PSUMJ
PSU MEDICAL JOURNAL

Review Article

Advancements in Early Gastric Cancer Management: A Focus on Minimally Invasive Techniques

Supakool Jerania, M.D., Wongsakorn Chaochankit, M.D.

Department of Surgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

ABSTRACT

Early gastric cancer (EGC) is a significant, global health concern. However,screening programs have improved early detection and outcomes; particularly in East Asia. The management of EGC has evolved from radical gastrectomy with lymph node dissection to minimally invasive approaches that preserve gastric function, while ensuring oncological safety. Endoscopic techniques; such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), offer effective treatment for select patients, with low risk of lymph node metastasis. These approaches provide comparable survival rates to surgery, while reducing postoperative complications, hospitalization and recovery time. Lymph node metastasis remains a key prognostic factor in EGC management. While radical surgery is necessary for cases with lymphatic spread, function-preserving surgeries; including pylorus-preserving gastrectomy (PPG) and proximal gastrectomy (PG), aim to maintain gastric function and improve quality of life. The sentinel lymph node concept has further refined surgical strategies by minimizing unnecessary lymphadenectomy. Risk stratification tools; such as the eCura scoring system, assist in predicting lymph node involvement and guiding individualized treatment decisions. Patients classified as low-risk may benefit from endoscopic resection alone, while those at higher risk may require additional surgical intervention. The growing role of laparoscopic approaches has further advanced minimally invasive treatment, demonstrating comparable oncologic outcomes to open surgery. As treatment paradigms continue to shift, a multidisciplinary approach integrating endoscopic, surgical, and risk-based strategies is essential for optimizing patient outcomes. Future research will further refine treatment guidelines, ensuring a balance between oncological safety and functional preservation in EGC management.

Keywords: early gastric cancer; endoscopic resection; function-preserving gastrectomy; minimally invasive surgery; sentinel lymph node biopsy

Corresponding author: Wongsakorn Chaochankit, M.D.
Department of Surgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: thegunnerpump@hotmail.com
doi: 10.31584/psumj.2025278449
https://he01.tci-thaijo.org/index.php/PSUMJ/

PSU Med J 2025;5(2):91-103
Received 2 April 2025
Revised 24 May 2025
Accepted 29 May 2025
Published online 22 August 2025

INTRODUCTION

Gastric cancer is the fifth most common cancer worldwide, and the third leading cause of cancer-related deaths[1,2]. The disease is predominantly found in Asia, Latin America and Eastern Europe. A major risk factor for developing gastric cancer is *Helicobacter pylori* (H. pylori) infection, which leads to chronic and atrophic inflammation, followed by metaplasia and, eventually malignancy[3,4]. Over the past decade early, diagnosis and treatment have significantly reduced gastric cancer-related mortality[5].

Gastric cancer staging is classified according to the TNM system; established by the American Joint Committee on Cancer (AJCC) 8th edition, which has been validated across different populations[6]. Treatment strategies are stage-dependent and are categorized as follows:

- Early-stage gastric cancer (EGC): T1N0M0
- Locally advanced gastric cancer: T2-4N0-3M0
- Metastatic gastric cancer: AnyTAnyNM1

Relevant articles were identified through a literature search of PubMed using search terms; such as “early gastric cancer”, “minimally invasive surgery”, “endoscopic resection” and “function-preserving gastrectomy”. Priority was given to English language publications and studies from 2000 to 2024, with high methodological quality”. This review focuses on EGC; a term first introduced in the 1970s by Tadashige Murakami[7]. EGC is defined as: cancer confined to the mucosa or submucosa, with or without lymph node involvement[8,9]. Most patients are asymptomatic, and diagnoses are often made through upper gastrointestinal endoscopy or barium meal studies[8].

EGC is more prevalent in East Asian countries, particularly in Japan and South Korea, wherein nationwide screening programs have led to significantly higher survival rates compared to advanced-stage gastric cancer[10]. Moreover, in selected cases treatment may not require total gastrectomy or extensive lymph node dissection; thereby, reducing postoperative complications[11]. This narrative review aims to provide a comprehensive overview of minimally invasive techniques for EGC; including endoscopic and function-preserving surgical approaches, with a focus on their indications, outcomes and future perspectives.

Lymph node metastasis in gastric cancer

Lymph node metastasis is a crucial prognostic factor in gastric cancer[10]. As a result, the standard treatment for gastric cancer involves gastrectomy with lymph node dissection[10]. However, in early-stage gastric cancer, the necessity for surgery is debatable due to the low likelihood of lymph node involvement[11].

- In mucosal gastric cancer (T1a), the risk of lymph node metastasis is less than 3%.
- In submucosal gastric cancer (T1b), the risk of lymph node metastasis increases to 15–20%.
- The 5-year survival rate for patients with early-stage gastric cancer is approximately 94%.

Given the low rate of lymph node involvement in T1a disease, a key question arises: Is surgery and complete lymph node dissection necessary for all cases of early gastric cancer, or can less invasive treatment options be considered to reduce surgical complications?

Lymph node involvement remains the most important prognostic factor for survival[12]. Patients with early-stage gastric cancer without lymph node metastasis have a significantly better 3-year survival rate than those with nodal involvement[12].

In 1998, the Japanese Gastric Cancer Association (JGCA)[12] identified key risk factors for lymph node metastasis in EGC, including:

- Tumor size >2 cm
- Ulcerative lesions (based on biopsy)
- Undifferentiated histology (diffuse type)
- Lymphovascular invasion

Recent studies also suggest that an age of >40 years and tumor invasion depth are significant predictors of lymph node metastasis[12]. These factors play a critical role in determining the most appropriate treatment approach.

