupled with decreased hospital LOS, it is foreseeable that the cost comparison between different approaches may become more level.

Surgical learning curve

A surgeon's experience with the technical aspects of an operation can wield substantial influence on operative outcomes. Studies have identified phases of a surgeon's learning for both RG and LG based on changes in OR time, EBL, and complication rates after performing a discrete number of cases. Kim et al.[64] evaluated surgeons who had completed at least 60 RGs and identified four phases in the learning arc for RG: initial learning (1–25 cases), proficiency (26–65 cases), transitional

(66–86 cases), and mastery (≥89 cases). As surgeons reached the proficiency phase, they began performing more complex cases on higher risk patients, leading to a transient uptick in complications before mastering the procedure. Therefore, recognizing the difference in the participating surgeons' experience between studies (KLASS 01[22] surgeons had performed ≥50 LDGs, JCOG 0912[28] surgeons had performed ≥30 ODGs or LDGs, and surgeons in the RCT by Lu et al.[54] had performed ≥300 LGs and ≥ 50 RGs) is essential for determining the possible influence on outcomes.

CONCLUSION

Surgical management of GC involves numerous variables that affect patients' surgical and oncologic outcomes. Here, we have underscored the role of the extent of resection, the scope of lymphadenectomy, the method of reconstruction, and the potential for a minimally invasive operative approach. Although current literature suggests some benefits in postoperative recovery using minimally invasive approaches compared with OG, long-term oncologic outcomes often remain similar no matter the technique used. Ultimately, when applying outcomes from the literature to clinical patient care decisions, it is imperative to recognize the studies' variability in inclusion criteria that span patients originating from Eastern or Western countries, the use of NAC, the volume of surgeon experience, and the extent of gastrectomy, among others.

CONFLICTS OF INTEREST

Kevin K. Roggin reports expert witness testimony for Gazak Brown PSC as an independent contractor and other support from Intuitive Surgical outside the submitted work. Cecilia T. Ong and Jason L. Schwarz made no disclosures.

