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# Chinese national clinical practice guidelines on the prevention, diagnosis, and treatment of early gastric cancer

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**Abstract**

**Background:** Gastric cancer is one of the most common malignant tumors in the digestive system in China. Few comprehensive practice guidelines for early gastric cancer in China are currently available. Therefore, we created the Chinese national clinical practice guideline for the prevention, diagnosis, and treatment of early gastric cancer.

**Methods:** This clinical practice guideline (CPG) was developed in accordance with the World Health Organization's recommended process and with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) in assessing evidence quality. We used the Evidence to Decision framework to formulate clinical recommendations to minimize bias and increase transparency in the CPG development process. We used the Reporting Items for practice Guidelines in HealThcare (RIGHT) statement and the Appraisal of Guidelines for Research and Evaluation II (AGREE II) as reporting and conduct guidelines to ensure completeness and transparency of the CPG.

**Results:** This CPG contains 40 recommendations regarding the prevention, screening, diagnosis, treatment, and follow-up of early gastric cancer based on available clinical studies and guidelines. We provide recommendations for the timing of *Helicobacter pylori* eradication, screening populations for early gastric cancer, indications for endoscopic resection and surgical gastrectomy, follow-up interval after treatment, and other recommendations.

**Conclusions:** This CPG can lead to optimum care for patients and populations by providing up-to-date medical information. We intend this CPG for widespread adoption to increase the standard of prevention, screening, diagnosis, treatment, and follow-up of early gastric cancer; thereby, contributing to improving national health care and patient quality of life.

**Keywords:** Early gastric cancer; Prevention; Screening; Diagnosis; Treatment; Follow-up

## Introduction

According to the data from GLOBOCAN 2020, there are an estimated 509,421 new cases of gastric cancer and 400,415 deaths in China annually. Additionally, both the incidence and mortality of gastric cancer in China are the third-highest among malignant tumors.[1] Correa and Piazuelo[2] proposed that most gastric cancers involve a series of pathological changes, namely atrophic gastritis, intestinal metaplasia, dysplasia, and adenocarcinoma, and the risk of gastric cancer increases gradually with progression through the cascade. Most patients with early gastric cancer and precancerous lesions have no specific symptoms. Owing to the lack of inexpensive and convenient early screening methods, the early diagnosis and treatment rate of gastric cancer in China is less than 10%, and the 5-year survival rate is low (31.3%); much lower than that in Japan and South Korea.[3,4] Therefore, early diagnosis and treatment of gastric cancer and precancerous lesions are essential to reduce mortality and prolong survival time.

Recently, the basic and clinical research on early gastric cancer has made great progress. The focus of this clinical practice guideline (CPG) is on the prevention, screening, diagnosis, treatment, and surveillance of gastric cancer. This CPG is intended to provide whole-process utility

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**Table 1: Summary and strengths of the recommendations.**

| No. | Recommendation | Strength of recommendation |
|---|---|---|
| **Prevention** | | |
| 1.1 | We recommend eradication of *Helicobacter pylori (H. pylori)* before the development of atrophy and/or intestinal metaplasia. | Strong recommendation, moderate certainty of evidence |
| 1.2 | We suggest against a "test-and-treat" strategy for *H. pylori* infection for asymptomatic children to protect against gastric cancer development. | Weak recommendation, very low certainty of evidence |
| 1.3 | Eradication of *H. pylori* is conditionally suggested in elderly patients (≥80 years) with *H. pylori* infection. | Weak recommendation, very low certainty of evidence |
| 1.4 | Possible chemoprevention of gastric cancer | |
| 1.4.1 | Low-dose daily aspirin is suggested for the prevention of gastric cancer in patients with cardiovascular and cerebrovascular diseases who may benefit from the use of aspirin. | Weak recommendation, low certainty of evidence |
| 1.4.2 | Cyclooxygenase-2 (COX-2) inhibitors are not suggested for the prevention of gastric cancer. | Weak recommendation, low certainty of evidence |
| 1.4.3 | Metformin is not suggested for the prevention of gastric cancer. | Weak recommendation, very low certainty of evidence |
| **Screening** | | |
| 2.1 | We suggest endoscopic screening, in accordance with Li *et al*'s prediction model to obtain health economic benefits. | Weak recommendation; very low certainty of evidence |
| 2.2 | Patients older than 40 years with *H. pylori* infection and other risk factors for gastric cancer (male, smoking, pernicious anemia, immediate relatives with gastric cancer, severe atrophic gastritis, intestinal metaplasia, adenoma, and etc.) are recommended for gastric cancer screening. A combination of *H. pylori* detection and the pepsinogen I and pepsinogen I/II ratio are recommended as gastric cancer screening indicators. | Strong recommendation, low certainty of evidence |
| 2.3 | Magnetically controlled capsule gastroscopy, as a beneficial supplement and the best alternative to conventional gastroscopy, can be used for gastric cancer screening. For special populations (people who decline or cannot tolerate conventional gastroscopy, or those who have a high risk of complications during gastroscopy), magnetically controlled capsule gastroscopy is recommended for gastric cancer screening after exclusion of any contraindications. | Strong recommendation; moderate certainty of evidence |
| **Diagnosis** | | |
| 3.1 | It is recommended to use mucolytic agents (such as pronase or N-acetylcysteine) to dissolve and remove gastric mucus before gastroscopy, and to use defoaming agents (such as simethicone or dimethicone) to reduce gastric foam, which can improve the visibility of the mucosa and may increase the detection rate of early gastric cancer. | Strong recommendation, moderate certainty of evidence |
| 3.2 | For patients with severe gastric peristalsis, which interferes with clear observation, L-menthol spray on the gastric mucosa is suggested to inhibit gastric peristalsis. | Weak recommendation, moderate certainty of evidence |
| 3.3 | Sedatives and analgesics are suggested for patients who are extremely anxious and/or unable to cooperate during gastroscopy. Painless endoscopy may improve the detection rate of early gastric cancer. | Weak recommendation, low certainty of evidence |
| 3.4 | Adequate time for gastroscopy is helpful in the detection of early gastric cancer. We recommend no less than 7 minutes for a complete esophagogastroduodenal examination. | Strong recommendation, low certainty of evidence |
| 3.5 | Diagnostic value of imaging examination for early gastric cancer | |
| 3.5.1 | Clinical tumor stage (cT stage) | |
| | Endoscopic ultrasonography (EUS) is recommended to identify the cT stage in patients with early gastric cancer. | Strong recommendation, moderate certainty of evidence |
| | Multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI) are conditionally suggested to identify the cT stage because these methods tend to perform slightly worse for cT staging of early gastric cancer compared with EUS, with moderate accuracy, sensitivity, and specificity. | Weak recommendation, moderate certainty of evidence |
| | Positron emission tomography (PET) is not suggested to define the cT stage of early gastric cancer. | Weak recommendation, moderate certainty of evidence |
| 3.5.2 | Clinical lymph node stage (cN stage) | |
| | MDCT is recommended to assess the cN stage in patients with early gastric cancer. | Strong recommendation, moderate certainty of evidence |
| | EUS is suggested to assess regional metastatic lymph nodes in early gastric cancer. | Weak recommendation, moderate certainty of evidence |
| | When MDCT findings cannot confirm the cN stage, MRI and PET are recommended to provide supplemental information to determine the cN stage of early gastric cancer. | Strong recommendation, moderate certainty of evidence |
| 3.5.3 | Clinical metastatic stage (cM stage) | |
| | MDCT is recommended to identify the cM stage in patients with early gastric cancer. | Strong recommendation, high certainty of evidence |
| | When MDCT findings cannot confirm the cM stage, MRI is recommended to define the diagnosis of liver metastases in patients with early gastric cancer. | Strong recommendation, high certainty of evidence |
| | If metastases are suspected clinically, PET is recommended to identify the cM stage when MDCT and MRI findings cannot confirm the diagnosis. | Strong recommendation, moderate certainty of evidence |
| **Treatment** | | |
| 4.1 | Patients are suggested to undergo endoscopic treatment when there is an extremely low probability of lymph node metastasis, and when the size and site of the lesion are feasible for *en bloc* resection. | Weak recommendation, low certainty of evidence |
| 4.2 | We conditionally suggest that patients with early signet ring cell carcinoma undergo endoscopic submucosal dissection (ESD) as treatment. | Weak recommendation, low certainty of evidence |

(*continued*)

Table 1

(Continued).