Management of early gastric cancer

Radical gastrectomy with lymph node dissection remains the standard treatment for gastric cancer, as it improves survival rates and reduces recurrence[12]. Since lymph node involvement is a key prognostic factor, surgical resection with lymphadenectomy continues to be a primary treatment approach[13,14]. However, both open surgery and laparoscopic gastrectomy are associated with longer hospital stays, increased treatment costs, slower gastrointestinal recovery and delayed remission[15]. These factors can negatively impact a patient's quality of life. Therefore, less invasive treatment options; such as endoscopic resection and function-preserving gastrectomy, have been developed[16]. Function-preserving gastrectomy incorporates the sentinel lymph node concept, which aims to minimize unnecessary lymphadenectomy[17]. The details of these treatment approaches are outlined below.

1. Endoscopic treatment

Endoscopic treatment is a minimally invasive alternative for early-stage gastric cancer; particularly for tumors confined to the mucosa (T1a), wherein the risk of lymph node metastasis is very low[18]. This approach allows for tumor removal without lymph node dissection, making it a less invasive option with comparable long-term outcomes.

Endoscopic resection (ER) includes two main techniques:

1.1. Endoscopic Mucosal Resection (EMR)

EMR involves submucosal injection of hypertonic or normotonic fluid to create a lifting effect, followed by resection using a high-frequency steel snare[18].

- Recurrence rates: 84% at 5 years and 64% at 10 years.
- Survival rate: As high as 99% at 10 years.

1.2 Endoscopic Submucosal Dissection (ESD)

ESD is a more advanced technique that allows for en bloc resection of larger or more complex lesions[19].

- The procedure begins with circumferential marking approximately 5 mm from the tumor edge, followed by submucosal injection of dye and precise dissection using a high-frequency electric knife[20].
- Compared to EMR, ESD has a lower recurrence rate; however, it requires greater technical expertise as well as having a higher risk of perforation[20].

Indications for ER

According to the JGCA 5th edition[21], indications for ER are classified into three categories:

1. Absolute indication

For EMR, tumors with a less than 1% risk of lymph node metastasis, where endoscopic treatment achieves survival and recurrence rates equivalent to surgery[21]:

- Intramucosal lesion (T1a)
- Well-differentiated intestinal-type adenocarcinoma
- Lesion ≤2 cm
- No ulceration (neoplastic ulcer-negative)
- No lymphovascular invasion
- Negative margins (deep and horizontal)

For ESD, absolute indications include[21]:

1. Differentiated-type adenocarcinoma without ulceration (T1a, any size).

2. Differentiated-type adenocarcinoma with ulceration (T1a, diameter ≤3 cm).

The JCOG 0607 trial demonstrated that when ER is performed according to these criteria, the 5-year survival rate is 97%, comparable to surgical treatment (94%)[22].

2. Expanded indication

Cases with <1% risk of lymph node metastasis, where short-term outcomes are favorable, but long-term data are limited[23]: Undifferentiated mucosal tumors (T1a), ≤2 cm, without ulceration.

Long-term results are under investigation in the JCOG 1009/1010 trial.

3. Relative indication

Cases not meeting absolute or expanded criteria, but where endoscopic treatment may still be considered due to high surgical risk[24]:

- Elderly patients
- Patients with severe comorbidities

There is a growing trend toward expanding the indications for ER, particularly in cases where the lesion extends into the submucosa (T1b)[25]. If the depth of invasion does not exceed one-third of the submucosal layer (sm1), the risk of lymph node metastasis remains low[26]. However, in clinical practice, biopsy limitations make it difficult to precisely determine the depth of invasion within the muscularis propria[27]. Although the total submucosal depth cannot always be accurately measured, a general threshold of 500 microns is used to define sm1 involvement[28]. Studies have shown that if the tumor invades beyond 500 microns, the risk of lymph node metastasis increases significantly. Therefore, while ER may be considered in select T1b cases it should be performed with caution, particularly outside of absolute indications[28]. A study conducted at the National Cancer Center Hospital and Cancer Institute Hospital evaluated lymph node metastasis rates in patients having undergone lymphadenectomy following ER[29-31]. The results, which assessed ER indications, are summarized in Table 1. According to the NCCN Guidelines (Version 4.2019), ER remains recommended only for tumors ≤2 cm and is not advised for cancers invading the submucosa (T1b). Additionally, endoscopic ultrasonography (EUS) is recommended for all cases to assess tumor (T) staging prior to treatment[31].

Maintenance and follow-up after gastrointestinal endoscopy

Following ESD, gastric ulcers commonly develop at the site of tissue removal[32]. To promote healing and reduce ulcer size, proton pump inhibitors (PPIs) are recommended for all post-ESD patients. Studies indicate that a prophylactic dose of esomeprazole (20 mg once daily) is as effective as 20 mg twice daily, making the lower dose sufficient for ulcer prevention[33]. Additionally, testing for Helicobacter pylori (H. pylori) is recommended in all patients. If infection is detected, eradication therapy should be initiated after ER, so as to reduce the risk of recurrence[29,30].

Follow-up recommendations

- Re-laparoscopy is advised within 6 months post-ER to reassess the gastric mucosa and confirm the absence of residual or recurrent cancer[35].
- Synchronous gastric cancer is detected in 9% of ESD patients, and 19% of these cases are missed during the initial endoscopic evaluation[36].
- To minimize missed invasive cancer, 1-2 endoscopic follow-ups per year are recommended[37].

