

Review

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Precision and Progress: Evaluating the Role of Robotic Surgery Gastric Cancer Treatment – A Comprehensive Review by TROGSS – The Robotic Global Surgical Society & EFISDS - European Federation International Society for Digestive Surgery Joint Working Group

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Review

Precision and Progress: Evaluating the Role of Robotic Surgery Gastric Cancer Treatment—A Comprehensive Review by TROGSS—The Robotic Global Surgical Society & EFISDS—European Federation International Society for Digestive Surgery Joint Working Group

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Abstract: Introduction: Robotic-assisted minimally invasive gastrectomy (RAMIG) represents a significant advancement in the surgical management of gastric cancer, offering superior dexterity, enhanced visualization, and improved ergonomics compared to laparoscopic gastrectomy (LG). This review systematically evaluates the current evidence on perioperative outcomes, oncological efficacy, learning curves, and economic considerations, providing insights into RAMIG's potential role in modern gastric cancer surgery. Methods: A thorough analysis of retrospective, prospective, and meta-analytic studies was conducted to compare RAMIG with LG. Key outcomes, including operative time, intraoperative blood loss, lymph node retrieval, postoperative complications, learning curve duration, and cost-effectiveness, were assessed. Emphasis was placed on both shortterm and long-term oncological outcomes to determine the clinical value of RAMIG. Results: Evidence indicates that RAMIG is associated with reduced intraoperative blood loss, lower morbidity rates, and a shorter learning curve, with proficiency achieved after 11-25 cases compared to 40-60 cases for LG. The robotic platform's articulated instruments and enhanced three-dimensional visualization enable more precise lymphadenectomy, particularly in complex anatomical regions. Despite these advantages, operative time remains longer, and costs remain higher due to system acquisition, maintenance, and consumable expenses. However, emerging data suggest a gradual narrowing of cost disparities. While short-term outcomes are favorable, further high-quality, multicenter studies are needed to validate long-term oncological efficacy and survival outcomes. Conclusion: RAMIG offers significant technical and clinical advantages over conventional LG, particularly in terms of precision and learning efficiency. However, the long-term oncological benefits and economic feasibility require further validation. Future research should focus on cost optimization, advanced technological integration such as near-infrared fluorescence and artificial intelligence, and multicenter trials to solidify RAMIG's role as a standard approach for gastric cancer surgery.

Keywords: Robotic-assisted gastrectomy; Minimally invasive surgery; Gastric cancer surgery; Learning curve; Lymphadenectomy

1. Introduction

Minimally invasive techniques for gastric cancer surgery have been increasingly utilized to enhance postoperative recovery for patients undergoing gastrectomy [1]. These approaches have demonstrated benefits such as reduced postoperative pain, decreased complication rates, minimal blood loss, shorter durations of hospitalization, and quicker resumption of daily activities [2]. Since its introduction in the late 1990s, robotic surgery has gained widespread adoption, with significant advancements and growing expertise over time [3,4]. Notably, robotic systems have addressed several limitations inherent to conventional laparoscopy by offering enhanced precision through tremor filtration, articulated instruments with wrist-like motion, seven degrees of freedom, and motion scaling capabilities [5,6].

Numerous proficient laparoscopic surgeons have adopted robotic surgery techniques for the treatment of gastric cancer. Within a decade of its initial application for early-stage gastric cancer, robotic gastrectomy has emerged as a safe and viable alternative to traditional laparoscopic approaches [7,8]. Despite its advantages, challenges such as high costs and the need to establish its oncological efficacy for advanced gastric cancer remain significant hurdles to broader adoption [9]. This review, conducted by a joint working group on behalf of the RObotic Global Surgical Society (TROGSS) and the European Federation of the International Society for Digestive Surgery (EFISDS), aims to provide an in-depth analysis of the current evidence surrounding robotic gastrectomy, including its clinical applications, perioperative outcomes, cost considerations, learning curve, oncological outcomes, and potential future developments. This study represents the largest review of its kind in the literature to date on RAMIG in comparison to LG. It analyzes safety outcomes in depth and includes a discussion on multidisciplinary management as well as suggestions for the as advancement of robotics in the field of minimally invasive gastrectomy for cancer.

2. Materials and Methods

We conducted a comprehensive literature search across several online databases, including the Cochrane Library, Embase, PubMed, and Web of Science, to identify studies on robotic-assisted minimally invasive gastrectomy (RAMIG) published up to June 2024. The search strategy employed a combination of subject headings and text words, incorporating terms such as "robotic" "gastrectomy," and their synonyms to ensure comprehensive coverage and minimize the chance of missing relevant studies. We included studies that compared RAMIG to conventional approaches, such as laparoscopic or open surgery, for the treatment of both cardia and non-cardia gastric cancer. Additionally, non-comparative studies and those focusing solely on robotic techniques without comparisons to conventional surgery were also included. Eligibility criteria required studies to be written in English and to report data on more than 10 patients. Articles such as reviews, study protocols, invited commentaries, studies without full-text availability, and duplicates were excluded.