| No. | Recommendation | Strength of recommendation |
|---|---|---|
| 4.3 | For patients with early gastric cancer that cannot be treated by ESD, combined ESD and laparoscopic lymph node dissection is suggested. | Weak recommendation, low certainty of evidence |
| 4.4 | Management of complications associated with ESD for early gastric cancer | |
| 4.4.1 | Routine second-look endoscopy is not recommended to prevent bleeding after gastric ESD. | Strong recommendation, high certainty of evidence |
| 4.4.2 | Endoscopic closure methods are suggested to be the first choice for post-gastric ESD perforation. When panperitonitis develops, emergency surgery is indicated. | Weak recommendation, low certainty of evidence |
| 4.5 | Additional surgical treatment is suggested for early gastric cancer after noncurative resection with ESD. However, close follow-up or additional endoscopic treatment is suggested when a positive horizontal margin is the only noncurative resection factor, especially in elderly patients. | Weak recommendation, low certainty of evidence |
| 4.6 | Routine detection and eradication of *H. pylori* after early gastric cancer surgery are recommended to prevent metachronous cancer. | Strong recommendation, high certainty of evidence |
| 4.7 | Quality of life in early gastric cancer patients after super- minimally invasive surgery is better than that with traditional and minimally invasive surgery. | Strong recommendation, moderate certainty of evidence |
| 4.8 | Radical gastrectomy (RG) is recommended for tumors that do not meet the endoscopic resection indication (T1b) and with the possible presence of lymph node metastasis, as suggested by preoperative examinations, and among patients with noncurative ESD resection of eCura C-2 gastric cancer. | Strong recommendation, low certainty of evidence |
| 4.9 | Both preoperative and intraoperative gastroscopy are suggested for the localization of early gastric cancer. | Weak recommendation, very low certainty of evidence |
| 4.10 | Laparoscopic gastrectomy for the treatment of early gastric cancer | |
| 4.10.1 | Laparoscopic surgery is recommended for distal gastrectomy in early gastric cancer. | Strong recommendation, high certainty of evidence |
| 4.10.2 | Laparoscopic surgery is recommended for total gastrectomy in early gastric cancer. | Strong recommendation, high certainty of evidence |
| 4.10.3 | Laparoscopic surgery is suggested for proximal gastrectomy and other functional sparing surgeries in early gastric cancer. | Weak recommendation, low certainty of evidence |
| 4.11 | For early gastric cancer, RG should fully ensure the resection margin distance to the tumor edge. For stage T1 tumors, the recommended resection margin is >2 cm from the tumor. The standard operations are distal gastrectomy and total gastrectomy. With sufficient resection margins, functional-preserving gastrectomy can be selected based on the tumor location. Regarding upper-third lesions, if >50% of the stomach can be preserved, proximal gastrectomy can be performed. Regarding middle-third lesions, if the distal lesion is >4 cm from the pylorus, pylorus-preserving gastrectomy can be chosen. | Strong recommendation, low certainty of evidence |
| 4.12 | Total gastrectomy is suggested for hereditary diffuse early gastric cancer. | Weak recommendation, low certainty of evidence |
| 4.13 | Subtotal gastrectomy is suggested for multiple early gastric cancer that is unsuitable for endoscopic treatment. | Weak recommendation, very low certainty of evidence |
| 4.14 | D2 lymphadenectomy is recommended for cT1N$^+$ tumors, and D1/1$^+$ lymphadenectomy is recommended for cT1N0 tumors. | Strong recommendation, low certainty of evidence |
| 4.15 | Additional surgical resection with lymphadenectomy for eCura C1/2 patients | |
| 4.15.1 | Surgical resection with lymphadenectomy is an option (others include repeat ESD or careful follow-up) for eCura C1 patients based on the status of the primary tumor(s). | Conditional recommendation, low certainty of evidence |
| 4.15.2 | Surgical resection with lymphadenectomy is recommended for eCura C2 patients. | Strong recommendation, low certainty of evidence |
| 4.16 | The recommended extent of gastrectomy for early gastric cancer patients who have undergone noncurative ESD is the same extent as that for early gastric cancer. | Strong recommendation, low certainty of evidence |
| 4.17 | The suggested timing of additional surgery for early gastric cancer patients after noncurative ESD is within 3 months after ESD. | Weak recommendation, very low certainty of evidence |
| **Follow-up** | | |
| 5.1 | The suggested classification of postoperative recurrence of early gastric cancer is as gastric recurrence and extragastric metastasis (including lymph node metastasis, hematogenous metastasis, abdominal metastasis, and others). Extragastric metastasis is more common and occurs mainly in lymph nodes and the liver, while peritoneal metastasis is less common. Lymph node metastasis, lymphovascular invasion, and tumor invasion depth are suggested risk factors for postoperative recurrence in patients with early gastric cancer. | Weak recommendation, low certainty of evidence |
| 5.2 | The follow-up after R0 resection for early gastric cancer is recommended to be divided into two stages, as follows: stage I, every 6 months for the first 2 years after surgery, and stage II, annually for 2–5 years after surgery. Regular follow-up is recommended to comprise at least the following: (1) clinical history, physical examination, body weight; (2) blood tests, namely blood routine examination, biochemical examination, tumor markers (carcinoembryonic antigen [CEA], carbohydrate antigen 19-9 [CA19-9], and others); and (3) imaging examination, such as computed tomography (CT) and/or ultrasonography (US) and endoscopy. | Strong recommendation, low certainty of evidence |
| 5.3 | Patients with low-grade intraepithelial neoplasia (LGIN) detected by biopsy should undergo an intensive endoscopic examination. Lesions with risk factors (such as clear boundaries or obvious protuberances and depressions) are suggested to undergo endoscopic minimally invasive treatment. For patients with no obvious abnormalities after the examination, endoscopic examination is suggested every 6–12 months. | Weak recommendation, moderate certainty of evidence |

for Chinese clinicians and patients to improve patients' health outcomes. This article provides a synopsis of 40 key recommendations, with summaries of clinical study data supporting each recommendation [Table 1]. We aim to update this CPG in 2025.

## Methods

### Guideline development group

A multidisciplinary group of 43 experts on gastroentology, general surgery, medical imaging, pathology, and methodology from regions across China forms the guideline development group (GDG). The members' conflicts of interest were collected and assessed in accordance with the principles listed on the Guideline International Network (GIN). All GDG members were free of financial and intellectual conflicts of interest and were permitted full participation. This CPG is registered on the GIN website (https://guidelines.ebmportal.com/node/70434).

### Guideline development

This CPG was developed in accordance with the World Health Organization's recommended process and with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) for assessing evidence quality, and using the Evidence to Decision framework to formulate clinical recommendations. This process minimized bias and increased the transparency of the process. Quality of evidence indicates the degree of certainty of the findings. GRADE categorizes the quality of evidence into high, moderate, low, and very low by assessing various aspects of the body of evidence, namely risk of bias, inconsistency, indirectness, imprecision, and publication bias. The strengths of the recommendations in this CPG are categorized as strong, weak, and conditional. The factors that promoted strong recommendation were high certainty of evidence, similarity in stakeholders' values and preferences, cost effectiveness, and sharp contrast between benefit and harm.[5]

The GDG identified important clinical questions through discussion, which were later converted into research questions using the problem/patient/population, intervention/exposure, comparisons, outcomes (PICO) format to pave the way for systematic reviews. The GDG held several meetings between 2022 and 2023 to review the evidence under each PICO question, and to reach a consensus on the corresponding recommendations. Consensus was reached in each case through open discussion and voting, where 70% defined the threshold to pass a recommendation.

The full CPG report was sent for review to external guideline methodologists and clinicians without direct involvement in the current CPG development. The feedback was collected and incorporated, as appropriate. We referenced Appraisal of Guidelines for Research and Evaluation II (AGREE II) before and during the creation of this CPG to ensure quality, and we followed the Reporting Items for practice Guidelines in HealThcare (RIGHT) statement for reporting.[6,7]

### Evidence synthesis

The systematic review team searched PubMed, Embase, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, China Biomedical Database, and WanFang Database between October 2021 and March 2022 without date or language limits. Additionally, reviewers hand searched the references of all included articles for further relevant studies, and contacted clinicians for potentially relevant studies. Two separate sets of searches were performed to identify studies on efficacy and safety, and studies on cost-effectiveness, values and preferences, acceptability, and feasibility. Quality of evidence was evaluated using GRADE, as stated in the preceding section.

## Recommendations and Evidence Profiles

### Part 1. Prevention

**Clinical question 1.1:** Can the risk of developing gastric cancer be reduced effectively using eradication treatment before the development of atrophy and/or intestinal metaplasia?

**Recommendation 1.1:** We recommend eradication of *Helicobacter pylori (H. pylori)* before the development of atrophy and/or intestinal metaplasia (strong recommendation, moderate certainty of evidence).

The development of intestinal-type gastric cancer is a multifactorial and multistage process (Correa cascade) that is characterized by the following progression: normal gastric mucosa–superficial gastritis–atrophic gastritis–intestinal metaplasia–dysplasia–gastric cancer.[2] *H. pylori* infection mainly plays a role early in carcinogenesis (before gastric mucosal atrophy and/or intestinal metaplasia). Many studies have shown that early eradication of *H. pylori* can eliminate gastric inflammation, reverse the progression of carcinogenesis, and reduce or even eliminate the risk of gastric cancer.[8] Additionally, many evidence-based studies have confirmed that *H. pylori* eradication reduces the risk of gastric cancer.[9–12] Recent published meta-analyses showed that *H. pylori* eradication in healthy individuals significantly reduced the risk of gastric cancer (relative risk [RR] = 0.54; 95% confidence interval [CI]: 0.40–0.72) and the associated mortality (RR = 0.61; 95% CI: 0.40–0.92).[3] In addition to gastric mucosal atrophy or intestinal metaplasia status, follow-up time, patient age, *H. pylori* reinfection rate, antioxidant supplementation, and other factors may have an important impact on the effect of intervention.