Table 1 Lymph node metastases classified by endoscopic resection indication: green absolute indication, yellow expanded[31-34]

Depth	Ulceration		Differentiated type		Undifferentiated type	
M	UL0	Tumor diameter	≤2 cm	>2 cm	≤2 cm	>2 cm
		Nodal metastasis	0% (0/437)	0% (0/493)	0% (0/310)	2.8% (6/214)
	UL1	Tumor diameter	≤3 cm	>3 cm	≤2 cm	>2 cm
		Nodal metastasis	0% (0/488)	3% (7/230)	2.9% (8/271)	5.9% (44/743)
SM1		Tumor diameter	≤3 cm	>3 cm	Any diameter	
		Nodal metastasis	0% (0/145)	2.6% (2/78)	10.6% (9/85)	

indication and red relative indication21 (M=mucosa; SM1=1/3 of submucosa; UL=ulcerative lesion; 0=negative; 1=positive)

Imaging for recurrence and metastasis

• Endoscopic ultrasonography (EUS) has been shown to improve sensitivity in detecting tumor recurrence[36].

• Computed tomography (CT) or abdominal ultrasound should be performed in cases where biopsy results suggest undifferentiated-type carcinoma, so as to assess potential metastasis to other organs[36].

After endoscopic treatment, the curability of endoscopic resection (eCura) should be evaluated based on two key factors[37]:

1. Complete removal of the cancerous tissue
2. Risk of lymph node metastasis

Based on these criteria, endoscopic outcomes are classified into eCura A, B, C1, and C2 (Table 2)[31].

The eCura system, developed by W. Hatta et al., is a scoring model designed to evaluate treatment outcomes following endoscopic resection. It works by estimating the probability of lymph node metastasis[35]. This system assigns a total score of 7, based on key pathological factors, and categorizes patients into three risk groups: low (0–1), intermediate (2–4), and high (5–7). The rates of lymph node metastasis for each group were: 2.5%, 6.7%, and 22.7%, respectively[35].

The stratification of patients, according to the eCura score, provides a clinical framework for treatment decision-making[35]. Patients in the low-risk group exhibited a low probability of lymph node metastasis, making ESD without additional intervention an acceptable treatment approach[36]. Conversely, high-risk patients demonstrated a significantly increased risk of metastasis, necessitating radical surgery as the recommended treatment strategy[36].

The eCura scoring system is based on five pathological factors:

1. Tumor size >3 cm
2. Venous invasion
3. Submucosal invasion (pT1b >SM1)
4. Positive vertical margin
5. Lymphatic invasion (assigned a weight of 3 points due to its high prognostic significance)

Among these variables, lymphatic invasion exhibited the highest odds ratio (OR 3.99, 95% CI 2.43–6.55), underscoring its importance in predicting lymph node dissemination. It is important to note that the eCura model was derived from a retrospective study focused on identifying factors associated with lymph node metastasis[38]. In the low-risk group, where additional treatment was not pursued, the 5-year cancer-specific survival rate was 99.6%, with a 5-year recurrence rate of 0.7%[39]. However, in the intermediate- and high-risk groups, the need for additional surgical intervention was evident, as the hazard ratios (HR) for recurrence were 7.73 and 18.1, while the HRs for cancer-related mortality were 6.11 and 16.1, respectively[39].

Table 2 The curability of endoscopic resection and treatment guidelines[21]

eCura	Cell type	pT stage	Size	UL	VM	Ly	V	HM	Management
A	Diff.	T1a	Any size	0	0	0	0	0	Observe
	Diff.	T1a	≤3 cm	1	0	0	0	0	
B	Diff.	T1b (sm1)	≤3 cm	0	0	0	0	0	Observe
	Undiff.	T1a	≤2 cm	0	0	0	0	0	
C1	eCuraA or eCuraB							1	Observe, re-ESD, coagulation, surgery
C2	Unmatched all above rows								Add surgery

eCura=endoscopic curability; UL=ulcer; VM=vertical margin; Ly=lymphatic invasion; V=vascular invasion; HM=horizontal margin; Diff=differentiated; Undiff=undifferentiated; 0=negative; 1=positive

Traditional surgical approach

Radical gastrectomy with lymph node dissection remains the standard surgical treatment for both early-stage and metastatic gastric cancer[21]. In patients with early-stage gastric cancer, radical gastrectomy achieves a 5-year survival rate of 98%[38]. The current standard procedure for gastric cancer is D2 gastrectomy, which involves the removal of the stomach with extensive lymphadenectomy[21]. However, for early-stage patients who are not candidates for ER but still require surgical intervention, a D1 or D1+ gastrectomy is considered sufficient to minimize postoperative risks and complications[35].

Classification of gastric resection procedures[21]

Gastric cancer surgery consists of two major components:

1. Gastric resection
2. Lymph node dissection

According to the JGCA, gastric resection procedures are classified as follows[21]:

1. Total gastrectomy – Complete removal of the stomach; including the cardia and pylorus.
2. Distal gastrectomy – Removal of at least two-thirds of the stomach; including part of the pylorus, while preserving the cardia.
3. Pylorus-preserving gastrectomy (PPG) – Resection of the upper one-third of the stomach; including the pylorus and parts of the antrum, while preserving the right gastric artery and the pyloric branch of the vagus nerve.
4. Proximal gastrectomy – Resection of the upper portion of the stomach; including the esophagogastric junction (EGJ), while retaining the pylorus.
5. Segmental gastrectomy – Circumferential resection of the stomach, while preserving both the cardia and pylorus.
6. Local resection – Removal of only the tumor and surrounding tissue, without circumferential resection.
7. Non-resection surgery – Palliative procedures; such as gastrojejunostomy, gastrostomy or jejunostomy, performed to relieve symptoms rather than cure the disease.