3. Clinical Applications, Perioperative Outcomes, and Emerging Technologies

3.1. Evolving Indications and Applications of Robotic Gastrectomy in Gastric Cancer Management

The application of RAMIG has undergone significant evolution, paralleling advancements in laparoscopic gastrectomy (LG) for the management of gastric cancer. Initially, RAMIG was primarily indicated for early-stage gastric cancer in patients without clinical evidence of lymph node metastasis. Over time, its indications have broadened to include clinical stage T1–T2 tumors, irrespective of perigastric lymph node involvement, except for lesions suitable for endoscopic submucosal dissection (ESD) [10,11]. This expansion reflects technological advancements and an increasing body of clinical expertise. Robot-assisted surgery has become an integral part of clinical practice for GC worldwide, mirroring its adoption in other fields of abdominal and pelvic surgery. RAMIG aims to provide benefits comparable to those of LG while addressing ergonomic limitations inherent to conventional laparoscopy. Key features of robotic systems include high-resolution three-

dimensional imaging with a surgeon-controlled stable camera, tremor suppression, and articulated instruments with greater degrees of freedom, all of which contribute to an optimized surgical environment. However, the significantly higher procedural cost remains a substantial barrier to widespread adoption [12–14]. The integration of minimally invasive techniques, including RAMIG and LG, for advanced GC involving serosal invasion has been limited, particularly in regions like Korea and Japan. Nonetheless, emerging data suggest that serosal involvement may not represent an absolute contraindication for minimally invasive surgical approaches. Despite these advancements, specific limitations persist, particularly in scenarios involving large tumors, extensive lymphadenopathy, or cases requiring multi-organ resection, which can constrain the feasibility of these techniques [7,15]. Achieving an R0 resection, a critical surgical objective, necessitates precise determination of the proximal resection margin. For tumors that are either small or non-palpable, methods such as preoperative endoscopic placement of radiopaque hemoclips or intraoperative endoscopic localization have been advocated to facilitate accurate tumor localization [16–19].

The scope of lymphadenectomy in RAMIG adheres to the guidelines outlined in the Japanese Classification of Gastric Carcinoma. For clinically early-stage gastric cancer without lymph node metastasis, a D1+lymphadenectomy is recommended, whereas D2 dissection is advised for advanced gastric cancer or cases with confirmed regional lymph node involvement [15]. Notably, recent evidence indicates that RAMIG achieves lymph node retrieval rates comparable to, or even exceeding, those of LG, particularly in anatomically complex regions such as the splenic hilum and the suprapancreatic area [9]. Asian surgeons have led the exploration of RAMIG's feasibility, safety, and efficacy. In 2021, two randomized controlled trials (RCTs) comparing RAMIG to LG demonstrated lower postoperative morbidity, faster recovery, and a higher lymph node yield with RAMIG in one of the trials [13,14]. These findings were corroborated by a large propensity scorematched cohort study involving over 3,500 patients[12]. Despite these promising results, concerns about prolonged operative time and high costs remain. Ongoing research is focused on refining surgical techniques, including resection, reconstruction, anastomosis, and lymphadenectomy [20]. A Japanese phase III RCT (JCOG1907, MONA LISA study) is currently evaluating whether RAMIG can achieve superior outcomes compared to LG, particularly in reducing postoperative complications [21]. As experience with RAMIG grows, further advancements are expected. However, it remains uncertain whether these improvements will translate into better long-term survival outcomes for patients.

3.2. Evolution of Minimally Invasive Techniques in Robotic Gastrectomy

Since the first laparoscopic distal gastrectomy (LDG) was performed by Kitano in 1991 and described in 1994[22], minimally invasive approach has been accepted as the gold standard approach for distal gastrectomies[23–27].

The evidence is different for total gastrectomy because of technical difficulties of the procedure. Azagra et al first described laparoscopic total gastrectomy (LTG) for cancer in 1993[28]. Since then, many authors described the feasibility and safety of the LTG for early and recently for advanced gastric cancer(8–18). The limited adoption of LTG primarily stems from two factors: achieving adequate lymphadenectomy and performing esophagojejunostomy (EJ). The first one impacts on the oncologic safety and the second one impacts on the surgical safety. Both impact the patient's prognosis[40–44].

Various techniques of EJ construction have been described, including mechanic and hand-sewn (HS). Mechanical methods use the circular stapler (CS) and the linear stapler (LS). Up to now there is no standard on superiority and no consensus for EJ construction [41,45–48].

LTG most commonly is a laparoscopic assisted total gastrectomy (LATG) because the EJ is performed using a CS by a mini-laparotomy[49–54]. With the spread of LS by the laparoscopic approach many authors have described the advantages of side-to-side LS EJ versus end-to-side CS EJ with lower anastomotic related complication rates to performing a total laparoscopic total gastrectomy (TLTG) [37,40,48,55]. The HS EJ has already been described as feasible and safe, but it is

not frequently performed by surgeons around the world most of all because of its technical difficulties[42–44,56–59]. Many are the theoritical advantages of HS EJ: it does not require a long esophageal stump exposure, it has better blood supply, there is less tension on the sutures, and it allows an higher esophageal transection when needed and last but not least, it saves costs[60]. Another important point is the surgeon's feeling: every suture is made under good control of view by the surgeon which provides a better feeling of safety. Concerning the LS EJ, especially when it is high on the esophageal stump, the higher point of the anastomosis is poorly visualized and it is also the tension point of the EJ. Concerning the CS EJ a good visualization requires extra manipulation of the anastomosis with a risk of iatrogenic injury.

The only relevant limiting factor of the HS EJ is the difficulty of the procedure. A simplified technique using barbed suture has been described by Azagra et al (standardized Azagra's technique) to try to make this step of the surgery more simple and consequently more reproducible [56,58,59]. The authors have shown excellent results in terms of anastomotic related complications with no leakage reported.

