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# Current role of minimally invasive approaches in the treatment of early gastric cancer

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## Abstract

Despite declining incidence, gastric cancer remains one of the most common cancers worldwide. Early detection in population-based screening programs has increased the number of cases of early gastric cancer, representing approximately 50% of newly detected gastric cancer cases in Asian countries. Endoscopic mucosal resection and endoscopic submucosal dissection have become the preferred therapeutic techniques in Japan and Korea for the treatment of early gastric cancer patients with a very low risk of lymph node metastasis. Laparoscopic and robotic resections for early gastric cancer, including function-preserving resections, have propagated through advances in technology and surgeon experience. The aim of this paper is to discuss the recent advances in minimally invasive approaches in the treatment of early gastric cancer.

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**Key words:** Endoscopy; Endoscopic resection; Endo-

scopic mucosal resection; Endoscopic submucosal dissection; Laparoscopic resection; Early gastric cancer; Pylorus preserving gastrectomy; Sentinel lymph node; Robotic gastrectomy

**Core tip:** Early gastric cancer (EGC) is associated with favorable prognosis and there have been many efforts made to minimize the invasiveness of resection. Curative minimally invasive approaches utilized for EGC include endoscopic, laparoscopic and robotic approaches, and sentinel lymph node biopsy. Endoscopic resections have been shown to be safe and effective treatments for carefully selected patients with EGC. In patients with EGC that are not candidates for endoscopic resection, laparoscopic and robotic resections allow for the appropriate curative resection and lymphadenectomy with the benefits of minimally invasive surgery, including improved pain, reduced blood loss, and shorter hospital length of stay.

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## INTRODUCTION

Although the incidence of gastric cancer has declined, it remains one of the most common causes of cancer-related mortality worldwide<sup>[1,2]</sup>. There are noted regional differences in gastric cancer epidemiology between East Asian and Western nations. In Japan and Korea, where the incidence of gastric cancer remains high, population-based screening with double-contrast barium radiography and/or endoscopy has allowed for earlier detection and presumably better survival<sup>[3,4]</sup>. Analysis of a Japanese nationwide

registry of gastric cancer revealed that 48.8% of cases currently treated are early stage disease<sup>[5]</sup>. However, in the West, late presentation of the disease still predominates<sup>[6]</sup>.

Surgical resection remains the cornerstone of treatment in gastric cancer and prognosis is dependent on the stage at time of detection. Early gastric cancer (EGC) is defined as cancer in which tumor invasion is confined to the mucosa or submucosa (T1 cancer), regardless of lymph node involvement<sup>[7]</sup>. Long term survival data from Japan revealed that the 5-year cancer specific survival rates of EGC are 99% when limited to the mucosa and 96% when the submucosa is invaded<sup>[8,9]</sup>. Furthermore, depth of cancer invasion plays a role in the risk of lymph node (LN) metastasis. When gastric cancer is limited to the mucosa, the incidence of LN metastasis is less than 3% and rises to approximately 20% with submucosal involvement<sup>[8,9]</sup>.

As EGC is associated with favorable prognosis, there have been many efforts made to minimize the invasiveness of resection. Minimally invasive approaches utilized for curative treatment of EGC include endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), laparoscopic and robotic approaches, and sentinel lymph node biopsy<sup>[10]</sup>. The aim of this paper is to describe and discuss the recent advances in minimally invasive approaches in the treatment of EGC.