Extent of gastrectomy and lymphadenectomy

The definition of standard gastrectomy includes resection of at least two-thirds of the stomach with D2 lymphadenectomy[21]. Surgical procedures that remove less than two-thirds of the stomach or involve fewer lymph nodes than D2 lymphadenectomy are classified as modified surgeries[21]. Conversely, procedures extending beyond D2 lymphadenectomy are categorized as extended surgeries[21]. Resection Margin Recommendations.

Appropriate resection margins depend on the tumor stage and growth pattern[8,21]. The National Comprehensive Cancer Network (NCCN) 2019 guidelines recommend the following:

- For T1b-T3 lesions, a minimum margin of 4 cm from the tumor should be maintained.
- For T1 lesions (JGCA ver.5), a minimum margin of 2 cm is recommended.
- For T2 and above lesions, resection margins should be:
  - At least 3 cm for expansive growth patterns.
  - At least 5 cm for infiltrative growth patterns.

Lymph node dissection in gastric cancer surgery

Lymph node dissection is performed, based on the extent of gastric resection, and is classified into standard and modified approaches. Standard gastrectomy, which includes total gastrectomy and distal gastrectomy, typically incorporates D2 lymphadenectomy, while modified surgeries may involve more limited lymph node removal (D1 or D1+)[27].

A study comparing D2 resection and standard D1 resection in early-stage gastric cancer found no significant difference in overall survival rates between the two approaches[26]. However, this finding is applicable only under specific conditions—namely; that the tumor is

confined to the mucosa (T1a), is well-differentiated and is ≤2 cm in size. In cases where the cancer has invaded the submucosa (T1b), is poorly differentiated or exceeds 2 cm, more extensive lymph node dissection may be necessary[21].

Lymph node metastasis in submucosal (T1b) gastric cancer

For T1b lesions that have invaded the submucosal layer, the likelihood of lymph node metastasis is significantly increased. Studies indicate that in such cases, lymph node involvement is most commonly observed at stations 7, 8a, and 9[39]. Consequently, the JGCA guidelines recommend D1+ lymphadenectomy for T1b tumors >1.5 cm in size or those with undifferentiated histology, as these patients exhibit a higher risk of lymphatic spread, making standard D1 dissection insufficient[40].

Spleen-preserving approaches in total gastrectomy with D2 lymphadenectomy

A notable advancement in total gastrectomy with D2 lymphadenectomy is the recommendation to omit splenic hilar lymph node dissection (station 10) to preserve the spleen. Studies have shown that patients undergoing spleen-preserving D2 lymphadenectomy demonstrate 5-year survival rates comparable to those having undergone splenectomy with station 10 dissection[40]. However, these findings are not applicable to tumors located in the greater curvature region, where splenic hilar lymph node involvement remains a concern[40].

Comparison of laparoscopic and open surgery in early-stage gastric cancer

Laparoscopic and open gastrectomy are both widely used surgical approaches for the treatment of early-stage gastric cancer[41]. Studies have shown that laparoscopic surgery is associated with fewer complications compared to open surgery, while achieving a similar extent of lymph node dissection[42]. The number of lymph nodes removed in laparoscopic gastrectomy is comparable to that in open surgery, suggesting that the oncological efficacy of both techniques is equivalent[43].

Advantages of laparoscopic surgery

Laparoscopic surgery offers several advantages over open gastrectomy, including:

• Smaller surgical incisions, leading to reduced postoperative pain and faster recovery[44].

• Lower opioid analgesic requirements, minimizing the risk of opioid-related side effects[45].

• Lower incidence of surgical site infections and reduced risk of respiratory complications[45].

Long-term outcomes and survival rates

The KLASS-01 trial, a large-scale study conducted in South Korea, compared laparoscopic distal gastrectomy with open distal gastrectomy in patients with early-stage gastric cancer[41]. The results demonstrated no significant difference in long-term survival rates between the two approaches; including 5-year overall survival and cancer-specific survival[41]. These findings support laparoscopic gastrectomy as both a viable and effective alternative to open surgery for early-stage gastric cancer treatment[41].

Function-preserving gastrectomy

Function-preserving gastrectomy is a modified surgical approach designed to retain a greater portion of the stomach, while selectively removing lymph nodes[46]. This technique aims to minimize postoperative complications and improve patients' quality of life compared to standard gastrectomy[47].

To achieve this, limited surgical approaches have been developed, including:

- Pylorus-preserving gastrectomy
- Proximal gastrectomy
- Local resection with sentinel lymph node biopsy

Each of these techniques focuses on preserving gastric function, while maintaining oncological safety; thereby, offering a less invasive alternative to conventional gastrectomy[48]. The details of each approach are outlined below.

1. Pylorus-preserving gastrectomy (PPG)

PPG is a surgical approach indicated for early-stage gastric cancer located in the middle of the stomach without lymph node metastasis[46]. This procedure aims to retain gastric function by preserving the right gastric artery and the pyloric branch of the vagus nerve, while maintaining approximately 3 cm of the antral cuff[47]. To ensure oncological safety, the lower tumor margin should be at least 4 cm from the pylorus[47].

Advantages of PPG

PPG has been shown to reduce the incidence of postoperative complications commonly associated with traditional gastrectomy, including:

• Dumping syndrome, which involves rapid gastric emptying and regurgitation of gastric juice from the duodenum into the stomach[49].

• Reduced risk of gallstone formation, which is often observed following gastric bypass surgery[49].