**Clinical question 1.2:** Is screening for *H. pylori* infection in children necessary to prevent gastric cancer?

**Recommendation 1.2:** We suggest against a "test-and-treat" strategy for *H. pylori* infection for asymptomatic children to protect against gastric cancer development (weak recommendation, very low certainty of evidence).

*H. pylori* eradication reduces gastric cancer risk in the adult population[13,14] However, little evidence confirms

whether a "test-and-treat" strategy for *H. pylori* infection in children reduces the risk of gastric cancer development during adulthood. Notably, North American, European, and Japanese pediatric guidelines have recommended against a "test-and-treat" strategy for *H. pylori* infection in asymptomatic children.[15–17] Currently, little direct evidence supports the need to assess the risk of gastric cancer in children after screening and eradication of *H. pylori*. We should also consider that a "test-and-treat" strategy might result in negative effects in children, such as drug adverse events, reinfection rates, induction of antimicrobial resistance, and modifying the potential beneficial effects of *H. pylori* in allergic/atopic disease during childhood. In any case, the "test-and-treat" strategy is currently not suggested for asymptomatic children.

**Clinical question 1.3:** In elderly patients with *H. pylori* infection, does eradication of *H. pylori* reduce the morbidity and mortality of gastric cancer compared with no eradication?

**Recommendation 1.3:** Eradication of *H. pylori* is conditionally suggested in elderly patients (≥80 years) with *H. pylori* infection (weak recommendation, very low certainty of evidence).

*H. pylori* is associated with chronic gastritis, peptic ulcers, and other diseases, and is also considered the most important risk factor for gastric cancer.[18] Some guidelines recommend *H. pylori* eradication and clearly indicate that eradication can reduce the morbidity and mortality of gastric cancer and effectively prevent gastric cancer.[19] However, little direct evidence indicates that *H. pylori* eradication reduces the risk of gastric cancer in elderly patients (≥ 80 years) with *H. pylori* infection. Further studies are needed to examine the long-term clinical effects of *H. pylori* eradication in elderly patients.[20]

**Clinical question 1.4:** Do pharmaceuticals, such as nonsteroidal anti-inflammatory drugs and metformin, have preventive effects regarding gastric cancer?

**Recommendation 1.4.1:** Low-dose daily aspirin is suggested for the prevention of gastric cancer in patients with cardiovascular and cerebrovascular diseases who may benefit from the use of aspirin (weak recommendation, low certainty of evidence).

A recent meta-analysis analyzed data for 10 cohort studies on aspirin and the risk of gastric cancer (comprising 14,933 events and 2,378,794 participants).[21] The results revealed an overall 33% reduced risk (RR = 0.67, 95% CI: 0.52–0.87; $P = 0.003$) of gastric cancer with regular aspirin use, with high heterogeneity and no indication of bias. A subgroup analysis of long-duration (≥5 years) use showed a significant association (three studies; RR = 0.6, 95% CI: 0.38–0.94; $P = 0.027$). Dose-response analysis revealed no significant association between aspirin dose and gastric cancer risk ($R^2 = 0.00$; $P = 0.948$). Regarding adverse events, a study of regular-dose aspirin in the primary prevention of cardiovascular events showed that the overall incidence of treatment-related adverse events was low.[22] Therefore, on the basis of this evidence of efficacy and safety, we suggest that low-dose aspirin can be prescribed in patients with the need for primary prevention of cardiovascular and cerebrovascular diseases, especially those with high-risk factors for gastric cancer.

**Recommendation 1.4.2:** Cyclooxygenase-2 (COX-2) inhibitors are not suggested for the prevention of gastric cancer (weak recommendation, low certainty of evidence).

A recent systematic review and meta-analysis[23] of five studies of the relationship between COX-2 inhibitors and the risk of gastric cancer (three case–control studies, one cohort study, and one RCT) suggested that COX-2 inhibitors are effective in gastric cancer prevention (RR = 0.45, 95% CI: 0.29–0.70). Dose-response analysis revealed that a COX-2 inhibitor dose of 200 mg/d significantly reduced the risk of gastric cancer (RR = 0.50, 95% CI: 0.30–0.84; $P = 0.009$). However, considering the possible adverse effects associated with COX-2 inhibitors, such as cardiovascular adverse events (hypertension, heart failure, and others), digestive adverse events (abdominal pain, indigestion, heartburn, and others), and kidney adverse events,[24,25] COX-2 inhibitors are not suggested for the prevention of gastric cancer.

**Recommendation 1.4.3:** Metformin is not suggested for the prevention of gastric cancer (weak recommendation, very low certainty of evidence).

Metformin is the most commonly prescribed oral glucose-lowering drug and is widely used in the treatment of type 2 diabetes. Recently, metformin has been found to have a therapeutic effect in cancer. Several *in vivo* and *in vitro* studies showed that metformin reduced the migration and invasion of gastric cancer cells[26] and restrained the carcinogenic properties of gastric cancer stem cells.[27] A meta-analysis of cohort studies suggested that metformin might decrease the risk of gastric cancer.[28] However, another recent meta-analysis showed that the relationship between metformin use and gastric cancer risk has been exaggerated as a result of the presence of immortal time bias.[29]

## *Part 2. Screening*

**Clinical question 2.1:** Does endoscopic screening, which is based on gastric cancer risk stratification, achieve health economic benefits?

**Recommendation 2.1:** We suggest endoscopic screening in accordance with Li *et al*'s prediction model to obtain health economic benefits (weak recommendation; very low certainty of evidence).

Endoscopy combined with histopathological biopsy is the most important and reliable method for gastric cancer screening. A population-based multicenter cohort study from China showed that endoscopic screening significantly reduced gastric cancer mortality in high-risk areas.[30] However, large-scale screening in China is difficult to perform because of the excessive work required of doctors. Currently, a number of gastric cancer risk stratification methods are used as the initial prescreening tool before endoscopy, and one of the most effective methods

was proposed by Li *et al*.[31,32] However, few studies have investigated the health economic benefits of endoscopic screening in China. A Japanese study showed that the "ABC method" combined with endoscopic screening was cost-effective.[33]

**Clinical question 2.2:** What is the best risk stratification method for gastric cancer screening?

**Recommendation 2.2:** Patients over 40 years of age with *H. pylori* infection and other risk factors for gastric cancer (male, smoking, pernicious anemia, immediate relatives with gastric cancer, severe atrophic gastritis, intestinal metaplasia, and adenoma) are recommended for gastric cancer screening. *H. pylori* detection with pepsinogen (PG) I measurement and the PG I/II ratio are recommended as gastric cancer screening indicators (strong recommendation, low certainty of evidence).

*H. pylori* infection is one of the most common chronic infections in humans. The numbers of new cases and deaths from gastric cancer in China annually are approximately half of all patients with gastric cancer worldwide. Approximately 90% of noncardiac cancers are attributed to *H. pylori* infection.[34] *H. pylori* was classified as a Class I (definite) carcinogen in human gastric cancer by the International Agency for Research on Cancer of the World Health Organization in 1994.[35] PG is a precursor of pepsin, a gastric mucosa-specific functional enzyme, with PG I and PG II subgroups. The serum PG concentration can reflect the morphology and function of the gastric mucosa in different parts of the stomach, and combined PG I measurement with the PG I/II ratio is useful as a "serological biopsy" of the gastric mucosa.[36] The combined detection of PG and *H. pylori* is of great importance in the early detection and treatment of gastric cancer and is worthy of clinical application. The Consensus Opinions on Early Gastric Cancer Screening and Endoscopic Diagnosis and Treatment in China (April 2014, Changsha)[37] suggested that the risk of gastric cancer could be effectively stratified based on the results of serum PG and *H. pylori* antibody measurement, and further examination strategies could be determined.

**Clinical question 2.3:** Gastroscopy is the most effective method for gastric cancer screening. Are other noninvasive techniques, including magnetically controlled capsule gastroscopy, also effective methods for gastric cancer screening?

**Recommendation 2.3:** Magnetically controlled capsule gastroscopy, as a beneficial supplement and the best alternative to conventional gastroscopy, can be used for gastric cancer screening. For certain populations (i.e., people who decline or cannot tolerate conventional gastroscopy, or those who have a high risk of complications during gastroscopy), magnetically controlled capsule gastroscopy is recommended for gastric cancer screening after exclusion of any contraindications (strong recommendation, moderate quality of evidence).