REFERENCES

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin*. 2022;72(1):7-33.
2. Li X, Gong S, Lu T, et al. Proximal gastrectomy versus total gastrectomy for Siewert II/III adenocarcinoma of the gastroesophageal junction: a systematic review and meta-analysis. *J Gastrointest Surg*. 2022;26(6):1321-1335.
3. Pu Y, Gong W, Wu Y, Chen Q, He T, Xing C. Proximal gastrectomy versus total gastrectomy for proximal gastric carcinoma. A meta-analysis on postoperative complications, 5-year survival, and recurrence rate. *Saudi Med J*. 2013;34(12):1223-1228.
4. Li S, Gu L, Shen Z, Mao D, Khadaroo PA, Su H. A meta-analysis of comparison of proximal gastrectomy with double-tract reconstruction and total gastrectomy for proximal early gastric cancer. *BMC Surg*. 2019;19(1):117.
5. Nunobe S, Ida S. Current status of proximal gastrectomy for gastric and esophagogastric junctional cancer: a review. *Ann Gastroenterol Surg*. 2020;4(5):498-504.
6. Tanioka T, Waratchanont R, Fukuyo R, et al. Surgical and nutritional outcomes of laparoscopic proximal gastrectomy versus total gastrectomy: a meta-analysis. *Surg Endosc*. 2020;34(3):1061-1069.
7. Katai H, Mizusawa J, Katayama H, et al. Single-arm confirmatory trial of laparoscopy-assisted total or proximal gastrectomy with nodal dissection for clinical stage I gastric cancer: Japan Clinical Oncology Group Study JCOG1401. *Gastric Cancer*. 2019;22(5):999-1008.
8. Bozzetti F, Marubini E, Bonfanti G, Miceli R, Piano C, Gennari L. Subtotal versus total gastrectomy for gastric cancer: five-year survival rates in a multicenter randomized Italian trial. *Ann Surg*. 1999;230(2):170-178.
9. Kwon OK, Yu B, Park KB, Park JY, Lee SS, Chung HY. Advantages of distal subtotal gastrectomy over total gastrectomy in the quality of life of long-term gastric cancer survivors. *J Gastric Cancer*. 2020;20(2):176-189.
10. Ajani JA, D'Amico TA, Almhanna K, et al. Gastric Cancer, Version 3.2016. NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2016;14(10):1286-1312.
11. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer*. 2011;14(2):113-123.
12. Sano T, Sasako M, Mizusawa J, et al. Randomized controlled trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. *Ann Surg*. 2017;265(2):277-283.
13. Sasako M, Sano T, Yamamoto S, et al. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Engl J Med*. 2008;359(5):453-462.
14. Hartgrink HH, Van De Velde CJH, Putter H, et al. Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch Gastric Cancer Group Trial. *J Clin Oncol*. 2004;22(11):2069-2077.
15. Songun I, Putter H, EM-Kl K, Sasako M, van de Velde C. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol*. 2010;11(5):439-449.
16. Cuschieri A, Joypaul V, Fayers P, et al. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. *Lancet*. 1996;347(9007):995-999.
17. De Steur WO, Hartgrink HH, Dikken JL, Putter H, Van De Velde CJH. Quality control of lymph node dissection in the Dutch Gastric Cancer Trial. *Br J Surg*. 2015;102(11):1388-1393.
18. Mocellin S, Mcculloch P, Kazi H, Gama-Rodrigues JJ, Yuan Y, Nitti D. Extent of lymph node dissection for adenocarcinoma of the stomach. *Cochrane Database Syst Rev* 2015;2015(8):CD001964, 2015.
19. Douridas GN, Pierrakakis SK. Is there any role for D3 lymphadenectomy in gastric cancer? *Front Surg*. 2018;5:27.
20. Marrelli D, Pedrazzani C, Neri A, et al. Complications after extended (D2) and superextended (D3) lymphadenectomy for gastric cancer: analysis of potential risk factors. *Ann Surg Oncol*. 2007;14(1):25-33.
21. Wang G, Jiang Z, Zhao J, et al. Assessing the safety and efficacy of full robotic gastrectomy with intracorporeal robot-sewn anastomosis for gastric cancer: a randomized clinical trial. *J Surg Oncol*. 2016;113(4):397-404.
22. Kim HH, Hyung WJ, Cho GS, et al. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer an interim report—a phase III multicenter, prospective, randomized trial (KLASS trial). *Ann Surg*. 2010;251(3):417-420.
23. Kitano S, Shiraishi N, Fujii K, Yasuda K, Inomata M, Adachi Y. A randomized controlled trial comparing open vs. laparoscopy-assisted distal gastrectomy for the treatment of early gastric cancer: an interim report. *Surgery*. 2002;131(1 suppl):S306-S311.
24. Huscher CGS, Mingoli A, Sgarzini G, et al. Laparoscopic versus open subtotal gastrectomy for distal gastric cancer: five-year results of a randomized prospective trial. *Ann Surg*. 2005;241(2):232-237.
25. Strong VE, Devaud N, Allen PJ, Gonen M, Brennan MF, Coit D. Laparoscopic versus open subtotal gastrectomy for adenocarcinoma: a case-control study. *Ann Surg Oncol*. 2009;16(6):1507-1513.
26. Ji X, Jin C, Ji K, et al. Double tract reconstruction reduces reflux esophagitis and improves quality of life after radical proximal gastrectomy for patients with upper gastric or esophagogastric adenocarcinoma. *Cancer Res Treat*. 2021;53(3):784-794.
27. van der Wielen N, Straatman J, Daams F, et al. Open versus minimally invasive total gastrectomy after neoadjuvant chemotherapy: results of a European randomized trial. *Gastric Cancer*. 2021;24(1):258-271.
28. Katai H, Mizusawa J, Katayama H, et al. Survival outcomes after laparoscopy-assisted distal gastrectomy versus open distal gastrectomy with nodal dissection for clinical stage IA or IB gastric cancer