Lymph node dissection and oncological outcomes

According to the JGCA guidelines, D1+ lymphadenectomy is recommended for PPG[47]. Studies have demonstrated that the long-term survival rate following PPG is comparable to that of distal gastrectomy, despite the exclusion of suprapyloric lymph node dissection[47].

The Postgastrectomy Syndrome Assessment Study (PGSAS) further confirmed that PPG surgery results in fewer postoperative complications; such as diarrhea and dumping syndrome, while maintaining similar oncological outcomes to traditional distal gastrectomy[48].

2. Proximal gastrectomy (PG)

PG is an alternative surgical approach for early-stage gastric cancer located in the upper third of the stomach[50]. While total gastrectomy remains the standard treatment, PG offers several advantages; particularly in terms of preserving gastric function and enhancing postoperative quality of life[51].

Advantages of proximal gastrectomy

Compared to total gastrectomy, PG provides the following benefits:

• Improved nutritional status by preserving a portion of the stomach[50].

• Reduced risk of postoperative anemia due to the retention of gastric acid production[51].

• Maintenance of gastrin and intrinsic factor secretion, which plays a crucial role in vitamin B12 absorption and overall digestive function[52].

Studies have demonstrated that omitting lymph node dissection of the right gastric artery and right gastroepiploic artery in early-stage gastric cancer does not negatively impact survival rates[53,54].

Reconstruction after proximal gastrectomy

Following PG, reconstruction is a critical step to restore digestive continuity[48]. Several reconstruction techniques exist[50]. Although, total gastrectomy is often preferred. This is due to concerns regarding postoperative complications; such as stenosis and severe reflux esophagitis. Additionally, long-term studies have shown that PG is not associated with a higher incidence of stenosis[47].

Moreover, evidence suggests that proximal gastrectomy carries a lower risk of severe reflux esophagitis compared to total gastrectomy[52]. Meta-analyses further supports the use of double tract reconstruction after PG, as it significantly reduces the incidence of both reflux esophagitis and anastomotic stenosis; therefore, improving overall patient outcomes[54].

3. Function-preserving gastrectomy based on the sentinel node concept

The sentinel lymph node biopsy (SLNB) technique, originally developed for breast cancer and melanoma, is increasingly being applied in the management of early-stage gastric cancer[55]. This approach aims to minimize excessive lymph node dissection; thereby, reducing surgical complications and improving postoperative recovery[56].

By integrating sentinel lymph node mapping with function-preserving gastrectomy various surgical techniques can be employed, including:

- Wedge resection
- Proximal gastrectomy
- Pylorus-preserving gastrectomy
- SLNB combined with endoscopic resection

These procedures are particularly suitable for patients whom do not meet the criteria for endoscopic treatment alone but still require gastric resection with limited lymphadenectomy[57].

Sentinel lymph node mapping techniques

The dual-tracer method is currently the most widely used sentinel lymph node mapping technique in gastric cancer surgery[58]. This method employs both a radioactive tracer and a dye tracer to enhance accuracy in detecting sentinel nodes[59].

Commonly Used Tracers

1. Radioactive Tracers
   - Technetium-99m tin colloid
   - Technetium-99m sulfur colloid
   - Technetium-99m antimony sulfur colloid
2. Dye Tracers
   - Isosulfan blue dye
   - Indocyanine green (ICG)

Tracer injection and sentinel node detection

According to the study of Takeuchi et al.[55], the tracer injection protocol involves:

- Radioactive tracer administration:
  - 2 mL of Technetium-99m colloid (150 MBq) is injected submucosally in four quadrants around the tumor site one day before surgery[55].
  - The colloid reaches the sentinel lymph nodes within 2 hours and persists for approximately 20 hours before being cleared by macrophages[55].
- Dye tracer administration:
  - Isosulfan blue dye or ICG is injected submucosally in four quadrants immediately before surgery[55].
  - The sentinel node becomes visible within 15 minutes after injection[55].
- Detection method:
  - A gamma probe detector is used intraoperatively to locate radioactive sentinel nodes[55].

Lymphatic drainage and sentinel node distribution

The lymphatic drainage pattern of the stomach is categorized into five primary pathways, based on major arterial supply[58]:

1. Left gastric artery (stations 1, 3a, 7)
2. Right gastric artery (stations 3b, 5, 8a)
3. Right gastroepiploic artery (stations 4d, 6)
4. Left gastroepiploic artery (stations 4sa, 4sb)
5. Posterior gastric artery (station 11p)

By accurately identifying sentinel lymph nodes, surgeons can selectively remove affected nodes, while preserving uninvolved lymphatic structures; thereby, reducing the extent of lymphadenectomy and postoperative morbidity[57,58]. The sentinel lymph node mapping method has demonstrated a high identification rate of 94–100%, and a predictive accuracy of 85–100% for lymph node distribution[56]. The dual-tracer technique further enhances accuracy, making it the preferred approach[56]. However, gastric cancer differs from breast cancer and melanoma in that skip metastasis can occur; wherein, the cancer

spreads directly to N2 lymph nodes without first involving N1 nodes[55]. This phenomenon complicates sentinel node mapping, as undetected skip metastases may lead to inaccurate staging and suboptimal treatment[55,56].

In the JCOG 0302 trial, sentinel node biopsy yielded a false-negative rate of 46%, with some cases exhibiting lymph node metastasis outside the sentinel lymphatic basin[55]. A contributing factor was the use of indocyanine green (ICG) as a single dye, rather than a dual-tracer technique[59]. Additionally, the study included larger tumors (T2–T3, >4 cm in size), which may have increased the likelihood of false-negative results[59].