## ROLE OF THERAPEUTIC ENDOSCOPY IN THE TREATMENT OF EARLY GASTRIC CANCER

### *Endoscopic resection techniques in the treatment of EGC*

Endoscopic approaches in the treatment of EGC were first performed in Japan in 1974<sup>[8]</sup>, but it was not until 1984 that EMR was first described<sup>[11]</sup>. Initially, EMR technique involved injecting saline under the lesion thus raising the tissue and allowing it to be grasped for snaring<sup>[11]</sup>. Over time, EMR has evolved through the use of different injection solutions, such as hypertonic saline with dilute epinephrine, addition of cap-fitted panendoscopes, and variceal ligation devices to capture the lesions<sup>[12-15]</sup>. The main disadvantage of EMR is that for lesions larger than 15mm, a piecemeal pathological specimen is inevitable, greatly impacting pathologists' ability to adequately stage patients<sup>[8,16]</sup>. ESD was developed at the National Cancer Center Hospital in Japan to overcome the limitations of EMR. In comparison with EMR, ESD allows for the resection of larger EGC lesions *en bloc* by dissection along the submucosal plane, thus preserving the specimen for more accurate pathologic assessment<sup>[17-20]</sup>. Resection with ESD, however, requires more advanced endoscopic skills and instrumentation to perform.

### *Pathological specimen processing*

Endoscopic resection provides a specimen that will allow for assessment of the depth of tumor invasion, degree of differentiation and presence of lymphovascular invasion<sup>[21,22]</sup>.

Assessment of the horizontal and vertical margins of the specimen are completed to confirm adequate resection<sup>[23]</sup>. Although, no lymph nodes are assessed pathologically, this information allows for prediction of the risk of LN metastasis based on published data of patients with similar pathological staging<sup>[24]</sup>. Importantly, both EMR and ESD allow for pathological staging without undermining any future surgical intervention.

### *Indications for endoscopic resection*

EGC carries a favorable prognosis when treated with standard surgical resection and lymphadenectomy. Since EMR and ESD are not accompanied by lymphadenectomy, it is imperative to carefully determine the indications for endoscopic resection<sup>[25]</sup>. Ideally, endoscopic resection would be reserved for small, intramucosal EGC of intestinal histology type, in which LN involvement is very unlikely<sup>[8,25]</sup>. Large lesions, or those with diffuse histology type, are more likely to invade into the submucosa and exhibit metastasis to the LNs, making them poor candidates for endoscopic resection<sup>[26]</sup>. In Japan, indications for EMR and ESD are for well-differentiated EGC confined to the mucosa (depth T1a), measuring less than 2 cm in diameter, and without ulceration<sup>[23]</sup>. In the United States, National Comprehensive Cancer Network guidelines for tumors confined to the mucosa state that EMR is considered appropriate for lesions less than 1.5 cm, and ESD for lesions less than 3 cm<sup>[27]</sup>. Lesions selected for endoscopic resection should be devoid of lymphovascular invasion<sup>[28]</sup>. Importantly, these guidelines recommend that endoscopic resection for EGC be performed at high-volume centers.

The application of ESD has been explored beyond the standard indications for cancers with a very low probability of LN metastasis. Extended indications were proposed following the study of 5265 patients with EGC who underwent a gastrectomy and D2 lymphadenectomy by Gotoda *et al.*<sup>[29]</sup>, which revealed that these patients had no risk or a lower risk of lymph node metastasis than risks of mortality from a gastrectomy. Proposed extended indications for ESD include T1a tumors that are (1) differentiated without ulceration beyond 2 cm in size; (2) differentiated with ulceration up to 3 cm; and (3) undifferentiated without ulceration up to 2 cm. Large scale feasibility studies showed no differences in the 5-year overall (97.1%) and disease-specific (100%) survival rate of curative resection between the primary and expanded indications for endoscopic resections<sup>[30]</sup>. However, these extended indications remain investigational. Long-term ESD results from prospective clinical trials by the Japan Clinical Oncology Group (JCOG 0607 study) are pending, which may validate the expanded ESD indications<sup>[31]</sup>. JCOG 0607 study, a phase II trial with 330 patients enrolled from 26 institutions, aims to evaluate the efficacy, safety and 5-year overall survival (OS) of patients undergoing ESD resection of T1a EGC under the expanded endoscopic treatment guidelines<sup>[31]</sup>.