(JCOG0912): a multicentre, non-inferiority, phase 3 randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2020;5(2):142-151.
29. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer* 2021;24(1):1–21.
30. Kim W, Kim HH, Han SU, et al. Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage i gastric cancer short-term outcomes from a multicenter randomized controlled trial (KLASS-01). *Ann Surg*. 2016;263(1):28-35.
31. Kim HH, Han SU, Kim MC, et al. Effect of laparoscopic distal gastrectomy vs. open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. *JAMA Oncologia*. 2019;5(4):506-513.
32. Hu Y, Huang C, Sun Y, et al. Morbidity and mortality of laparoscopic versus open D2 distal gastrectomy for advanced gastric cancer: a randomized controlled trial. *J Clin Oncol*. 2016;34(12):1350-1357.
33. Yu J, Huang C, Sun Y, et al. Effect of laparoscopic vs. open distal gastrectomy on 3-year disease-free survival in patients with locally advanced gastric cancer: the CLASS-01 randomized clinical trial. *JAMA*. 2019;321(20):1983-1992.
34. Huang C, Liu H, Hu Y, et al. Laparoscopic vs. open distal gastrectomy for locally advanced gastric cancer: five-year outcomes from the CLASS-01 randomized clinical trial. *JAMA Surg*. 2022;157(1):9-17.
35. Katai H, Mizusawa J, Katayama H, et al. Short-term surgical outcomes from a phase III study of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer: Japan Clinical Oncology Group Study JCOG0912. *Gastric Cancer*. 2017;20(4):699-708.
36. Lee HJ, Hyung WJ, Yang HK, et al. Short-term outcomes of a multicenter randomized controlled trial comparing laparoscopic distal gastrectomy with D2 lymphadenectomy to open distal gastrectomy for locally advanced gastric cancer (KLASS-02-RCT). *Ann Surg*. 2019;270(6):983-991.
37. Hyung WJ, Yang HK, Park YK, et al. Long-term outcomes of laparoscopic distal gastrectomy for locally advanced gastric cancer: the KLASS-02-RCT randomized clinical trial. *J Clin Oncol*. 2020;38(28):3304-3313.
38. Li Z, Shan F, Ying X, et al. Assessment of laparoscopic distal gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: a randomized clinical trial. *JAMA Surg*. 2019;154(12):1093-1101.
39. Liu F, Huang C, Xu Z, et al. Morbidity and mortality of laparoscopic vs. open total gastrectomy for clinical stage i gastric cancer: the CLASS02 multicenter randomized clinical trial. *JAMA Oncologia*. 2020;6(10):1590-1597.
40. Aiolfi A, Lombardo F, Matsushima K, et al. Systematic review and updated network meta-analysis of randomized controlled trials comparing open, laparoscopic-assisted, and robotic distal gastrectomy for early and locally advanced gastric cancer. *Surgery*. 2021;170(3):942-951.
41. Beyer K, Baukloh AK, Kamphues C, et al. Laparoscopic versus open gastrectomy for locally advanced gastric cancer: a systematic review and meta-analysis of randomized controlled studies. *World J Surg Oncol*. 2019;17(1):1-19.
42. Seoul National University Hospital. Comparison of Laparoscopic Pylorus Preserving Gastrectomy Versus Laparoscopic Distal Gastrectomy (KLASS-04). ClinicalTrials.gov identifier NCT02595086. US National Library of Medicine; 2015. Accessed June 8, 2022. https://clinicaltrials.gov/ct2/show/NCT02595086
43. Guerra F, Giuliani G, Iacobone M, Pietro BP, Coratti A. Pancreas-related complications following gastrectomy: systematic review and meta-analysis of open versus minimally invasive surgery. *Surg Endosc*. 2017;31(11):4346-4356.
44. Farrow NE, Freischlag KW, Adam MA, Blazer DG. Impact of minimally invasive gastrectomy on use of and time to adjuvant chemotherapy for gastric adenocarcinoma. *J Surg Oncol*. 2020;121(3):486-493.
45. Hendriksen BS, Brooks AJ, Hollenbeak CS, Taylor MD, Reed MF, Soybel DI. The impact of minimally invasive gastrectomy on survival in the USA. *J Gastrointest Surg*. 2020;24(5):1000-1009.