Conversely, the SENORITA trial, which specifically examined T1N0M0 tumors smaller than 3 cm, used a standardized procedural checklist and reported a 100% sensitivity rate; with a false-negative rate of 0%[60]. While these findings support the feasibility of SLNB in early-stage gastric cancer, long-term outcomes remain under investigation[60].

Long-term oncologic outcomes of function-preserving gastrectomy have shown promising results. PPG offers comparable 5-year survival to distal gastrectomy (94–98%), with lower rates of dumping syndrome. PG maintains nutritional status with similar recurrence-free survival to total gastrectomy. Sentinel node navigation surgery in selected EGC patients demonstrates excellent accuracy in nodal staging, although its long-term impact is still under investigation[48–50]. To facilitate clinical application and enhance reader comprehension, we summarize the key characteristics of each technique in Table 3.

Checklist for quality control of sentinel lymph node biopsy in gastric cancer surgery[60]

Tracer Injection Process[60]

1. Submucosal injection

Ensure that the tracer is injected into the submucosal layer via intraoperative esophagogastroduodenoscopy (EGD).

2. Injection sites

Confirm that the tracer is injected at four different sites using intraoperative EGD.

3. Leakage check

Assess for any intraluminal or extraluminal leakage of the tracer during injection via intraoperative EGD.

4. Time requirement

Ensure that the four injections are completed within 3 minutes from the first to the last injection during intraoperative EGD.

Sentinel Basin Node (SBN) Identification and Evaluation[60]

5. Lymph node detection

Verify that at least one sentinel basin (SB) node is identified during laparoscopic surgery.

6. Frozen biopsy analysis

Table 3 Summary of minimally invasive techniques in early gastric cancer

Technique	Indication	Key advantages	Limitations/Risks
Endoscopic Submucosal Dissection (ESD)	T1a EGC, well-differentiated, ≤2–3 cm	Organ preservation, fast recovery	Requires expertise, perforation risk
Pylorus-Preserving Gastrectomy (PPG)	Mid-stomach EGC, no nodal metastasis	Reduced dumping, better QoL	Technically demanding
Proximal Gastrectomy (PG)	Upper-third EGC, no high-risk features	Nutritional benefits, acid retention	Risk of reflux, anastomotic stenosis
Sentinel Node Navigation Surgery	Selected EGC cases, cT1N0 <3 cm	Tailored resection, avoids over-surgery	False-negative risk if not well controlled

EGD=early gastric cancer; cm=centimeter; QoL=quality of life

Evaluate the SBN using intraoperative frozen biopsy.

7. Minimum node count

Ensure that at least five SBNs (hot nodes, green nodes, hot & green nodes, basin nodes) are identified and analyzed at the back table and frozen section.

CONCLUSION

Surgery, combined with lymph node dissection, remains the primary treatment for gastric cancer. However, in EGC, where the tumor is confined to the mucosal or submucosal layer, the need for extensive surgery depends on lymph node involvement. While some cases may exhibit lymphatic spread, alternative treatment strategies can help minimize surgical complications and improve patient outcomes. For appropriately selected patients, ER has emerged as a highly effective, minimally invasive treatment option; demonstrating favorable recurrence and survival rates. Avoiding excessive surgery in early-stage cases can significantly reduce postoperative complications, shorten hospitalization duration and accelerate recovery.

A critical aspect of treatment planning involves assessing the risk of lymph node metastasis following resection. Lymph node involvement is a key prognostic factor in gastric cancer, and its presence necessitates surgical intervention. The eCura system currently serves as the primary tool for risk assessment, guiding decisions on whether additional surgery is required. In cases where a lesion poses a high risk of lymphatic spread, gastrectomy with lymph node dissection remains the standard treatment.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424.
2. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. Prz Gastroenterol 2019;14:26–38.
3. Luo G, Zhang Y, Guo P, Wang L, Huang Y, Li K. Global patterns and trends in stomach cancer incidence: age, period and birth cohort analysis. Int J Cancer 2017;141:1333–44.
4. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999;83:18–29.
5. Park YH, Kim N. Review of atrophic gastritis and intestinal metaplasia as a premalignant lesion of gastric cancer. J Cancer Prev 2015;20:25–40.
6. In H, Solsky I, Palis B, Langdon-Embry M, Ajani J, Sano T. Validation of the 8th edition of the AJCC TNM staging system for gastric cancer using the national cancer database. Ann Surg Oncol 2017;24:3683–91.
7. Saragoni L. Upgrading the definition of early gastric cancer: better staging means more appropriate treatment. Cancer Biol Med 2015;12:355–61.
8. National Comprehensive Cancer Network. Gastric Cancer: NCCN guidelines with NCCN evidence blocks [homepage on the Internet]. NCC: Plymouth Meeting, PA; 2020. Available from: https://www.nccn.org/home
9. Fernández-Esparrach G, Calderón Á, De-la-Peña J, Díaz-Tasende JB, Esteban JM, Gimeno-García AZ, et al. Endoscopic submucosal dissection. Sociedad Española de Endoscopia Digestiva (SEED) clinical guideline. Rev Esp Enferm Dig 2014;106:120–32.
10. Li X, Liu S, Yan J, Peng L, Chen M, Yang J, et al. The Characteristics, prognosis, and risk factors of lymph node metastasis in early gastric cancer. Gastroenterol Res Pract 2018;2018:6945743.
11. Zhao X, Cai A, Xi H, Chen L, Peng Z, Li P, et al. Predictive factors for lymph node metastasis in undifferentiated early gastric cancer:a systematic review and meta-analysis. J Gastrointest Surg 2017;21:700–11.
12. Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma – 2nd English Edition. Gastric Cancer 1998;1:10–24.
13. Dohi O, Yagi N, Majima A, Horii Y, Kitaichi T, Onozawa Y, et al. Diagnostic ability of magnifying endoscopy with blue laser imaging for early gastric cancer: a prospective study. Gastric Cancer 2017;20:297–303.
14. Kim SM, Lee H, Min B-H, Kim JJ, An JY, Choi M-G, et al. A prediction model for lymph node metastasis in early-stage gastric cancer:toward tailored lymphadenectomy. J Surg Oncol 2019;120:670–5.
15. Fang WL, Huang KH, Lan YT, Chen MH, Chao Y, Lo SS, et al. The risk factors of lymph node metastasis in early gastric cancer. Pathol Oncol Res POR 2015;21:941–6.
16. Kim Y, Kim YW, Choi IJ, Cho JY, Kim JH, Kwon JW, et al. Cost comparison between surgical treatments and endoscopic submucosal dissection in patients with early gastric cancer in Korea. Gut Liver 2015;9:174–80.
17. Liu Q, Ding L, Qiu X, Meng F. Updated evaluation of endoscopic submucosal dissection versus surgery for early gastric cancer: a systematic review and meta-analysis. Int J Surg Lond Engl 2020;73:28–41.
18. Uedo N, Iishi H, Tatsuta M, Ishihara R, Higashino K, Takeuchi Y, et al. Longterm outcomes after endoscopic mucosal resection for early gastric cancer. Gastric Cancer 2006;9:88–92.