The implementation of robotic surgery for gastric cancer may play a role in the implementation of HS EJ because the limiting factor will be overcome by using a robot, when compared to a "sewing machine".

The EJ related complications are reported ranging from 2 to 14%[61–65]. The main two are leakage and stenosis. The KLASS-03 trial for laparoscopic total gastrectomy by the Korean Laparoendoscopic Gastrointestinal Surgery Study Group reported 3,2% the incidence of anastomosis related complications[66]. The Japanese nationwide surgical case registration system study reported it as 4,4% after open total gastrectomy[67]. Particularly concerning the EJ leakage rate is reported ranging between 1,7 and 15% (average incidence 4,4%) with a related mortality up to 30%[61,63,67–70]. The Italian Research Group for Gastric Cancer (GIRCG) recently reported an EJ leakage rate of 6,6% with a related mortality of 8,6%[46]. EJ after TLTG remains a surgical and clinical challenge and the intracorporeal EJ is a controversial topic [71–73].

Mechanical methods (CS and LS) are the two worldwide most performed techniques for EJ for minimally invasive total gastrectomy. The CS is popular mostly because surgeons were familiar with the technique since the open approach and more recently, with the LS technique [49–54].

CS EJ does not require a large exposure of the esophageal stump and the esophageal transection can be higher than it is required for LS. The limiting factors of CS EJ are two: how to introduce and fix the anvil and the introduction of the instrument by a mini-laparotomy. Many techniques have been described for the introduction of the anvil including trans-oral insertion (OrVil tm), hand-sewn purse string suturing, pursestring instrument, the lift-up method and needle through esophageal stump[49,54,74–77]. Intra-corporeal purse string application of the anvils has been described but is not very easy to perform[78]. The OrVil method can cause iatrogenic damage to esophageal mucosa and to the muscular layers [49,54,74–77].

The mini-laparotomy for circular stapler insertion and the excessive traction of the incision made by the instrument can increase postoperative pain and anastomotic bleeding[50].

With minimally invasive surgery for gastric cancer LS EJ has increased in adoption and frequency recently. It can be performed during TLTG without a mini-laparotomy and it contributes to cost saving by using a cartridge of the same stapler used for other steps of the surgery. The most significant limitation of LS EJ is the inablility to construct it at a higher, more proximal localization on the esophagus. Thus, this technique requires significant dissection of the esophageal stump with, potentially, a poorer vascularization. Many authors have described the advantages of LS EJ versus CS EJ after LTG with a lower rate of anastomosis-related complications, in particular lower rates of EJ stenosis and comparable rates of leakage[37,40,48,55,79].

Robotic CS EJ has two main limiting factors: firstly the stapler needs to be manipulated by the bed-side assistant, making the procedure dependent on the technical skills of the assistant. Secondly, the robotic arms limit the access to the abdominal wall making it very difficult for the assistant to introduce and manipulate the circular stapler. For this reason LS EJ and HS EJ are the two techniques

of choice for alimentary tract reconstruction after robotic total gastrectomy. The implementation of laparoscopic surgery has enabled surgeons to become more familiar with and proficient at intracorporeal suturing and hand-sewn anastomosis construction. For this reason and with the spreading of robotic surgery, intracorporeal HS EJ could gain a central role in alimentary tract reconstruction after total gastrectomy. In 2011 So et al first described the hand-sewn technique for intracorporeal EJ following TLTG. They reported as an important advantages that it does not require a large mobilization of the esophageal stump and it has lower tension on the EJ[44]. Since then, a few other authors have described the hand-sewn EJ with excellent results[41–44,57,60,80–83]. The learning curve and experience needed to perform an HS EJ have been discussed in literature[41,81,82,84,85] and the use of barbed suture has proven to significantly shorten the suturing time by minimally invasive surgery[56,86–93].

The results of barbed HS EJ are very convincing and comparable to those in literature concerning non-barbed HS EJ making the technique much more simple to perform [41,42,44,57,80–82,94].

Robotic surgery may overcome the two main reasons behind the low implementation of minimally invasive approach for total gastrectomy, hence allowing an adequate lymphadenectomy and performing a safe and reproducible esophagojejunostomy according to surgeon's preferences. The hand-sewn esophagojejunostomy after robotic total gastrectomy may eventually become the gold standard.

3.3. Perioperative Outcomes

3.3.1. Operative Time

Numerous studies, including randomized controlled trials (RCTs), have consistently demonstrated that RAMIG typically requires longer operative times compared to LG. Reported durations for RAMIG range from 202 to 439 minutes, while LG durations vary between 171 and 361 minutes [7,95,96]. Specific RCTs have confirmed this difference, with Wang G et al. reporting mean durations of 242.7 minutes for RAMIG versus 192.4 minutes for LG (p = 0.002), Lu et al. documenting 201.2 minutes for RAMIG compared to 181.6 minutes for LG (p < 0.001), and Ojima T et al. noting 297 minutes for RAMIG versus 245 minutes for LG (p = 0.001) [13,14,97]. Similarly, a non-randomized prospective study by Kim H et al. found RAMIG to take significantly longer than LG, with durations of 221 and 178 minutes, respectively (p < 0.001) [98]. Other prospective studies have reported RAMIG durations ranging from 313 to 372 minutes [99–101]. Retrospective studies, both multi-institutional and single-center, have also demonstrated longer operative times for RAMIG, with differences typically ranging from 20 to 50 minutes compared to LG [12,102–107].