### Outcomes for endoscopic resection

Although no randomized controlled studies (RCTs) exist comparing endoscopic resections with formal surgical resections<sup>[32]</sup>, cohort studies have revealed that EMR treated patients had 5 and 10 year disease-specific survival of greater than 95% and the incidence of recurrence is approximately 6%<sup>[33]</sup>. In addition, these studies revealed that endoscopic approaches had favorable complication rates and quality of life compared to formal surgical resections<sup>[33]</sup>. ESD has also been shown to result in higher complete resection rates and recurrence-free rates when compared to EMR<sup>[34]</sup>.

Complications from endoscopic resections include pain, bleeding and perforation. To prevent delayed bleeding following therapeutic endoscopy, patients are kept fasting the day of the surgery and are asked to begin fluid intake the day following resection and to resume a regular diet the second day after resection<sup>[8]</sup>. Resected gastric submucosal beds close within 6-8 wk, and patients are discharged on proton pump inhibitors for that duration<sup>[8,25]</sup>. Perforations are commonly closed with the aid of endoclips and often do not require additional surgical intervention<sup>[8,25]</sup>. Although Oda *et al*<sup>[34]</sup>, in their retrospective multicenter study, revealed that the 3-year recurrence-free rate was higher with ESD than EMR (97.6% *vs* 92.5% respectively), ESD also proved to be associated with higher perforation rates (3.6% *vs* 1.2% respectively).

### Follow-up after endoscopic resection

Endoscopic surveillance following definitive treatment of gastric cancer is required to monitor for evidence of recurrence. Abnormalities including mucosal surface changes, wall thickening or stricture, should be investigated with multiple biopsies (4-6) and alongside endoscopic ultrasound (EUS)<sup>[27]</sup>. Treatment of recurrence with further endoscopic resections is controversial.

## ROLE OF LAPAROSCOPY IN THE TREATMENT OF EARLY GASTRIC CANCER

### Laparoscopic resection techniques in the treatment of EGC

Although therapeutic endoscopy has become a standard treatment modality for selected EGC lesions, formal gastrectomy with lymphadenectomy remains the gold standard for most gastric cancers. Increasingly, laparoscopic resection has been used in the minimally invasive treatment for EGC<sup>[10,35]</sup>. Laparoscopic approaches that have been described for the treatment of EGC cancer include (1) Laparoscopic intragastric mucosal resections (LIGMR); (2) Laparoscopic wedge resection (LWR); and (3) Laparoscopic gastrectomy (LG).

Initially, laparoscopic resection techniques were used in the treatment of EGC that was strictly limited to the mucosa with no risk of lymph node involvement<sup>[36]</sup>. LIGMR, which was first described by Ohashi *et al*<sup>[37]</sup>,

involves the placement of 3 balloon trocars into the abdomen and into the lumen of the stomach through the anterior wall. The balloon equipped ports, one for the laparoscope and two for laparoscopic instruments, prevent air leak and fix the ports to the gastric wall<sup>[37]</sup>. LIGMR enabled mucosal resection of any part of the stomach except for the anterior wall while preserving the muscularis propria<sup>[37]</sup>. LWR, which allows for a full-thickness resection of lesions from the anterior stomach wall, was performed after endoscopic confirmation of an accessible lesion. Two approaches have been described. LWR can be performed using the "lesion lifting method", which entails introduction of a hollow needle at the point of the lesion for the application of a T-tack in the lumen of the stomach. The T-tack serves as an anchor lifting the lesion allowing it to be resected with a laparoscopic stapler<sup>[38]</sup>. The second method for LWR, first described by Kitano *et al*<sup>[39]</sup>, involves making an incision in the seromuscular layer of the anterior stomach wall over the lesion, causing the mucosal lesion to bulge through and allowing for resection. The seromuscular layer is then sutured to close the defect<sup>[39]</sup>. As endoscopic techniques of EMR and ESD have become established as safe and effective treatment strategies for EGC confined to the mucosa, the use of LIGMR and LWR have largely decreased<sup>[36]</sup>.