With conventional gastroscopy and histopathological examination as the gold standards, a number of studies have shown that magnetically controlled capsule gastroscopy has high sensitivity, specificity, and overall accuracy in the diagnosis of gastric diseases, such as gastric cancer, and is better tolerated by people. Therefore, magnetically controlled capsule gastroscopy can be used as a beneficial supplement and best alternative to conventional gastroscopy for gastric cancer screening.[38–41] Magnetically controlled capsule endoscopy has been recommended as a screening modality for gastric cancer in asymptomatic populations by the China Experts Consensus on the Protocol of Early Gastric Cancer Screening (2017, Shanghai) and the Chinese Guideline on Magnetically Controlled Capsule Gastroscopy (2021, Shanghai).[42,43] Other noninvasive detection methods for gastric cancer screening, namely serum tumor marker testing, X-rays, barium swallow radiography, and spiral CT, have limited value in early gastric cancer screening and are not recommended.[44]

### *Part 3. Diagnosis*

**Clinical question 3.1:** Should mucolytic agents and defoaming agents be used before gastroscopy to improve the visibility of the gastric mucosa and increase the detection rate of early gastric cancer?

**Recommendation 3.1:** It is recommended to use mucolytic agents (such as pronase or N-acetylcysteine) to dissolve and remove gastric mucus before gastroscopy, and to use defoaming agents (such as simethicone or dimethicone) to reduce gastric foam. These methods can improve the visibility of the mucosa and may increase the detection rate of early gastric cancer (strong recommendation, moderate certainty of evidence).

A clear visual field is the prerequisite for high-quality endoscopic examination.[45] The presence of foam and mucus can prolong examination time and may affect the detection of gastric mucosal lesions. Administering defoaming and mucolytic agents before endoscopy can remove bubbles and mucus in the stomach, improve gastric visibility scores, and decrease the need for water lavage, with no increase in endoscopic examination time.[46] A clear image is conducive to the detection of minimal gastric mucosal lesions, including early gastric cancer.[47,48]

There are conflicting results regarding whether premedication with defoaming and mucolytic agents before gastroscopy increases the detection rate of early gastric cancer. One study showed that defoaming and mucolytic agents increase the detection rate of precancerous lesions and early gastric cancer (36.4% in the test group *vs*. 26.8% in the control group; $P = 0.000$).[49] Two other multicenter studies showed that premedication with pronase alone or combined with simethicone may not increase the detection rate of early gastric cancer.[50,51]

**Clinical question 3.2:** In patients with severe gastric peristalsis, which interferes with clear observation, can antispasmolytic drugs that inhibit gastric peristalsis (such as butylscopolamine, glucagon, menthol oil, and L-menthol) be considered? Can gastric peristalsis inhibitors improve the detection rate of early gastric cancer?

**Recommendation 3.2:** For patients with severe gastric peristalsis, which interferes with clear observation, L-menthol spray on the gastric mucosa is suggested to inhibit gastric peristalsis (weak recommendation, moderate certainty of evidence).

L-menthol is a nontoxic substance that relaxes smooth muscle in the gastrointestinal tract by blocking calcium ions from entering the smooth muscle cells. Multiple meta-analyses and clinical trials have demonstrated that L-menthol sprayed directly on the gastrointestinal mucosa significantly inhibits gastrointestinal peristalsis with minimal adverse effects.[52–54] Intravenous injections of butylscopolamine or glucagon have also been used to inhibit gastrointestinal peristalsis. However, this treatment lacks meta-analysis support, and there are safety concerns.[55,56] Studies have shown that butylscopolamine may have adverse effects on the ophthalmic, urinary, and cardiovascular systems, and may lead to severe anaphylactic shock.[57–59] Additionally, glucagon may cause nausea, vomiting, delayed hypoglycemia, and allergic reactions.[60,61] A previous clinical trial showed that gastric peristalsis inhibitors did not improve the detection rate of early gastric cancer.[62]

**Clinical question 3.3:** Can painless endoscopy improve the detection rate of early gastric cancer?

**Recommendation 3.3:** Sedatives and analgesics are suggested for patients who are extremely anxious and/or unable to cooperate during gastroscopy. Painless endoscopy may improve the detection rate of early gastric cancer (weak recommendation, low certainty of evidence).

In the United States, more than 98% of gastroscopies are performed with sedation; however, in China, many routine gastroscopies are performed without sedation. Painless gastroscopy can relieve patients' anxiety and discomfort, and enable their cooperation to improve the quality of the procedure.[63–65] Sedation may improve the detection rate of early gastric cancer, likely owing to enhancing the use of accessary endoscopic techniques, prolonging observation time, and permitting more biopsies in different locations. A few systematic reviews have analyzed the effect of sedation on the performance of endoscopy and found that moderate sedation can provide a high level of physician and patient satisfaction without increasing the incidence of serious or life-threatening adverse events.[63,66,67] A multicenter retrospective study investigated the influence of sedation on the endoscopic detection rate of upper gastrointestinal early cancer and precancerous lesions and found that sedation statistically increased the detection rate of early gastric cancer (0.12% in the nonsedation group *vs.* 0.16% in the sedation group; $P = 0.02$).[68]

**Clinical question 3.4:** The duration of observation in the stomach is related to the detection rate of early gastric cancer; therefore, it is recommended that the stomach be observed for a sufficient length of time. What is the exact length of time?

**Recommendation 3.4:** Adequate time for gastroscopy is helpful in the detection of early gastric cancer. We recommend no less than 7 minutes for a complete esophagogastroduodenal examination (strong recommendation, low certainty of evidence).

To improve the detection rate of early gastric cancer, systematic observation should be performed in the stomach. To date, four papers have been published about the relationship between the duration of upper gastrointestinal endoscopy and the detection rate of early gastric cancers.[69–72] The detection of early gastric cancer is related to the observation time in the stomach. Sufficient examination time is helpful for lesion detection, and the stomach should be systematically observed to ensure that there are no blind spots; however, extremely long examination time is unnecessary.

**Clinical question 3.5:** Can imaging, namely computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography (EUS), and positron emission tomography (PET), be used to diagnose early gastric cancer?

**Recommendation 3.5.1:** EUS is recommended to identify the clinical tumor stage (T-stage) of early gastric cancer (strong recommendation, moderate certainty of evidence). The diagnostic accuracy of both multidetector CT (MDCT) and MRI to determine the T-stage varies compared with EUS; moreover, less experience has been gained with MDCT or MRI (weak recommendation, moderate certainty of evidence). PET/CT is not suggested as a routine imaging modality to determine gastric cancer T-stage (weak recommendation, moderate certainty of evidence).

The clinical T-stage of gastric cancer can be identified based on the intramural depth of tumor invasion detected by EUS, CT, or MRI. One meta-analysis of 46 studies involving 2742 patients demonstrated that EUS can distinguish T1 and T2 gastric cancer, with a pooled sensitivity and specificity of 85% (95% CI: 78%–91%) and 90% (95% CI: 85%–93%), respectively.[73] Moreover, another meta-analysis indicated that stage T1a or T1b gastric cancer can be differentiated by EUS, with a pooled sensitivity and specificity of 87% (95% CI: 81%–92%) and 75% (95% CI: 62%–84%), respectively.[73] Regarding the identification of T1 stage gastric cancer, one meta-analysis showed that the sensitivity of EUS (82%) was significantly higher than that of MDCT (41%), and the specificity of EUS and MDCT was 89% and 97%, respectively, with no significant difference.[74] Although one meta-analysis showed that the accuracy of MRI in the identification of T1 stage gastric cancer was 86.3%, the study involved only 109 patients.[75] The ability of PET to determine early gastric cancer T-stage cannot be confirmed.[75] These studies indicate that the most experience has been gained with EUS for the accurate diagnosis of early gastric cancer T-stage. Few MDCT studies and even fewer MRI studies are available for meta-analysis.

**Recommendation 3.5.2:** MDCT is recommended to identify the clinical lymph node stage (N-stage) in patients with early gastric cancer (strong recommendation, moderate certainty of evidence). EUS could be used to detect

regional metastatic lymph nodes (weak recommendation, moderate certainty of evidence). MRI and PET can provide supplemental information to determine the N-stage of early gastric cancer when MDCT cannot confirm a final decision (strong recommendation, moderate certainty of evidence).

The identification of gastric cancer N-stage using EUS, MDCT, and MRI is based mainly on the short-axis diameter of the lymph nodes. MDCT is recommended as the first choice to determine the N-stage of early gastric cancer. Compared with other imaging methods, EUS is more accurate in the diagnosis of regional metastatic lymph nodes because it can detect the detailed structure of the lymph nodes surrounding the stomach. The accuracy of MRI to determine the N-stage can be improved by adding diffusion-weighted imaging (DWI) because metastatic lymph nodes show higher signal intensity.[76] The higher signal intensity is induced by denser cellularity compared with that of benign lymph nodes.[76] Additionally, regarding determination of the early gastric cancer N-stage, PET has higher specificity compared with MDCT and MRI owing to the higher glucose metabolism of metastatic lymph nodes compared with benign lymph nodes.