An umbrella review of 14 systematic reviews and meta-analyses further confirmed that RAMIG involves longer operative times compared to LG, encompassing 146 primary studies and over 37,500 patients [9]. Statistically significant differences in operative duration were observed in eleven studies [6,108–117]. This prolonged operative time has been attributed to additional steps, such as robotic docking and undocking, as reported in the literature [118]. However, the evidence supporting this association is relatively weak. Liu et al. analyzed contributing factors and found that while the effective operative time and frequency of instrument exchanges were similar between RAMIG and LG, "junk time," including robotic arm setup and positioning, was significantly longer for RAMIG [119].

Despite advancements in surgical expertise and familiarity with robotic systems, extended operative time remains a notable limitation of RAMIG. A prior meta-analysis confirmed a mean operative time of 267.34 minutes for RAMIG compared to 220.48 minutes for LG (p < 0.001) [120]. Conflicting findings do exist; Pan et al. reported no significant differences in operative times between RAMIG and LG [121], while Omori T et al. recently indicated that RAMIG could achieve shorter operative times than LG through training and accumulated expertise [122].

3.3.2. Blood Loss

Blood loss during RAMIG has been extensively studied, with varying results across investigations. Several analyses have demonstrated a significant reduction in intraoperative blood loss with RAMIG compared to LG, with estimates ranging from 46 to 176 mL for RAMIG and 34 to 212 mL for LG [5,95,96]. Furthermore, three RCTs reported significantly lower intraoperative blood loss during RAMIG compared to LG or open gastrectomy (OG). Wang G et al. documented mean blood loss of 94.2 mL for RAMIG versus 152.8 mL for LG, Pan HF et al. observed 41.3 mL for RAMIG compared to 83.7 mL for LG, and Lu J et al. reported 41.2 mL for RAMIG versus 55.7 mL for LG [14,97,121]. However, some studies have reported conflicting findings. An RCT by Ojima T et al. found no significant difference in blood loss between RAMIG and LG (25 mL for both, p = 0.18) [13], while a non-randomized prospective study by Kim H et al. also found similar results (50 mL vs. 55 mL, p = 0.318) [98]. Despite these discrepancies, most studies report a reduction in intraoperative bleeding with RAMIG, with only three studies failing to show statistical significance in this difference [105,123,124]. This reduction may be attributed to the enhanced visualization provided by the robotic 3D optical system, combined with superior precision in fine movements and tremor-filtering capabilities [125].

Prospective studies from Japan have further highlighted minimal intraoperative blood loss during RAMIG, with estimates ranging from 15 to 20 mL [99–101]. Retrospective studies have produced more variable outcomes. For instance, Li et al. observed significantly lower blood loss with RAMIG compared to LG (126.8 vs. 142.5 mL, p < 0.0001) [12], whereas another study indicated no significant differences (20 vs. 15 mL, p = 0.149) [102]. Among seven single-center retrospective studies, four demonstrated the superiority of RAMIG in reducing intraoperative blood loss [105–107,122], while two reported no significant differences between RAMIG and LG [104,126]. Interestingly, one study observed slightly higher blood loss with RAMIG compared to LG (37 vs. 28 mL, p = 0.005) [103]; however, the small volumes in both groups limit the practical significance of these findings. Across most studies, the difference in estimated intraoperative blood loss between RAMIG and LG was approximately 20 mL.

Meta-analyses provide further clarity, showing significantly lower blood loss during RAMIG compared to LG (98.77 vs. 115.02 mL, p < 0.001) [120]. This reduction is largely attributed to the technological innovations of RAMIG, including high-resolution 3D visualization and tremor-filtered, articulated instruments, which enhance vascular identification and control of intra-abdominal bleeding. Although the short-term clinical significance of reduced blood loss may be minimal, its potential impact on long-term oncological outcomes, particularly in advanced gastric cancer, remains an important area of research [102,127].

3.3.3. Morbidity

To reliably evaluate morbidity, only complications classified as Clavien–Dindo (CD) grade \geq IIIa were included in most analyses, as these events are potentially life-threatening and often require surgical, endoscopic, or radiological interventions. Such complications can lead to prolonged hospital stays and increased healthcare costs [128,129]. While many studies have reported similar overall complication rates between RAMIG and LG, the specific findings vary. A recent multicenter prospective study observed complication rates of 11.9% for RAMIG and 10.3% for LG, with major complications (CD grade \geq IIIa) occurring at a rate of 1.1% in both groups [98]. Conversely, Ojima T et al. reported significantly fewer overall complications with RAMIG compared to LG (5.3% vs. 16.2%, p=0.01), although no significant differences were observed for intra-abdominal infectious complications such as anastomotic leakage, pancreatic fistula, or abscesses [13]. Another study highlighted significantly lower rates of pancreatic fistula in RAMIG compared to LG (2.3% vs. 11.4%), which was attributed to the precision of the robotic system, reducing pressure on the pancreas and minimizing parenchymal injury [124].

When CD grade II complications were included, two RCTs by Lu J et al. (7.7% vs. 16.9%, p = 0.006) and Ojima T et al. (8.8% vs. 19.7%, p = 0.02) demonstrated superior outcomes for RAMIG

compared to LG [14,124]. Non-randomized studies corroborate these findings. Kim HI et al. reported a morbidity rate of 1.1% for both RAMIG and LG, with no significant difference (p = 0.999) [98]. A multi-institutional prospective study showed that RAMIG significantly reduced morbidity rates compared to LG (2.45% vs. 6.4%, p = 0.0018) [99]. Single-arm prospective studies by Okabe H et al. and Tokunaga M et al. also reported low morbidity rates for RAMIG, with CD grade \geq IIIa rates of 2.6% and 3.3%, respectively [100,101]. Multi-institutional retrospective studies have similarly reported low morbidity rates for RAMIG (1.3% to 5.4%), which are comparable to those of LG (2.9% to 4.7%) [12,102,130].