19. Facciorusso A, Antonino M, Di Maso M, Muscatiello N. Endoscopic submucosal dissection vs endoscopic mucosal resection for early gastric cancer: a meta-analysis. World J Gastrointest Endosc 2014;6:555–63.
20. Takizawa K, Ono H, Muto M. Current indications of endoscopic submucosal dissection for early gastric cancer in Japan. Jpn J Clin Oncol 2019;49:797–802.
21. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2020.
22. Hasuike N, Ono H, Boku N, Mizusawa J, Takizawa K, Fukuda H, et al. A non-randomized confirmatory trial of an expanded indication for endoscopic submucosal dissection for intestinal-type gastric cancer (cT1a): the Japan Clinical Oncology Group study(JCOG0607). Gastric Cancer 2018;21:114–23.
23. Takizawa K, Takashima A, Kimura A, Mizusawa J, Hasuike N, Ono H, et al. A phase II clinical trial of endoscopic submucosal dissection for early gastric cancer of undifferentiated type: Japan Clinical Oncology Group study JCOG1009/1010. Jpn J Clin Oncol 2013;43:87–91.
24. Azari FS, Roses RE. Management of early stage gastric and gastroesophageal junction malignancies. Surg Clin North Am 2019;99:439–56.
25. Lim JH, Kim J, Kim SG, Chung H. Long-term clinical outcomes of endoscopic vs. surgical resection for early gastric cancer with undifferentiated histology. Surg Endosc 2019;33:3589–99.
26. Park DJ, Lee HK, Lee HJ, Lee HS, Kim WH, Yang HK, et al. Lymph node metastasis in early gastric cancer with submucosal invasion: feasibility of minimally invasive surgery. World J Gastroenterol 2004;10:3549–52.
27. Abdelfatah MM, Barakat M, Lee H, Kim JJ, Uedo N, Grimm I, et al. The incidence of lymph node metastasis in early gastric cancer according to the expanded criteria in comparison with the absolute criteria of the Japanese Gastric Cancer Association: a systematic review of the literature and meta-analysis. Gastrointest Endosc 2018;87:338–47.
28. Ko J, Kim SJ, Kang DH, Choi CW, Kim HW, Park SB. Dose-related healing of artificial ulcers after endoscopic submucosal dissection using esomeprazole: a randomized controlled study. Medicine (Baltimore) 2019;98:e15701.
29. Choi J, Kim SG, Yoon H, Im JP, Kim JS, Kim WH, et al. Eradication of helicobacter pylori after endoscopic resection of gastric tumors does not reduce incidence of metachronous gastric carcinoma. Clin Gastroenterol Hepatol 2014;12:793-800.
30. Fukase K, Kato M, Kikuchi S, Inoue K, Uemura N, Okamoto S, et al. Effect of eradication of helicobacter pylori on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomized controlled trial. Lancet Lond Engl 2008;372:392–7.
31. Kato M, Nishida T, Yamamoto K, Hayashi S, Kitamura S, Yabuta T, et al. Scheduled endoscopic surveillance controls secondary cancer after curative endoscopic resection for early gastric cancer: a multicentre retrospective cohort study by Osaka University ESD study group. Gut 2013;62:1425–32.
32. Nakajima T, Oda I, Gotoda T, Hamanaka H, Eguchi T, Yokoi C, et al. Metachronous gastric cancers after endoscopic resection: how effective is annual endoscopic surveillance? Gastric Cancer 2006;9:93–8.
33. Lightdale CJ, Botet JF, Kelsen DP, Turnbull AD, Brennan MF. Diagnosis of recurrent upper gastrointestinal cancer at the surgical anastomosis by endoscopic ultrasound. Gastrointest Endosc 1989;35:407–12.
34. Hirasawa T, Gotoda T, Miyata S, Kato Y, Shimoda T, Taniguchi H, et al. Incidence of lymph node metastasis and the feasibility of endoscopic resection for undifferentiated-type early gastric cancer. Gastric Cancer 2009;12:148–52.
35. Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, et al. A scoring system to stratify curability after endoscopic submucosal dissection for early gastric cancer: "eCura system". Am J Gastroenterol 2017;112:874–81.
36. Youn HG, An JY, Choi MG, Noh JH, Sohn TS, Kim S. Recurrence after curative resection of early gastric cancer. Ann Surg Oncol 2010;17:448–54.
37. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1–19.
38. Degiuli M, Calvo F. Survival of early gastric cancer in a specialized European center. Which lymphadenectomy is necessary? World J Surg 2006;30:2193–203.
39. Kinami S, Nakamura N, Tomita Y, Miyata T, Fujita H, Ueda N, et al. Precision surgical approach with lymph-node dissection in early gastric cancer. World J Gastroenterol 2019;25:1640–52.
40. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, Yoshikawa T, et al. Randomized controlled trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. Ann Surg 2017;265:277–83.
41. Lee HJ, Hyung WJ, Yang HK, Han SU, Park YK, An JY, 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;270:983–91.
42. Fujiya K, Tokunaga M, Nishiwaki N, Furukawa K, Omori H, Kaji S, et al. Feasibility of laparoscopic distal gastrectomy for stage i gastric cancer in patients outside of clinical trials. J Soc Surg Aliment Tract 2018;22:1665–71.
43. Katai H, Sasako M, Fukuda H, Nakamura K, Hiki N, Saka M, et al. Safety and feasibility of laparoscopy-assisted distal gastrectomy with suprapancreatic nodal dissection for clinical stage I gastric cancer: a multicenter phase II trial (JCOG 0703). Gastric Cancer 2010;13:238–44.
44. Zhang CD, Yamashita H, Zhang S, Seto Y. Reevaluation of laparoscopic versus open distal gastrectomy for early gastric cancer in Asia: a meta-analysis of randomized controlled trials. Int J Surg Lond Engl 2018;56:31–43.
45. Kim HH, Han SU, Kim MC, Kim W, Lee HJ, Ryu SW, 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 Oncol 2019;5:506–13.
46. Nunobe S, Sasako M, Saka M, Fukagawa T, Katai H, Sano T. Symptom evaluation of long-term postoperative outcomes after pylorus-preserving gastrectomy for early gastric cancer. Gastric Cancer 2007;10:167–72.
47. Morita S, Katai H, Saka M, Fukagawa T, Sano T, Sasako M. Outcome of pylorus- preserving gastrectomy for early gastric cancer. Br J Surg 2008;95:1131–5.
48. Fujita J, Takahashi M, Urushihara T, Tanabe K, Kodera Y, Yumiba T, et al. Assessment of postoperative quality of life following pylorus-preserving gastrectomy and Billroth-I distal gastrectomy in gastric cancer patients: results of the nationwide postgastrectomy syndrome assessment study. Gastric Cancer 2016;19:302–11.
49. Hiki N, Nunobe S, Kubota T, Jiang X. Function-preserving gastrectomy for early gastric cancer. Ann Surg Oncol 2013;20:2683–92.
50. Katai H, Morita S, Saka M, Taniguchi H, Fukagawa T. Long-term outcome after proximal gastrectomy with jejunal interposition for suspected early cancer in the upper third of the stomach. Br J Surg 2010;97:558–62.
51. Ikeguchi M, Kader A, Takaya S, Fukumoto Y, Osaki T, Saito H, et al. Prognosis of patients with gastric cancer who underwent proximal gastrectomy. Int Surg 2012;97:275–9.
52. Sugoor P, Shah S, Dusane R, Desouza A, Goel M, Shrikhande SV. Proximal gastrectomy versus total gastrectomy for proximal third gastric cancer: total gastrectomy is not always necessary. Langenbecks Arch Surg 2016;401:687–97.
53. Son MW, Kim YJ, Jeong GA, Cho GS, Lee MS. Long-term outcomes of proximal gastrectomy versus total gastrectomy for upper-third gastric cancer. J Gastric Cancer 2014;14:246–51.
54. Xu Y, Tan Y, Wang Y, Xi C, Ye N, Xu X. Proximal versus total gastrectomy for proximal early gastric cancer: a systematic review and meta-analysis. Medicine (Baltimore) 2019;98:e15663.
55. Takeuchi H, Kitagawa Y. New sentinel node mapping technologies for early gastric cancer. Ann Surg Oncol 2013;20:522–32.
56. Wang Z, Dong ZY, Chen JQ, Liu JL. Diagnostic value of sentinel lymph node biopsy in gastric cancer: a meta-analysis. Ann Surg Oncol 2012;19:1541–50.
57. Siewert JR, Sendler A. Potential and futility of sentinel node detection for gastric cancer. Recent Results Cancer Res Fortschritte Krebsforsch Progres Dans Rech Sur Cancer 2000;157:259–69.
58. Mpallas KD, Lagopoulos VI, Kamparoudis AG. Prognostic significance of solitary lymphnode metastasis and micrometastasis in gastric cancer. Front Surg 2018;5:63.
59. Lee YJ, Jeong SH, Hur H, Han SU, Min JS, An JY, et al. Prospective multicenter feasibility study of laparoscopic sentinel basin dissection for organ preserving surgery in gastric cancer: quality control study for surgical standardization prior to phase III trial. Medicine (Baltimore) 2015;94:e1894.
60. Park JY, Kim YW, Ryu KW, Nam BH, Lee YJ, Jeong SH, et al. Assessment of laparoscopic stomach preserving surgery with sentinel basin dissection versus standard gastrectomy with lymphadenectomy in early gastric cancer-A multicenter randomized phase III clinical trial (SENORITA trial) protocol. BMC Cancer 2016;16:340.