One meta-analysis of 10 studies and 708 patients demonstrated that MDCT could identify gastric cancer N-stage, with a pooled sensitivity and specificity of 80.0% (95% CI: 62.5%–91.9%) and 77.8% (50.0%–87.9%), respectively.[77] Regarding EUS in the identification of gastric cancer N-stage, one meta-analysis of 44 studies and 3573 patients indicated that the sensitivity and specificity were 83% (95% CI: 79%–87%) and 67% (95% CI: 61%–72%), respectively.[73] Moreover, better results appeared not to be achievable with MRI or PET compared with MDCT.[75] Another meta-analysis of 12 retrospective studies and 3 prospective studies that involved 1301 patients aimed to compare the accuracy of DWI with PET/CT in the identification of gastric cancer N-stage. The pooled accuracy, sensitivity, and specificity of DWI and PET/CT in the meta-analysis were 79% (95% CI: 73%–85%) and 69% (95% CI: 61%–77%); 81% (95% CI: 77%–84%) and 52% (95% CI: 39%–64%); and 88% (95% CI: 61%–97%) and 66% (95% CI: 62%–70%), respectively.[78]

**Recommendation 3.5.3:** MDCT is recommended to identify the clinical metastatic stage (M-stage) in patients with early gastric cancer (strong recommendation, high certainty of evidence). When MDCT cannot be used to confirm liver metastases, MRI is recommended to confirm the diagnosis (strong recommendation, high certainty of evidence). If distant metastases are suspected clinically, but neither MDCT nor MRI findings are sufficient to support a diagnosis, PET is recommended to provide additional information in the identification of M-stage (strong recommendation, moderate certainty of evidence).

The identification of M-stage in patients with early gastric cancer is a key point in determining the treatment strategy. The guidelines for gastric cancer recommend MDCT as the first choice in the determination of the M-stage, including liver and peritoneal metastases. If MDCT cannot diagnose liver metastases, MRI combined with DWI and the administration of gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (EOB-Gd-DTPA) is strongly recommended to make the final decision. MDCT tends to misdiagnose micro- or miniperitoneal metastases, especially those close to the organs. DW-MRI or PET/CT is best to identify peritoneal metastases.

One meta-analysis evaluated liver metastases assessed by MDCT, MRI, and PET/CT and included 36 studies.[79] The pooled sensitivity of MDCT (11 studies involving 2151 lesions), MRI (12 studies involving 2301 lesions), and PET/CT (13 studies involving 1846 lesions) in the analysis were 82.1% (95% CI: 74.0%–88.1%), 93.1% (95% CI: 88.4%–96.0%), and 74.1% (95% CI: 62.1%–83.3%), respectively. The pooled specificity of MDCT, MRI, and PET/CT were 73.5% (95% CI: 53.7%–86.9%), 87.3% (95% CI: 77.5%–93.2%), and 93.9% (95% CI: 83.9%–97.8%), respectively. MRI with Gd-EOB-DTPA showed higher sensitivity in the diagnosis of liver metastases compared with MDCT and PET/CT, with a similar specificity to that of PET/CT. Additionally, DWI to diagnose liver metastases had a pooled sensitivity and specificity of 87% (95% CI: 0.84%–0.89%) and 90% (95% CI: 0.87%–0.93%),[80] respectively. Another meta-analysis of peritoneal metastases included 20 studies of MDCT, 10 studies of PET/CT, and 7 studies of DWI. The sensitivity, specificity, and diagnostic odds ratio (OR) of CT, PET/CT, and DWI were 68% (95% CI: 46%–84%), 88% (95% CI: 81%–93%), and 15.9 (95% CI: 4.4–58.0); 80% (95% CI: 57%–92%), 90% (95% CI: 80%–96%), and 36.5 (95% CI: 6.7–199.5); and 92% (95% CI: 84%–96%), 85% (95% CI: 78%–91%) and 63.3 (95% CI: 31.5–127.3), respectively.[81]

### *Part 4. Treatment*

**Clinical question 4.1:** What are the indications for endoscopic treatment for early gastric cancer?

**Recommendation 4.1:** Generally, patients are suggested to undergo endoscopic treatment when there is an extremely low probability of lymph node metastasis, and when the size and site of the lesion indicate that *en bloc* resection is feasible (weak recommendation, low certainty of evidence).

Once a patient has been diagnosed with early gastric cancer, endoscopic or surgical therapy is recommended. As a stomach-preserving technique, endoscopic resection has been most widely used in the treatment of early gastric cancer.[82,83] According to the guidelines, the absolute indications for endoscopic mucosal resection/endoscopic submucosal dissection (ESD) are "UL0 cT1a differentiated-type carcinomas with a long diameter ≤2 cm". Absolute indications for ESD are "UL0 cT1a differentiated-type carcinomas with a long diameter >2 cm; UL1 cT1a differentiated-type carcinomas with a long diameter ≤3 cm; and UL0 cT1a undifferentiated-type carcinomas with a long diameter ≤2 cm" (UL0 = no ulceration).[84] Studies indicated that endoscopic treatment might lead to higher rates of recurrence compared with other therapies. Therefore, strict long-term postoperative surveillance is required after endoscopic treatment.[85]

**Clinical question 4.2:** Can the indications for ESD for early gastric signet ring cell carcinoma be expanded?

**Recommendation 4.2:** We conditionally suggest that patients with early gastric signet ring cell carcinoma undergo ESD (weak recommendation, low certainty of evidence).

Currently, undifferentiated cancer measuring <2 cm is an expanded indication for ESD.[86,87] However, owing to the high risk of lymph node metastasis and recurrence of undifferentiated cancer, especially signet ring cell cancer, whether patients with early signet ring cell cancer should be treated with ESD remains controversial.[88] Current studies have shown that in undifferentiated cancer patients, ESD has similar efficacy and safety compared with surgery, especially in cases with expanded indications.[88–90] However, the complete resection rate of lesions in the ESD group in previous studies was relatively low, and the recurrence rate was significantly higher than that in the operation group.[89,90] Therefore, whether patients with early gastric signet ring cell carcinoma should receive ESD still requires careful consideration.

**Clinical question 4.3:** Can endoscopic full-thickness gastric resection, based on the concept of super-minimally invasive surgery, and the combination of ESD and laparoscopic lymph node dissection broaden the indications for endoscopic treatment for gastric cancer?

**Recommendation 4.3:** For patients with early gastric cancer that cannot be treated by ESD, combined ESD and laparoscopic lymph node dissection (LLND) is suggested (weak recommendation, low certainty of evidence).

Observational cohort studies indicated that combined ESD and LLND could avoid unnecessary gastrectomy in some early gastric cancer patients, enabling complete resection of the primary tumor and accurate histopathological assessment of the lymph node status. Five patients underwent combined ESD and LLND in a preliminary study. Histopathological examination revealed that all resected nodes were free of cancer cells in four patients; however, metastasis to the lymph nodes was confirmed in one patient who chose not to undergo additional surgery. During the follow-up, quality of life was restored in all patients, and no tumor recurrence was observed.[91] In a single-center prospective study, 100 patients underwent sentinel node navigation surgery. For patients with a negative sentinel node biopsy during the intraoperative examination, treatment recommendation was made based on the location and type of cancer and the patient's preference. Of 11 patients who underwent ESD, one patient also underwent distal gastrectomy because of tumor recurrence.[92]

**Clinical question 4.4:** How do we manage complications due to ESD for early gastric cancer?

**Recommendation 4.4.1:** Routine second-look endoscopy (SLE) is not recommended to prevent bleeding after gastric ESD (strong recommendation, high certainty of evidence).

Post-ESD bleeding is difficult to predict and can be a potentially life-threatening complication. Although the administration of proton pump inhibitors and prophylactic coagulation after ESD were reportedly effective for preventing post-ESD bleeding,[93–96] the incidence of bleeding after gastric ESD remains approximately 5%. Bleeding after ESD may result in serious events, such as hypovolemic shock; thus, prevention is important. Regarding the role of routine SLE in reducing the incidence of post-ESD bleeding, three RCTs reported that routine SLE did not reduce bleeding after gastric ESD in patients with an average risk of bleeding.[97–99] Furthermore, a recent meta-analysis revealed that SLE after ESD did not reduce the risk of delayed post-gastric ESD bleeding.[100]

**Recommendation 4.4.2:** Endoscopic closure methods are suggested to be the first choice for post-gastric ESD perforation. When panperitonitis develops, emergency surgery is indicated (weak recommendation, low certainty of evidence).

Delayed perforation is a rare but severe complication of ESD for early gastric cancer.[101] The reported incidence of perforation after gastric ESD ranges from 0.04% to 0.7%,[102–104] and almost half of the cases were managed by endoscopic methods; the remaining cases required emergency surgery.

**Clinical question 4.5:** Does additional surgery improve oncologic outcomes in early gastric cancer patients after noncurative resection with ESD?

**Recommendation 4.5:** Additional surgical treatment is suggested for early gastric cancer after noncurative resection with ESD. However, close follow-up or additional endoscopic treatment is suggested when a positive horizontal margin is the only noncurative resection factor, especially in elderly patients (weak recommendation, low certainty of evidence).