Among single-center retrospective studies employing propensity score-matched (PSM) analyses, several have demonstrated a clear advantage of RAMIG. Wang WJ et al. observed morbidity rates of 8.9% for RAMIG versus 17.5% for LG (p = 0.002), Shibasaki S et al. reported 3.7% for RAMIG versus 7.6% for LG (p = 0.033), and Omori M et al. noted rates of 1.0% for RAMIG compared to 4.8% for LG (p = 0.007) [126,131,132]. Furthermore, Hikage M et al. found that RAMIG significantly reduced CD grade \geq II intra-abdominal infectious complications compared to LG (4.4% vs. 9.4%, p = 0.015), although no significant difference was observed for total complications (RAMIG vs. LG: 13.2% vs. 18.4%, p = 0.074) [132].

A meta-analysis conducted by Guerrini G et al. further substantiated these findings, demonstrating significantly lower rates of CD grade \leq IIIa surgical complications in RAMIG compared to LG. The pooled analysis revealed complication rates of 4.13% (150/3631) for RAMIG versus 6.44% (498/7727) for LG, with an odds ratio (OR) of 0.66 (95% CI 0.49–0.88, p = 0.005) [120].

3.3.4. Mortality

No mortality was reported in four RCTs and four prospective studies evaluating RAMIG [13,97–101,121]. Similarly, large-scale multi-institutional retrospective analyses conducted in East Asia demonstrated exceptionally low mortality rates for RAMIG , ranging from 0% to 0.2%, with no statistically significant differences when compared to LG [12,102,130]. Single-center retrospective studies further supported these findings, with reported mortality rates ranging from 0% to 0.9% for RAMIG , again comparable to those of LG [103,105–107,122,126].

However, some studies reported conflicting trends. A multi-institutional retrospective analysis conducted in the United States observed slightly higher mortality rates for both RAMIG (4.5%) and LG (2.7%), though the difference was not statistically significant [133]. Similarly, six meta-analyses indicated a higher mortality rate with RAMIG compared to LG, while Hu LD et al. reported a lower mortality rate for RAMIG but none of these findings achieved statistical significance [108,109,111,112,114,117,134].

A recent meta-analysis by Guerrini G et al. further substantiated these observations, showing no significant difference in mortality rates between RAMIG and LG. The pooled mortality rates were 0.36% (16/4378) for RAMIG and 0.30% (31/10354) for LG, with an odds ratio (OR) of 1.43 (95% confidence interval [CI]: 0.77–2.65, p = 0.25) [120]. The peri-operative outcomes are detailed in Table 1.

Reference (year/country)	Study design	Patients for analysis (n)	≥ Stage II (%)	TG or SG (%)	Morbidity (%)	Operative time (min)	Estimated blood loss (mL)	Length of stay after procedure (days)
Kim et al. 2016, South Korea [98]	Prospective	RG: 185 LG: 185	19 10	16 16	1.1 1.1 (p = 0.999)	221 178 (p < 0.001)	50 55 (p = 0.318)	6 6 (p = 0.862)
Tokunaga et al. 2016, Japan [101]	Prospective	RG: 120	1	12	3.3	348.5	19	9
Wang et al.		RG: 151	76	37	2.6	243	94	5.6
2016, China [97]	RCT	OG: 145	79	31	2.8 ($p = 0.756$)	192 $(p = 0.002)$	153 (<i>p</i> < 0.001)	6.7 $(p = 0.021)$

Pan et al. 2017, China [121]	RCT	RG: 102 LG: 61	78 89	65 74	1.0 6.6 (N.D.)	153 152 (p = 0.717)	41 84 (<i>p</i> < 0.001)	3.8 5.4 (<i>p</i> < 0.001)
Okabe et al. 2019, Japan [100]	Prospective	RG: 115	30	37	2.6	372	15	12
Uyama et al. 2019, Japan [99]	Prospective	RG: 326	12	22	2.45	313	20	9
Wang et al. 2019, China [126]	Retrospective	RG: 354 LG: 354	76 76	43 44	$8.9 \\ 17.5 \\ (p = 0.002)$	242 238 $(p = 0.246)$		10.2 11.6 (<i>p</i> < 0.001)
Ryan et al. 2020, USA [133]	Retrospective	RG: 631 LG: 1262	66 66	28 28	N.D.	N.D.	N.D.	10.2 11.6 (<i>p</i> < 0.001)
Shibasaki et al. 2020, Japan [103]	Retrospective	RG: 354 LG: 354	38 37	30 29	3.7 7.6 $(p = 0.033)$	360 347 (p = 0.001)	37 28 (p=0.005)	$ \begin{array}{c} 12 \\ 13 \\ (p = 0.001) \end{array} $
Li et al. 2020, China [160]	Retrospective	RG: 1776 LG: 1776	35 35	31 31	2.5 2.9	248.5 220 (<i>p</i> < 0.001)	127 143 (<i>p</i> < 0.001)	9.2 9.3 (<i>p</i> = 0.371)
Ojima et al. 2021, Japan [13]	RCT	RG: 113 LG: 117	42 40	41 32	$5.3 \\ 16.2 \\ (p = 0.01)$	297 245 (p = 0.001)	25 25 $(p = 0.18)$	12 13 (p = 0.93)
Lu et al. 2021, China [14]	RCT	RG: 141 LG: 142	N.D.	0 0	1.4 1.4	201 182 (<i>p</i> < 0.001)	41 56 (p = 0.045)	7.9 8.2 $(p = 0.062)$
Suda et al. 2022, Japan [102]	Retrospective	RG: 2671 LG: 2671	N.D.	14 14	$4.9 \\ 3.9 \\ (p = 0.084)$	354 268 (<i>p</i> < 0.001)	20 15 (p = 0.149)	10 11 (p < 0.001)
Shimoike et al. 2022, Japan [103]	Retrospective	RG: 336	33	24	5.4	370	0	10