46. Bang YJ, Kim YW, Yang HK, et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. *Lancet*. 2012;379(9813):315-321.
47. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. *Lancet*. 2020;396(10251):635-648.
48. Caba Molina D, Lambreton F, Arrangoiz MR. Trends in robotic pancreaticoduodenectomy and distal pancreatectomy. *J Laparoendosc Adv Surg Tech A*. 2019;29(2):147-151.
49. Chen L, Wang Q, Liu Y, et al. A meta-analysis of robotic gastrectomy versus open gastrectomy in gastric cancer treatment. *Asian J Surg*. 2022;45(2):698-706.
50. Caruso S, Patriti A, Roviello F, et al. Robot-assisted laparoscopic vs. open gastrectomy for gastric cancer: systematic review and meta-analysis. *World J Clin Oncol*. 2017;8(3):273-284.
51. Solaini L, Bazzocchi F, Pellegrini S, et al. Robotic vs. open gastrectomy for gastric cancer: a propensity score-matched analysis on short- and long-term outcomes. *Int J Med Robot*. 2019;15(5):e2019.
52. Nakauchi M, Vos E, Janjigian YY, et al. Comparison of long- and short-term outcomes in 845 open and minimally invasive gastrectomies for gastric cancer in the United States. *Ann Surg Oncol*. 2021;28(7):3532-3544.
53. Park JY, Verma A, Tran ZK, Mederos MA, Benharash P, Girgis M. Disparities in utilization and outcomes of minimally invasive techniques for gastric cancer surgery in the United States. *Ann Surg Oncol*. 2022;29(5):3136-3146.
54. Lu J, Zheng CH, Xu B, et al. Assessment of robotic versus laparoscopic distal gastrectomy for gastric cancer: a randomized controlled trial. *Ann Surg*. 2021;273(5):858-867.
55. Ojima T, Nakamura M, Hayata K, et al. Short-term outcomes of robotic gastrectomy vs. laparoscopic gastrectomy for patients with gastric cancer: a randomized clinical trial. *JAMA Surg*. 2021;156(10):954-963.
56. Jin T, Liu HD, Yang K, Chen ZH, Zhang YX, Hu JK. Effectiveness and safety of robotic gastrectomy versus laparoscopic gastrectomy for gastric cancer: a meta-analysis of 12,401 gastric cancer patients. *Updates Surg*. 2022;74(1):267-281.
57. Guerrini GP, Esposito G, Magistri P, et al. Robotic versus laparoscopic gastrectomy for gastric cancer: the largest meta-analysis. *Int J Surg*. 2020;82:210-228.
58. Shin HJ, Son SY, Wang B, Roh CK, Hur H, Han SU. Long-term comparison of robotic and laparoscopic gastrectomy for gastric cancer a propensity score-weighted analysis of 2084 consecutive patients. *Ann Surg*. 2021;274(1):128-137.
59. Guerra F, Giuliani G, Formisano G, Bianchi PP, Patriti A, Coratti A. Pancreatic complications after conventional laparoscopic radical gastrectomy versus robotic radical gastrectomy: systematic review and meta-analysis. *J Laparoendosc Adv Surg Tech A*. 2018;28(10):1207-1215.
60. Kim HI, Han SU, Yang HK, et al. Multicenter prospective comparative study of robotic versus laparoscopic gastrectomy for gastric adenocarcinoma. *Ann Surg*. 2016;263(1):103-109.
61. Beane JD, Pitt HA, Dolejs SC, Hogg ME, Zeh HJ, Zureikat AH. Assessing the impact of conversion on outcomes of minimally invasive distal pancreatectomy and pancreatoduodenectomy. *HPB (Oxford)*. 2018;20(4):356-363.
62. Xie FN, Chen J, Li ZY, et al. Impact of laparoscopic converted to open gastrectomy on short- and long-term outcomes of patients with locally advanced gastric cancer: a propensity score-matched analysis. *J Gastrointest Surg*. 2021;25(10):2484-2494.
63. Ye M, Jin K, Xu G, et al. Short- and long-term outcomes after conversion of laparoscopic total gastrectomy for gastric cancer: a single-center study. *J BUON*. 2017;22(1):126-133.
64. Kim MS, Kim WJ, Hyung WJ, et al. Comprehensive learning curve of robotic surgery discovery from a multicenter prospective trial of robotic gastrectomy. *Ann Surg*. 2021;273(5):949-956.