Current meta-analyses showed that the additional surgical group had longer 5-year overall survival (OS), disease-free survival, and disease-specific survival compared with the nonsurgical group (follow-up observation).[105,106] Regarding close follow-up or endoscopic treatment in cases of a positive horizontal margin as the only noncurative resection factor, there were few additional endoscopic treatment cases, and all studies were retrospective cohort analyses; there is a lack of reviews and meta-analyses.

**Clinical question 4.6:** Is routine detection and eradication of *H. pylori* after early gastric cancer surgery recommended?

**Recommendation 4.6:** Routine detection and eradication of *H. pylori* after early gastric cancer surgery is recommended for the prevention of metachronous cancer (strong recommendation, high certainty of evidence).

Previous studies showed that the incidence of metachronous gastric cancer was significantly lower in the group that underwent detection and eradication of *H. pylori* after early gastric cancer surgery (including ESD) compared

with the undetected or uneradicated group.[107–110] Furthermore, there was a dose-response effect, with the benefit increasing with longer follow-up duration.[107–110]

**Clinical question 4.7:** Is quality of life for patients with early gastric cancer after super-minimally invasive surgery better than that with traditional and minimally invasive surgery?

**Recommendation 4.7:** Quality of life for early gastric cancer patients after super-minimally invasive surgery is better than that with traditional and minimally invasive surgery (strong recommendation, moderate certainty of evidence).

For early gastric cancer, partial or whole-stomach gastrectomy and gastrointestinal reconstruction is necessary as surgical treatment through a laparoscopic (minimally invasive surgery) or open approach (traditional surgery). Gastrectomy is associated with considerable adverse events, prolonged hospitalization, high cost, delayed recovery of gut function, and poor quality of life.[111–119] In contrast to minimally invasive and open surgery, super-minimally invasive surgery, which involves resecting the lesions while preserving anatomical integrity, is associated with enhanced recovery, minimal invasion, lower costs, and better quality of life.[113–120] The principle of super-minimally invasive surgery is to cure disease with quick recovery, and is a new treatment mode in medicine. In super-minimally invasive surgery, there are four channels, namely, the natural lumen, submucosal tunnel, multicavity channel, and transmural channel, and the methods comprise endoscopic mucosal resection, ESD, endoscopic submucosal tunnel dissection, and various modified endoscopic resection methods.[120]

**Clinical question 4.8:** What is the indication for surgical operation of early gastric cancer?

**Recommendation 4.8:** Radical gastrectomy is recommended for tumors that do not meet the endoscopic resection indications and with the possible presence of lymph node metastasis, as suggested by preoperative examinations, and patients with noncurative ESD resection of eCura C-2 (strong recommendation, low certainty of evidence).

A systematic review included 15 retrospective studies with 3737 patients in the endoscopic resection (ER) group and 4246 patients in the radical gastrectomy group. Although the 3- and 5-year survival rates were similar between the groups, the complication rate in the ER group was significantly lower than that in the radical gastrectomy group. ER is a good choice for patients with small early gastric cancer lesions without lymph node metastasis,[112] especially in older patients with various medical comorbidities and in patients who cannot tolerate abdominal surgery or decline surgery. In contrast, radical gastrectomy is recommended when preoperative examination suggests the possible presence of lymph node metastasis. A systematic review included five studies and described in detail the efficacy and safety of ESD or surgery in the treatment of undifferentiated cancer. The incidence of metachronous cancer in the ESD group was significantly higher than that in the operation group. Accordingly, radical gastrectomy can be used for early gastric cancer. Furthermore, additional surgery is occasionally necessary when patients have undergone noncurative ESD. Regarding distal gastrectomy for stage cTIN0 gastric cancer, laparoscopic surgery has similar safety compared with open surgery, with no significant difference in the long-term prognosis, and can be used as a routine treatment option.[121]

**Clinical question 4.9:** Which method is recommended for the localization of early gastric cancer?

**Recommendation 4.9:** Both preoperative and intraoperative gastroscopy are suggested for the localization of early gastric cancer (weak recommendation, very low certainty of evidence).

Recently, laparoscopic radical gastrectomy has developed rapidly in the field of gastric cancer treatment, and laparoscopic surgery has matured. When the gastric serosa is not involved, the specific location of the tumor is difficult to determine by observing the screen image during laparoscopic surgery. Therefore, the surgical resection scope of gastric cancer can be determined only by preoperative gastroscopic observation results or by experience and intuition. However, simple and effective methods for locating tumors in laparoscopic surgery for gastric cancer are lacking. Staining[122] and metal clip marking[123–126] can be used for preoperative gastroscopy, and endoscopy can be used for tumor localization, but there is no clear conclusion regarding the accuracy of these methods and which method is better. Therefore, both preoperative and intraoperative gastroscopy are recommended for the localization of early gastric cancer.

**Clinical question 4.10:** Is laparoscopic gastrectomy recommended for the treatment of early gastric cancer?

**Recommendation 4.10.1:** Laparoscopic surgery is recommended for distal gastrectomy in early gastric cancer (strong recommendation, high certainty of evidence).

**Recommendation 4.10.2:** Laparoscopic surgery is recommended for total gastrectomy in early gastric cancer (strong recommendation, high certainty of evidence).

**Recommendation 4.10.3:** Laparoscopic surgery is suggested for proximal gastrectomy and other functional sparing surgeries in early gastric cancer (weak recommendation, low certainty of evidence).

With developments in laparoscopic technology, laparoscopic gastrectomy has become widely used; however, surgical safety and OS after laparoscopic gastrectomy for early gastric cancer have not been confirmed. The evidence retrieval and evaluation team performed a systematic review. The systematic review included 37 studies[121,127–163] involving 12,172 patients. There were 23 studies of distal gastrectomy for early gastric cancer (6 RCTs, 2 prospective cohort studies, 15 retrospective studies). In the subgroup analysis by research type, six RCTs suggested a reduction in surgical complications with laparoscopic gastrectomy compared with open surgery

(hazard ratio [HR]: 0.60, 95% CI: 0.46–0.76). Additionally, 17 nonRCTs suggested a reduction in surgical complications with laparoscopic gastrectomy compared with open surgery (HR: 0.60, 95% CI: 0.40–0.90). Regarding OS, studies of distal gastrectomy, including three RCTs, suggested no significant difference in OS between laparoscopic and open surgery (HR: 0.93, 95% CI: 0.80–1.08), and five retrospective studies suggested no significant difference in OS between laparoscopic and open surgery (HR: 0.99, 95% CI: 0.68–1.44).

Three studies of total gastrectomy for early gastric cancer (one RCT and two retrospective studies) suggested that there was no significant difference in safety between laparoscopic and open total gastrectomy (HR: 1.09, 95% CI: 0.80–1.48). There was only one retrospective study of oncologic safety, which suggested no significant difference in OS between laparoscopic total gastrectomy and open total gastrectomy (HR: 0.96, 95% CI: 0.57–1.65).

Five studies, which focused on laparoscopic proximal gastrectomy and other functional sparing surgeries for early gastric cancer (all retrospective studies), reported no significant difference in surgical safety between laparoscopic gastric sparing surgery and open surgery (HR: 0.80, 95% CI: 0.51–1.25). There were no data on oncologic safety.

**Clinical question 4.11:** What is the recommended extent of gastrectomy for early gastric cancer?

**Recommendation 4.11:** For early gastric cancer, radical gastrectomy should fully ensure a safe margin distance from the tumor's edge. For stage T1 tumors, the recommended resection margin is >2 cm from the tumor. The standard operations are distal gastrectomy and total gastrectomy. With a sufficient resection margin, functional-preserving gastrectomy can be selected based on the tumor location. Regarding upper-third lesions, if more than 50% of the stomach can be preserved, proximal gastrectomy can be performed. Regarding middle-third lesions, if the distal lesion is >4 cm from the pylorus, pylorus-preserving gastrectomy can be chosen (strong recommendation, low certainty of evidence).

Surgery plays an important role in the treatment of early gastric cancer. To ensure R0 resection, the resection margin should be >2 cm from the tumor for stage T1 tumors.[164] The standard surgical procedures for gastric cancer are distal gastrectomy and total gastrectomy.[165] Many prospective clinical trials have shown that laparoscopic radical gastrectomy has become a routine choice for gastrectomy.[166,167] The prognosis of early gastric cancer is good; therefore, function-preserving gastrectomy can be selected based on the tumor location if the distance to the resection margin is sufficient. Proximal gastrectomy can be performed for upper gastric tumors if more than 50% of the stomach can be preserved.[168] Some studies suggest that proximal gastrectomy with double-tract or double-flap technique reconstruction provides excellent antireflux efficacy.[169,170] For tumors located in the middle third of the stomach, pylorus-preserving gastrectomy (PPG) can be performed if the distal lesion is >4 cm from the pylorus. A meta-analysis showed that the OS after PPG was not worse than that with distal gastrectomy, and PPG was associated with a lower incidence of postoperative weight loss and dumping syndrome.[171] The KLASS-04 study is designed to evaluate the difference between PPG and distal gastrectomy, and the study will provide high-level evidence regarding PPG.[172]

**Clinical question 4.12:** What is the recommended extent of gastrectomy for hereditary diffuse early gastric cancer?

**Recommendation 4.12:** Total gastrectomy is suggested for hereditary diffuse early gastric cancer (weak recommendation, low certainty of evidence).