3.3.5. Economic Evaluation

A clear cost-effectiveness analysis of robotic surgery for gastric cancer remains challenging due to limited data, with most studies providing only brief mentions of cost. Nonetheless, an extensive literature review was conducted, identifying publications that report substantial findings on the financial aspects of robotic surgery in gastric cancer [12,14,98,106,107]. Currently, the robotic approach is associated with higher overall costs, as confirmed by a recent systematic review and meta-analysis [135]. This is largely because many centers have only recently implemented robotic systems. The elevated costs primarily stem from system maintenance and the procurement of new equipment. In contrast, laparoscopic systems are widely available and, in most cases, already amortized. As a result, indirect costs, such as equipment depreciation, are the main contributors to the higher expenses associated with robotic surgery, whereas the direct, procedure-related costs of robotic surgery may actually be lower. It is also important to note that the majority of cost-related data originates from Asian centers, where cost calculations and billing practices differ significantly from those in Europe or the United States. Interestingly, a newly published randomized controlled trial reported only a modest difference of 3% in hospitalization costs between the robotic and

laparoscopic groups ($$15,953.41 \pm 3,533.91$ vs. $$12,198.26 \pm 2,761.27$, P < 0.001) [136]. This suggests that, similar to trends observed in bariatric surgery, the costs of robotic surgery for gastric cancer are expected to decrease steadily over time. As robotic systems become more prevalent and widely adopted, this trend will likely facilitate broader application of robotic technology in gastric cancer surgery.

3.3.6. Oncological Outcomes

The number of studies evaluating long-term outcomes in RAMIG has grown alongside reports on short-term outcomes. A total of nine studies and one meta-analysis were included in the assessment of long-term oncological outcomes [12,104,106,107,120,132,137–140]. Among these, only one prospective study specifically evaluated long-term outcomes following RAMIG. Hikage et al. reported highly favorable results, with 5-year OS and RFS rates of 96.7%, despite 12.5% of the patient cohort having advanced gastric cancer [132].

Two multi-institutional retrospective studies further analyzed long-term outcomes. Li et al. found that the 3-year and 5-year OS and DFS rates were comparable between RAMIG and LG [12]. In contrast, another study demonstrated significantly better 3-year OS rates for RAMIG compared to LG (96.3% vs. 89.6%, p = 0.009) using the inverse probability of treatment weighting method. Although a trend toward improved 3-year RFS was observed for RAMIG (92.3% vs. 87.2%), it did not reach statistical significance (p = 0.073) [137]. Subgroup analyses revealed that RAMIG significantly improved 3-year OS (99.7% vs. 94.4%, p = 0.004) and 3-year RFS (99.7% vs. 93.7%, p = 0.003) rates in patients with pathological stage IA disease [137]. Propensity score matching analysis further confirmed the superior 3-year OS (97.1% vs. 89.2%; p < 0.001) and RFS (94.2% vs. 86.7%; p = 0.002) rates in the RAMIG group compared to LG [137].

Six single-center retrospective studies also compared long-term oncological outcomes between RAMIG and LG. Most of these studies found no significant differences in 3-year or 5-year OS and RFS rates between the two approaches [104,106,107,138–140]. However, one study highlighted significantly improved 5-year OS (70.4% vs. 50.2%, p = 0.039) and 5-year RFS (74.1% vs. 44.5%, p = 0.005) rates for RAMIG in patients with pStage II/III GC after propensity score matching [140].

A meta-analysis further examined recurrence rates, reporting a lower but not statistically significant recurrence rate in the RAMIG group compared to the LG group (9.9% vs. 13.5%, p = 0.25) [120].

3.3.7. Learning Curve

One proposed advantage of RAMIG is its relatively shorter learning curve compared to LG, particularly for surgeons with prior experience in laparoscopic surgery. Evidence suggests that RAMIG can be performed safely during the initial phase when conducted by surgeons already proficient in LG techniques. Retrospective studies and systematic reviews have shown that experienced gastric cancer surgeons typically achieve competency in RAMIG after approximately 11–25 cases [100,106,122–124,130,131,141,142], whereas LG requires a longer learning period, with 40–60 cases needed to reach proficiency [5,107,138,143,144].

Zhou et al. reported that two surgeons with prior LG experience reached a learning plateau for RAMIG after 12 and 14 cases, as assessed using the cumulative summation score method [144]. Similarly, Park et al. demonstrated that three experienced laparoscopic surgeons achieved stable operative times after 6, 9.6, and 18.1 cases, respectively, using a nonlinear least-squares analysis [123]. Huang et al. further compared the learning curves for RAMIG and LG, showing that RAMIG operative and docking times stabilized after 25 cases, whereas LG required approximately 41 procedures for operative times to plateau [145].