LG is increasingly used for the treatment of EGC with potential lymph node involvement<sup>[36]</sup>. In Japan and Korea, EGC is considered the only indication for laparoscopic gastrectomy. Several RCTs have been published comparing laparoscopic to open gastric resection conducted mainly in patients with EGC<sup>[40-43]</sup>. These mostly single-center studies have favorably supported laparoscopic resection for EGC, with benefits including reduced operative blood loss, less post-operative pain and earlier discharge from hospital<sup>[44-46]</sup>. A recent meta-analysis has found that patients undergoing LG were associated with faster return of bowel function but longer operative times and less harvested lymph nodes<sup>[47]</sup>. Ongoing RCTs are being performed to determine whether there is a significant difference in oncologic outcomes between the two groups. The Japan Clinical Oncology Group (JCOG 0912 study) and the Korean Laparoscopic Gastrointestinal Surgery Study Group (KLASS 01 Study) have initiated large multi-center RCTs comparing long-term survival for EGC following laparoscopic gastrectomy and open gastrectomy<sup>[48,49]</sup>.

In addition, in Korea, a separate phase III study (KLASS 02) has been initiated to evaluate the feasibility of laparoscopic resection in advanced gastric cancer (AGC) patients<sup>[48]</sup>. As we await those results, a recent systematic review and meta-analysis comparing LG with OG for AGC, performed by Chen *et al*<sup>[50]</sup>, revealed similar safety and oncologic outcomes to those seen in the treatment of EGC. In the treatment of AGC, studies consistently revealed a reduction in intra-operative blood loss during LG in comparison to OG<sup>[50]</sup>. Although delicate dissection along with the complexity of performing



an adequate lymphadenectomy during LG was shown to be more time consuming and requiring extensive technical expertise<sup>[50]</sup>, studies have shown a learning curve of approximately 50 LG cases before operative times can be reduced<sup>[51-53]</sup> and that times were not longer for LGs performed in large high-volume specialized centers<sup>[54,55]</sup>. As shown in studies evaluating LG for EGC, Chen *et al*<sup>[50]</sup> also revealed a reduced number of post-operative complications (*i.e.*, wound infections, respiratory complications), reduced use of analgesic use, and earlier return of bowel function in the LG group for AGC. Furthermore, their systematic review revealed that LG for AGC had similar cancer recurrence and long-term survival rate to patients treated by OG<sup>[50]</sup>. Therefore existing studies show that LG for the treatment of AGC is both safe and feasible, and results from large multi-center RCTs with extended follow up will shed more light on its oncologic applicability<sup>[50]</sup>.

### Combination of endoscopic and laparoscopic approaches

Laparoscopic and endoscopic cooperative surgery (LECS) was developed by Hiki *et al*<sup>[56]</sup> and Nunobe *et al*<sup>[57]</sup> for the dissection of submucosal tumors of the stomach. The LECS technique involves initial endoscopic identification and confirmation of tumor location followed by ESD<sup>[56,57]</sup>. Laparoscopic serosal dissection is performed and a stapling device is applied to close the incision line<sup>[56,57]</sup>. LECS is indicated in the treatment of EGCs larger than 3 cm in diameter located at the greater curvature of the stomach or for lesions with extensive ulcerations that may not be amenable to ESD<sup>[57]</sup>. Importantly, LECS does not involve lymphadenectomy.

Combining endoscopic resection with laparoscopic lymphadenectomy has also been investigated in cases where lymph node involvement cannot be disregarded<sup>[58,59]</sup>. Abe *et al*<sup>[59]</sup> noted early and delayed gastric ischemia of the preserved stomach secondary to division of major feeding arteries during lymphadenectomy, which resulted in gastric perforation in 1 of 21 patients. In addition, 2 out of 21 patients exhibited gastric emptying problems, although preoperative quality of life was maintained with no dietary restrictions<sup>[59]</sup>. Further studies are necessary before this becomes an acceptable alternative to gastrectomy without compromising oncologic principles<sup>[59]</sup>.