Hereditary diffuse gastric cancer (HDGC) is caused by *CDH1* gene mutation with autosomal dominant inheritance.[173] People who carry the *CDH1* gene mutation have a lifetime risk of gastric cancer of up to 80%. Importantly, HDGC is difficult to diagnose in the early stage. Most patients are diagnosed as having HDGC in the advanced stage, which carries a poor prognosis. Only approximately 10% of patients with advanced HDGC diagnosed before the age of 40 years can undergo radical resection. The prognosis of HDGC is poor; the 5-year survival rate is <30% even with radical surgery with neoadjuvant or adjuvant chemotherapy.[174–177] Therefore, for people who carry the *CDH1* gene mutation, prophylactic total gastrectomy is suggested to eliminate the risk of gastric cancer and improve survival rates. More than 80%[178,179] of the patients who underwent prophylactic total gastrectomy were proven to have cancer on pathology. Most of the cancers were early gastric cancer, including advanced gastric cancer. Therefore, total gastrectomy is suggested for early gastric cancer that meets the diagnostic criteria of HDGC. Total gastrectomy and Roux-en-Y digestive tract reconstruction is suggested, and the proximal resection margin should include the distal esophagus with squamous epithelium to ensure no residual gastric mucosa. Owing to the small number of these patients, the level of evidence provided by the relevant literature is low. However, total gastrectomy is still suggested for patients with early gastric cancer meeting the diagnostic criteria of HDGC.

**Clinical question 4.13:** What is the recommended region (distal or total) for gastrectomy for multiple early gastric cancer (MEGC) that is unsuitable for endoscopic treatment?

**Recommendation 4.13:** Subtotal gastrectomy is suggested for MEGC that is unsuitable for endoscopic treatment (weak recommendation, very low certainty of evidence).

In 2020, Lee *et al*[180] performed a meta-analysis that included 25 cohort studies involving 3058 early gastric cancer patients. The results showed that the short-term outcome of radical subtotal gastrectomy was superior to that of radical total gastrectomy. Regarding the long-term outcomes, a meta-analysis that included two cohort studies involving 131 MEGC patients[181,182] reported that the 5-year OS after subtotal gastrectomy was comparable to that of total gastrectomy (OR = 1.40, 95% CI: 0.21–9.23).

Regarding short-term outcomes after subtotal *vs*. total gastrectomy, no direct evidence supports either approach in patients with MEGC. One meta-analysis included 25 cohort studies involving 3058 early gastric cancer patients. Compared with total gastrectomy, subtotal gastrectomy significantly reduced the operation time (weighted mean difference (WMD) = –17.89, 95% CI: –29.64 to –6.13) and intraoperative blood loss (WMD = –35.38, 95% CI: –61.27 to –9.48). Furthermore, no significant differences were observed between subtotal gastrectomy and total gastrectomy regarding hospitalization duration (WMD = –0.94, 95% CI: –2.73–0.85) or postoperative complications (OR = 0.84, 95% CI: 0.55–1.30).[180]

**Clinical question 4.14:** What is the recommended extent of lymph node dissection for early gastric cancer?

**Recommendation 4.14:** D2 lymphadenectomy is recommended for cT1N+ tumors, and D1/1+ lymphadenectomy is recommended for cT1N0 tumors (strong recommendation, low certainty of evidence).

Lymph node metastasis has an important impact on the prognosis of patients with early gastric cancer.[183] Studies have shown that approximately 5% of patients with mucosal cancer and 20% of patients with submucosal cancer have lymph node metastasis.[184,185] However, the rational extent of lymphadenectomy remains controversial. The risk of lymph node metastasis in early gastric cancer is much lower than that in advanced forms.[186] Invasion of the submucosa, poor differentiation, tumor size (diameter >2 cm), and ulceration are risk factors for lymph node metastasis in early gastric cancer.[105,187–189] In early gastric cancer that is unsuitable for endoscopic treatment (differentiated-type adenocarcinoma, UL0, T1a, diameter ≤2 cm), the Japanese Gastric Cancer Association guidelines suggest D1 or D1+ lymphadenectomy in cases with clinically-negative nodes. The 5-year disease-specific survival of D1/D1+ gastrectomy for early gastric cancer is 96%–98%,[159,190,191] which is similar to survival after D2 gastrectomy.[121,192,193] D2 lymphadenectomy should be performed for patients with cT1N+ tumors and whenever the possibility of nodal involvement cannot be dismissed.[87,194]

Currently, no consensus on the extent of lymphadenectomy for early gastric cancer is available. A systematic review that included 21 retrospective studies (4789 patients) showed that in patients with early gastric cancer who required salvage surgery after endoscopic surgery, those who underwent additional gastrectomy had longer 5-year OS (HR = 0.34; $P$ <0.001) and 5-year disease-free survival (HR = 0.52; $P$ = 0.001). Lymph node metastasis was associated with larger tumor size (>3 cm) (OR = 1.73; $P$ <0.001), elevated tumor type (OR = 1.60; $P$ = 0.035), deep tumor invasion (submucosal grade >1) (OR = 2.68; $P$ <0.001), lymphatic invasion (OR = 4.65; $P$ <0.001), and positive vertical margin (OR = 2.30; $P$ <0.001).[105]

**Clinical question 4.15:** What are the indications for surgical resection of early gastric cancer with noncurative ESD?

**Recommendation 4.15.1:** Surgical resection with lymphadenectomy is an option (others are repeat ESD or careful follow-up) for eCura C1 patients based on the status of the primary tumor(s) (conditional recommendation, low certainty of evidence).

**Recommendation 4.15.2:** Surgical resection with lymphadenectomy is recommended for eCura C2 patients (strong recommendation, low certainty of evidence).

Surgical resection with lymphadenectomy is the primary remedial measure for noncurative ESD in early gastric cancer. The eCura scoring system was developed in 2017 to categorize the curative degree of ESD.[195] In the Japanese gastric cancer treatment guidelines (v5, 2018),[196] the eCura system is used to evaluate the curability of ESD and determine additional treatment options. For patients with eCura C2, additional surgical treatment is recommended, but for eCura C1, additional surgery should be comprehensive, and the tumor status and ESD resection status should be considered. However, all of the current evidence regarding noncurative ESD is based on retrospective studies with different evaluation classifications for curative degree. Although there is low certainty of evidence, the Japanese eCura system is the best-evaluated system for patients who have undergone ESD.

A published meta-analysis, which included 10 studies from 2010 to 2018, found that additional surgery improved both OS and disease-specific survival compared with simple follow-up after noncurative ESD.[106]

**Clinical question 4.16:** What is the recommended extent of gastrectomy for early gastric cancer with noncurative ESD?

**Recommendation 4.16:** The recommended extent of gastrectomy for early gastric cancer patients with noncurative ESD is the same as that for early gastric cancer (strong recommendation, low certainty of evidence).

Few published studies have compared the extent of gastrectomy for early gastric cancer patients with noncurative ESD. In reality, early gastric cancer patients with noncurative ESD are still considered to have "early gastric cancer", and the extent of gastrectomy should not be influenced by previous ESD. Therefore, the extent of gastrectomy for early gastric cancer with or without noncurative ESD is the same as that for early gastric cancer and is consistent with the guidelines.[197] Therefore, we emphasize that the extent of gastrectomy for patients with noncurative ESD should be based on the treatment guidelines for early gastric cancer.

**Clinical question 4.17:** What is the optimal timing for additional surgery in patients with early gastric cancer following noncurative ESD?

**Recommendation 4.17:** The suggested timing of additional surgery for early gastric cancer patients after noncurative ESD is within 3 months after ESD (weak recommendation, very low certainty of evidence).

There is no clear conclusion regarding the best time for additional surgery after noncurative ESD for early gastric cancer. Studies have shown that ESD-induced ulcers are usually in the healing or scar formation stage 4–8 weeks after surgery. Inflammation and ulcers caused by ESD lead to inflammation and edema of local tissues in the gastric wall and swelling of lymph nodes around the lesion. The inflammatory response reaches its peak 1–2 weeks postoperatively and begins to resolve after 1 month.[198,199] With additional surgery performed less than 4 weeks after ESD, tissue separation and lymph node dissection become more difficult, the operation time is prolonged, and bleeding may increase. The recurrence rate and survival are not significantly affected by additional surgery performed >4 weeks postoperatively.