A multi-institutional retrospective study by Shimoike et al. evaluated surgeons transitioning to RAMIG after achieving certification under the Endoscopic Surgical Skill Qualification System (ESSQS), which validates expertise in LG. Among 20 surgeons, most had performed ≥100 LG procedures; however, at least 11 cases of RAMIG were required to achieve stable operative times and reduce surgeon fatigue. Interestingly, prior LG experience did not significantly impact operative time or morbidity rates in RAMIG [130].

The learning curve for younger-generation surgeons, who started RAMIG after acting as assistant surgeons in at least 50 procedures, has also been analyzed. Despite being early in their RAMIG experience, these surgeons—having acquired ESSQS certification—achieved learning plateaus after 5, 7, 7, 8, and 11 cases (median: 7 cases) [142]. This suggests that prior exposure as an

assistant and early familiarity with robotic systems significantly shortens the learning curve for RAMIG.

Notably, there is currently no direct evidence evaluating the learning curve for RAMIG among surgeons without prior LG experience. While such an analysis would provide valuable insights, it remains challenging due to the widespread adoption of LG as the standard minimally invasive approach in recent years.

Collectively, these findings underscore the shorter and more manageable learning curve of RAMIG compared to LG, especially for surgeons with substantial experience in LG or prior exposure to robotic systems. The enhanced visualization, tremor-filtered instrumentation, and ergonomic advantages of robotic platforms may contribute to this improved adaptability, ultimately facilitating quicker skill acquisition.

3.4. New Technologies: Image Guided Surgery

Fluorescent-guided surgery has significantly advanced over the past few years, contributing to safer and more precise procedures across various medical specialties. In gastric cancer, this technique shows promise in multiple stages of the operation. The primary applications of fluorescent image-guided surgery include the identification of lymphatic structures for accurate lymphadenectomy and sentinel node biopsy, tumor localization, perigastric vessel visualization, and intraoperative angiography. Currently, the da Vinci Xi® robotic system, developed by Intuitive Surgical Inc. (Sunnyvale, CA, USA), incorporates an integrated fluorescence imaging technology known as Firefly®. More recently, CMR Surgical Ltd. (Cambridge, UK) announced the development of vLimeLiteTM, a new integrated fluorescence system for its Versius® Plus surgical robotic platform.

3.4.1. Near Infrared Fluorescent Guided Lymphadenectomy

It has been established that standard D2 lymphadenectomy should be considered the gold standard for the treatment of locally advanced gastric cancer [146,147]. Intraoperative visualization of lymphatic vessels can facilitate proper lymph node dissection. Near-infrared fluorescence (NIRF)-guided lymphography has been shown to enhance lymph node visualization, increase the number of retrieved lymph nodes during lymphadenectomy, and potentially allow for tailored lymphadenectomy in cases of non-standard lymph node visualization outside the classic D2 template [148–151].

In a study by Jeon et al., a comparison of standard laparoscopy, indocyanine green (ICG)-guided laparoscopy, and ICG-guided robotic gastrectomy demonstrated that the robotic ICG-guided approach achieved the highest rate of proper lymphadenectomy [152]. Notably, in obese patients, where lymphadenectomy is typically more challenging, ICG-guided laparoscopic and robotic gastrectomy resulted in the resection of a greater number of lymph nodes. These approaches also demonstrated a significantly higher rate of retrieval of 16 or more lymph nodes, as well as 30 or more lymph nodes, compared to non-ICG-guided techniques [153].

A meta-analysis of NIRF-guided lymphadenectomy in robotic gastric cancer resection, based on five studies and 312 patients, found that the fluorescent-guided group retrieved a significantly higher number of lymph nodes. Moreover, this group experienced a shorter operative time [154]. However, in the Danish trial examining NIRF lymphography for gastroesophageal junction cancers, while more lymph nodes were retrieved in the fluorescence group, none of the additional lymph nodes were metastatic [155].

The recent phase 3 randomized clinical trial by Chen et al. demonstrated that the mean number of lymph nodes retrieved was significantly greater in the ICG group (50.5 vs. 42.0). Furthermore, both OS and DFS were significantly improved in the ICG group. Interestingly, the overall recurrence rate was considerably lower in the ICG group (18.8% vs. 31%) [156].

3.4.2. Near-Infrared Fluorescence-Guided Sentinel Node Biopsy

D2 lymphadenectomy remains the gold standard for the treatment of advanced gastric cancer; however, less extensive resections may be appropriate in early-stage disease. Due to the complex lymphatic drainage of the stomach, the concept of sentinel nodes is still under investigation. Several studies have described this approach in both open and laparoscopic surgeries [157]. In a preclinical animal model using the Da Vinci Si system, fluorescent sentinel node biopsy with ICG and mannose-labeled magnetic nanoparticles was successfully tested [158]. Additionally, sentinel node biopsy has been employed to preserve pyloric lymph nodes during robotic proximal gastrectomy, as demonstrated by Ikoma et al. [159].

3.4.3. Tumor Localization

The injection site for lymphography has been utilized as a landmark for tumor localization in early-stage gastric cancer to ensure proper margins during partial gastrectomy. Liu et al. used this approach to obtain adequate resection margins [160]. For instance, Nakanishi et al. described a method in which 0.1 mL of ICG was endoscopically injected 1 cm proximal to the tumor during preoperative preparation [161]. During robotic gastrectomy with the Firefly® mode, the fluorescent signal from the injection site was used to guide resections, with surgeons aiming to maintain a minimum of a 2 cm margin by resecting at the edge of the fluorescent signal.