## ROLE OF FUNCTION-PRESERVING RESECTIONS AND LAPAROSCOPY

Resection techniques have been developed with the aim of reducing the functional sequelae of radical gastric resections including dumping syndrome, reflux gastroesophagitis and weight loss<sup>[60]</sup>. Minimally-invasive procedures combining laparoscopic resections with function-preserving gastric surgery include (1) pylorus-preserving gastrectomy (PPG) for distal lesions; (2) proximal gastrectomy (PG) for proximal lesions; and (3) laparoscopic subtotal with small remnant gastric pouch for proximal

lesions.

### Laparoscopic pylorus-preserving gastrectomy

Pylorus-preserving gastrectomy (PPG), which was originally limited to the treatment of benign gastric diseases such as gastric ulcers<sup>[61]</sup>, has become an increasingly accepted treatment modality for EGC patients. The preservation of pyloric function in gastric resections has shown improvements over conventional distal gastrectomy in the prevention of dumping syndrome<sup>[62]</sup>, the prevention of bile reflux<sup>[63]</sup> and reduced post-operative weight loss<sup>[64]</sup>. Laparoscopic-assisted PPG (LAPPG), which introduces the benefits of laparoscopic surgery, including lower post-operative pain, shorter hospitalization, early return of bowel function, and better cosmesis, is a modality for the treatment of EGC in many institutions in Japan and South Korea<sup>[65]</sup>. LAPPG involves preservation of the right gastric artery and the pyloric branch of the vagus nerve required to maintain pyloric circulation and motility<sup>[64,66]</sup>. However, there are concerns that LAPPG does not allow for adequate suprapyloric lymph node dissection<sup>[67]</sup>. Studies that have evaluated the incidence of lymph node metastasis following distal gastrectomies for EGC have found a 4% rate of metastasis to the suprapyloric lymph nodes<sup>[68,69]</sup>, although 29%-34% of those patients were found to be T2-T3 gastric cancer after final pathological evaluation<sup>[67]</sup>. A retrospective survey of the Gastric Cancer Data Base in Japan by Akiyama *et al*<sup>[12]</sup> revealed a 0.2% metastasis rate of the suprapyloric lymph nodes after evaluation of 3646 cases of T1 tumors located in the body of the stomach.

Indications for performing LAPPG include (1) intramucosal or submucosal gastric adenocarcinoma without lymph node involvement (cT1, cN0); and (2) tumor lesion located in the distal stomach (4.5 cm to 5 cm proximal to the pyloric ring)<sup>[65]</sup>. A study performed by Morita *et al*<sup>[70]</sup>, evaluating 611 patients who underwent a PPG for T1 gastric cancer had a 5-year OS rate of 96.3%. Hiki *et al*<sup>[71]</sup> evaluated 305 patients treated by PPG and revealed a 5-year OS rate of 98%. While Jiang *et al*<sup>[72]</sup> evaluated 188 patients who underwent a LAPPG and revealed a 3-year OS rate and 3-year disease-specific survival rate of 97.8% and 99.3%.

### Laparoscopic proximal gastrectomy and laparoscopic subtotal gastrectomy with small remnant pouch

Proximal tumors are commonly treated with a total gastrectomy<sup>[73]</sup>. Laparoscopy-assisted total gastrectomy (LATG) is a technically difficult procedure relative to a laparoscopy-assisted distal gastrectomy (LADG) and is associated with higher rates of post-operative complications of increased operative blood loss and increased length of hospitalization<sup>[74,75]</sup>. In addition, Lee *et al*<sup>[76]</sup> showed that LATG was associated with an increased rate of anastomotic stricture in comparison to LADG (26.9% *vs* 8.0%, respectively).