3.4.4. Perigastric Vessel Localization

The localization of perigastric vessels plays a crucial role in ensuring vascular preservation during gastrectomy. In a study by Kim et al., ICG was injected immediately after right gastroepiploic vein ligation during laparoscopic and robotic gastrectomies to visualize the infrapyloric artery, crucial for pylorus-preserving gastrectomy, as well as the accessory splenic artery, necessary to prevent inferior polar infarction of the spleen [162]. The infrapyloric artery was visualized in 80% of cases, while the accessory splenic artery was detected in all cases. Lee et al. proposed an approach to localize the accessory left hepatic artery in 31 patients undergoing laparoscopic or robotic surgery. After clamping the artery near the left hepatic lobe, ICG was injected intravenously, and reduced fluorescence in the left hepatic lobe was observed to confirm its location [163].

Robotic distal gastrectomy has also been employed to mitigate the risk of remnant gastric ischemia associated with distal gastrectomy and distal pancreatectomy. Ito et al. demonstrated the visualization of the left inferior phrenic artery, which was found to sufficiently perfuse the remnant stomach even after splenic artery ligation [164].

3.4.5. Angiography

Anastomotic leakage remains one of the most serious complications following gastrectomy, with reported rates ranging from 1.2% to 6.7% [157,165,166]. Intraoperative ICG-based fluorescent angiography is a promising method to predict and potentially prevent anastomotic leakage. Hayakawa et al. evaluated blood flow in the duodenal wall using the Firefly® system during distal gastrectomy [167]. Among 55 patients, 10 were found to have insufficient blood supply, necessitating additional resection of the duodenal stump. Postoperative outcomes were comparable between patients with good and insufficient vascularization. Interestingly, patients with inadequate blood supply had a higher prevalence of aberrant branching of the left hepatic artery compared to those with adequate vascularization.

3.5. Current Achievements, Remaining Barriers, and Future Perspectives

The evolution of RAMIG marks a pivotal advancement in gastric cancer surgery, combining technological precision with clinical feasibility. The evidence synthesized in this review underscores several notable advantages of RAMIG over LG, including reduced intraoperative blood loss, lower morbidity rates, and a significantly shorter learning curve for surgeons proficient in laparoscopic techniques [13,137]. Enhanced three-dimensional visualization, tremor-filtered instruments, and

greater dexterity offered by robotic platforms have enabled safer, more precise lymphadenectomy, particularly in anatomically complex regions, such as the splenic hilum and around the celiac axis. Furthermore, advancements in reconstruction techniques, including robotic hand-sewn esophagojejunostomy, have improved procedural outcomes and minimized anastomotic complications [102,126]. These technical benefits have translated into improved short-term outcomes, with evidence suggesting comparable or superior oncological adequacy in lymph node retrieval and margin status when compared to LG [12,106,120].

Nevertheless, several challenges persist. The financial burden of RAMIG, primarily driven by system acquisition, maintenance costs, and consumables, remains a major limitation, particularly in Western healthcare settings where cost-effectiveness plays a critical role in surgical decision-making [135,136]. Encouragingly, recent studies show a narrowing cost gap between RAMIG and LG, suggesting that increasing adoption, system familiarity, and competition among robotic platforms may help drive costs down over time. Despite the promising short-term outcomes, long-term oncological efficacy, including OS and RFS, remains to be validated through large-scale, multicenter RCTs with extended follow-up periods [137].

This study has several limitations that are inherent to its design as a literature review, therefore relying on the available literature on reported data and the unavoidable issue of bias which may be a part of the individual studies analyzed. However, meticulous attention to detail on our review and analysis of the literature with strict search and inclusion criteria has procured minimizing these limitations with rigorous methodology.

Looking forward, further research should focus on several critical areas. Firstly, long-term oncological outcomes must be explored across diverse populations, particularly for patients with advanced gastric cancer, to confirm the oncological non-inferiority or superiority of RAMIG compared to LG and open gastrectomy. Secondly, the integration of emerging technologies such as NIRF-guided lymphadenectomy, real-time vascular assessment, and artificial intelligence-assisted navigation holds significant promise for improving surgical precision and enhancing patient outcomes [152,156,168] Comparative cost-effectiveness studies across healthcare systems in Asia, Europe, and the Americas will also be pivotal in addressing economic concerns and ensuring equitable access to robotic surgery.

4. Conclusions

RAMIG represents a highly promising technique in the surgical management of gastric cancer, offering clear advantages in technical precision, reduced complications, and a manageable learning curve. While financial constraints and long-term data gaps remain, the continued refinement of robotic platforms and the integration of adjunct technologies will likely solidify RAMIG as a cornerstone in gastric cancer surgery. Future collaborative efforts among surgeons, engineers, and healthcare policymakers will be essential to overcome existing barriers and fully harness the potential of robotic surgery for improved global patient care.

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Abbreviations

The following abbreviations are used in this manuscript:

RAMIG Robotic-assisted minimally invasive gastrectomy

LG Laparoscopic Gastrectomy

OG Open Gastrectomy

LTG Laparoscopic Distal Gastrectomy
LTG Laparoscopic Total Gastrectomy

LATG Laparoscopic Assisted Total Gastrectomy
TLTG Total Laparoscopic Total Gastrectomy

CS Circular Stapler
LS Linear Stapler
HS Hand-Sewn

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