PG has been proposed as a function-preserving approach for EGC<sup>[67]</sup>. Due to the association with mark-

edly higher rates of complications including anastomotic stenosis, reflux esophagitis and no change in nutritional status in comparison to total gastrectomies, An *et al*<sup>[77]</sup> concluded that PG are not a better option than total gastrectomy for proximal third EGC. There has been no apparent advantage with laparoscopic-assisted PG (LAPG)<sup>[78]</sup>.

To improve post-operative quality of life, Jiang *et al*<sup>[79]</sup> have developed a novel approach for selected patient with proximal EGC, laparoscopy-assisted subtotal gastrectomy (LAsTG), which involves preserving a small proximal gastric pouch. LAsTG carries some concerns pertaining to oncological and reconstruction safety with the preservation of a limited remnant stomach<sup>[67]</sup>. The indications for LAsTG include (1) a pre-operative diagnosis of T1N0 EGC; (2) tumor location is in the proximal third of the stomach; (3) distance between tumor and gastroesophageal junction (GEJ) of 5 cm; and (4) remnant gastric stump measuring 2-3 cm from GEJ<sup>[67]</sup>.

## ROLE OF ROBOTIC ASSISTED GASTRECTOMY IN THE TREATMENT OF EARLY GASTRIC CANCER

Robot-assisted gastrectomy (RAG) may allow surgeons to overcome some of the technical limitations of laparoscopic resections for EGC<sup>[80]</sup>. Robotics improves visualization by providing a magnified, high-definition, three-dimensional image that allows the surgeon to identify smaller anatomical structures<sup>[81]</sup>. In addition, manipulation of tissue is improved with the elimination of physiologic tremor and articulating tools providing seven degrees of freedom and reproducing the movement of the human hand<sup>[81]</sup>. Accordingly, RAG may be advantageous to performing the more technically challenging D2 lymphadenectomy<sup>[81]</sup>. Articulating robotic instruments may allow for the dissection of LNs from difficult lymphatic stations around major vessels and organs<sup>[81]</sup>.

Long-term survival results following RAG are required to assess oncological outcomes, however studies have shown this approach to be adequate in terms of resection margins, lymphadenectomy and staging<sup>[82,83]</sup>. No differences were noted in terms of the number of lymph nodes harvested when comparing open, laparoscopic and robotic gastrectomy, however the estimated blood loss was significantly less in the robotic group in comparison with the other two approaches<sup>[84]</sup>. A recent meta-analysis of three non-randomized controlled trials was performed by Xiong *et al*<sup>[85]</sup>. Operative time was significantly longer in the RAG group in comparison to the LG group but was associated with significantly less intra-operative blood loss<sup>[85]</sup>. Furthermore, the comparison of RAG with LG revealed no differences in the number of lymph nodes harvested, length of hospitalization, and morbidity and mortality rates<sup>[85]</sup>. In addition, several studies have reported shorter learning curves for RAG compared to LG (20 cases *vs* 50 cases, respectively). Further studies are

required to assess oncological outcomes following RAG, as well as addressing important concerns regarding cost-effectiveness<sup>[81]</sup>.

## ROLE OF SENTINEL LYMPH NODE BIOPSY IN THE TREATMENT OF EARLY GASTRIC CANCER

Accurate assessment of lymph node status is an integral part to determination of clinical outcomes and for therapeutic planning in gastric cancer. EGC is associated with 5-year OS rates of greater than 90% and pathological data have suggested that the majority of lymph nodes resected do not contain metastases<sup>[29,86-88]</sup>. Further, extensive lymphadenectomies are associated with increased risk of complications<sup>[89]</sup>. Sentinel lymph node (SLN) biopsy is well-established in the treatment of breast cancer and melanoma, and allows for lymph node assessment with limited dissection and reduced complications<sup>[90]</sup>. SLN biopsy has been investigated as an alternative to extensive lymphadenectomy in the treatment of EGC. Mapping for SLN biopsy has been completed with dye, radio-colloid, as well as combinations of dye and radio-colloid. Potential anatomical limitations to SLN mapping exist in gastric cancer, due to the complex and unpredictable lymphatic drainage of the stomach, increasing the likelihood of skip metastases.

A systematic review on the accuracy of SLN biopsy in gastric cancer was performed by Cardoso *et al*<sup>[91]</sup>. This study revealed an overall calculated false negative rate (FNR) of 34.7% with dye alone, 18.5% with radio-colloid alone, and 13.1% for the combination of dye and radio-colloid<sup>[91]</sup>. A recent systematic review performed by Can *et al*<sup>[92]</sup>, reveals accuracy rates ranged from 78% to 100%. In addition, there has been publication of the results of a multicenter trial (JCOG study 0302), which evaluated the feasibility and accuracy of diagnosis using SLN biopsy in T1 gastric cancer<sup>[93]</sup>. Final results revealed a high FNR and accrual was suspended early. Primary analysis revealed a FNR of 46% (13/28) and 7 of 13 patients had nodal metastases outside the lymphatic basin<sup>[93]</sup>. However, a recent prospective multicenter trial in Japan performed by Kitagawa *et al*<sup>[94]</sup>, revealed a higher accuracy of nodal evaluation for metastasis (93%) and lower FNR (7%) compared to JCOG 0302 results. This drastic difference in results may be explained by the difference in the procedural learning phase in both studies<sup>[94]</sup>. In JCOG 0302, only five cases were required as the minimum for the initial learning phase, while a minimum of 30 cases were required for the learning phase in the multicenter trial performed by Kitagawa *et al*<sup>[94]</sup>. Thus at present, SLN biopsy remains an experimental treatment modality in gastric cancer<sup>[93]</sup>.

## FUTURE DIRECTIONS

Novel surgical approaches, including natural orifice

transluminal endoscopic surgery (NOTES) and single-incision laparoscopic surgery (SILS), are currently being investigated as minimally-invasive treatment options for EGC<sup>[95]</sup>. NOTES entails incision-less surgery to access the peritoneal cavity through natural orifices<sup>[96]</sup>. Although it has been applied sporadically in bariatric surgery, Nakajima *et al*<sup>[97]</sup> have shown that transvaginal NOTES may represent an option for performing partial gastrectomy for patients with gastric submucosal tumors. Hybrid procedures are being developed including NOTES with SLN biopsy and NOTES with laparoscopy with the goal of expanding indications for its application<sup>[96,98]</sup>. In comparison to NOTES, which is still in early stages of development, SILS shows earlier promise in the treatment of gastric cancer. SILS is frequently applied in appendix, gallbladder, colon and bariatric surgery<sup>[95]</sup>. With favorable cosmetic results, Omori *et al*<sup>[99]</sup> demonstrated SILS distal gastrectomy as a feasible and safe approach for EGC, while Ahn *et al*<sup>[95]</sup> performed the first SILS total gastrectomy with D1 lymphadenectomy for proximal EGC. As instrumentation improves and surgeon experience increases, these novel approaches show potential in improving cosmesis and reducing post-operative pain in comparison to the current laparoscopic approaches.

## CONCLUSION

The prognosis of gastric cancer patients can be improved by early detection and treatment. Minimally-invasive approaches to patients with early gastric cancer have been developed to improve quality of life without compromising oncologic outcomes. EMR and ESD have been shown to be safe and effective treatments for carefully selected patients with EGC. Long term clinical trial results are still pending from Japan for extended criteria, and it is likely that endoscopic approaches have an increasing role in the treatment of EGC. In patients with EGC that are not candidates for endoscopic resection, laparoscopic and robotic resections allow for the appropriate curative resection and lymphadenectomy with the benefits of minimally invasive surgery, including improved pain, reduced blood loss, and shorter hospital length of stay. Growing interest in minimally invasive function-preserving resections will need to be supported with further study to assess oncologic safety. The roles of laparoscopy combined with endoscopic resections as well as SLN biopsy remains to be determined. Important to all these advancements in the treatment of EGC is the continued efforts to assess safety and function without compromising curability.

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