Few studies have focused on the optimal timing of additional surgery after noncurative ESD for early gastric cancer. In 2014, Kim *et al*[200] first suggested that 1 month after ESD was the best time for additional surgery. The study reviewed data for 154 patients with early gastric cancer who underwent additional surgery after ESD. The patients were divided into two groups: additional surgery ≤29 days after ESD and >29 days after ESD. The ≤29-day surgery group had longer operation times and more intraoperative blood loss compared with the >29-day group. In 2019, the research team in the study expanded the sample size to 302 patients and extended the follow-up time to 41.98 ± 21.23 months, which again showed that the delayed surgery group had shorter operation times and postoperative hospital stays.[201] The 5-year survival rate (99%) was higher in the later surgery group than that of the early surgery group (92%), but the difference was not statistically significant. Another retrospective study included 83 patients who were also divided into a ≤29-day additional surgery group and >29-day additional surgery group using the cutoff of 29 days after ESD. Compared with the early surgery group, the later surgery group had less intraoperative blood loss ($P = 0.011$). No significant differences for operation time, postoperative hospital stay, or postoperative complication rates were observed between the groups.

### *Part 5. Follow-up*

**Clinical question 5.1:** What is the common recurrence pattern in early gastric cancer patients after radical surgery, and what are the risk factors for recurrence?

**Recommendation 5.1:** The suggested classifications for postoperative recurrence of early gastric cancer are gastric recurrence and extragastric metastasis (lymph node metastasis, hematogenous metastasis, abdominal metastasis, and others). Extragastric metastasis is most common and occurs mainly in lymph nodes and the liver, while peritoneal metastasis is less common. Lymph node metastasis, lymphovascular invasion, and tumor invasion depth are risk factors for postoperative recurrence in patients with early gastric cancer (weak recommendation, low certainty of evidence).

The prognosis of early gastric cancer after radical surgery is good; however, a small number of patients may relapse after surgery. Therefore, identifying the risk factors associated with recurrence is important to guide postoperative follow-up and improve prognosis. A meta-analysis involving 14 studies showed that the recurrence modes of early gastric cancer after radical surgery comprised mainly local recurrence and extragastric metastasis.[114] The incidence of gastric recurrence was 0.4% (6/1597), and the incidence of extragastric metastasis was 0.4% (6/1555). A recent retrospective analysis with large numbers of patients ($n = 4149$) provided detailed information about extragastric metastases.[202] In the study, the local recurrence rate was 0.43% (18/4149), similar to that in the previous meta-analysis; however, the rate of extragastric metastasis was relatively high, at 1.5% (61/4149). Among the extragastric metastases, there were 23 cases of lymph node metastases, 17 cases of liver metastases, 5 cases of peritoneal metastasis, 4 cases of ovarian metastasis, and 12 cases of metastasis to other organs (lung, bone, pancreas, small intestine, and others). This pattern differed obviously from the postoperative recurrence pattern of advanced gastric cancer.

To assess the risk factors for postoperative recurrence of early gastric cancer, the evidence retrieval and evaluation team performed a meta-analysis that included 7 retrospective studies involving 12,289 patients diagnosed with early gastric cancer who underwent radical surgery.[203–209] The results showed that lymph node metastasis (metastatic/nonmetastatic RR = 3.58, 95% CI: 2.35–5.45), lymphovascular invasion (invaded/noninvaded RR = 1.90, 95% CI: 1.01–3.59), and tumor invasion depth (submucosal/mucosal RR = 1.90, 95% CI: 1.52–2.39) were risk factors associated with postoperative recurrence. In contrast, little evidence shows that differentiation (undifferentiated/differentiated RR = 1.10, 95% CI: 0.83–1.45), ulcer status (ulcerated/nonulcerated RR = 1.19, 95% CI: 0.81–1.75), and sex (male/female RR = 0.95, 95% CI: 0.78–1.17) were risk factors for postoperative recurrence. Additionally, several reports suggested that the amplification of *HER-2*,[210] eradication of *H. pylori*[211], and CD163 positivity[209] might also be used as predictors of early gastric cancer recurrence; however, additional studies are needed.

**Clinical question 5.2:** What is the recommended follow-up after surgery for early gastric cancer?

**Recommendation 5.2:** The recommended follow-up after R0 resection for early gastric cancer is divided into two stages, as follows: stage I, every 6 months for the first 2 years after surgery, and stage II, annually for 2–5 years after surgery. Regular follow-up is recommended to contain at least the following aspects:

(1) Clinical history, physical examination, and body weight;
(2) Blood tests, namely blood routine examination, biochemical examination, and tumor markers (e.g., carcinoembryonic antigen [CEA], carbohydrate antigen 19-9 [CA19-9]); and
(3) Imaging examination, such as CT and/or US and endoscopy (strong recommendation, low certainty of evidence).

Regular follow-up after radical gastrectomy for early gastric cancer can be used to assess the patient's general status, identify tumor recurrence early, and intervene appropriately. Follow-up should be performed based on tumor stage and patient-specific characteristics.[212] The frequency of follow-up for early gastric cancer is controversial.[87,197,213–215] Many studies have shown that intensive follow-up does not improve the long-term prognosis of gastric cancer patients who undergo curative treatment.[216,217] Therefore, we recommend that follow-up after R0 resection for early gastric cancer be divided into two stages, as follows: stage I, every 6 months for the first 2 years after surgery, and stage II, annually for 2–5 years after surgery. Regular follow-up should comprise at least the following aspects: general status, blood tests, and imaging examination. Regarding the patient's general status, the following should be evaluated, at a minimum: clinical history, performance status, body weight, and routine blood tests. Regarding the blood tests, the following measurements are necessary: routine blood examination, biochemical examination, and tumor markers (e.g., CEA, CA19-9). Endoscopy or CT should be performed based on the clinical findings.

**Clinical question 5.3:** What is the recommended follow-up for low-grade intraepithelial neoplasia?

**Recommendation 5.3:** Patients with low-grade intraepithelial neoplasia detected by biopsy should undergo an intensive endoscopic examination. Lesions with risk factors (such as clear boundaries or obvious protuberances and depressions) are suggested to undergo endoscopic minimally invasive treatment. For patients with no obvious abnormalities after the examination, endoscopic reexamination is suggested every 6–12 months (weak recommendation, moderate certainty of evidence).

In 2000, the World Health Organization introduced the concept of intraepithelial neoplasia in the new classification of digestive system tumors. On the basis of the degree of cellular and structural atypia, intraepithelial neoplasia is divided into low- and high-grades. Low-grade intraepithelial neoplasia is equivalent to mild to moderate dysplasia of the gastric mucosa; this is a precancerous lesion with the potential to transform into cancer.

Considering the possibility of biopsy error, current guidelines recommend that patients undergo at least one endoscopic examination and biopsy within the first year after surgery, to reduce the rate of biopsy errors. Combining different endoscopic techniques can help endoscopists observe lesion structures more accurately; thereby, making more accurate diagnoses. For example, magnifying endoscopy combined with narrow-band imaging can identify microvascular and microsurface structures under the epithelium. Confocal laser endomicroscopy can magnify the gastric epithelium cross-section by nearly 1000 times. A meta-analysis showed that the sensitivity of this method for detecting low- and high-grade intraepithelial neoplasia was 83% and 84%, respectively, and the combined specificity was 99%.[218]

Low-grade intraepithelial neoplasia is an important link in the Correa cascade towards gastric cancer development, usually progressing from atrophy and intestinal metaplasia. Therefore, regular endoscopic follow-up is necessary, with a suggested interval of 6–12 months, to detect lesions early and initiate timely endoscopic treatment.

## Discussion

Gastric cancer is the 5th most common cancer among all cancers worldwide and has become a huge problem threatening human health.[219,220] Early gastric cancer can be cured by minimally invasive surgery, such as ESD, and has a 5-year survival rate of >90%. In comparison, the prognosis of patients with advanced gastric cancer is relatively poor. Therefore, early detection of gastric cancer is critical to improve patients' prognosis.

Endoscopy combined with histopathological biopsy is the most important and reliable method for gastric cancer screening. However, as an invasive examination, conventional gastroscopy is poorly accepted by patients, which results in the delayed diagnosis of many patients with gastric cancer. Magnetically controlled capsule gastroscopy,[221] as a noninvasive examination, could be a beneficial alternative to conventional gastroscopy.

Tumor biomarkers also play important roles in cancer screening, especially in gastric cancer. However, owing to the poor sensitivity and specificity of conventional tumor biomarkers, such as CEA and CA72-4, the efficacy of tumor biomarkers in screening is poor. Among all screening methods, liquid biopsy is considered effective and has developed rapidly in the gastric cancer field. Circular RNAs (circRNAs) are one of the most popular liquid biopsy methods. Roy *et al*[222] identified a group of eight circRNAs as noninvasive biomarkers, with an area under receiver operating characteristic curve of 0.83 in the testing group. This eight circRNA panel distinguished early gastric cancer patients well. Circulating cell-free DNA (cfDNA) is another effective screening method. Liu *et al*[223] assessed the performance of targeted methylation analysis of cfDNA to detect cancers. The authors found that cfDNA sequencing, which provided informative methylation patterns, could detect more than 50 cancers regardless of stage, and might be a powerful method for cancer screening. Serum microRNAs (miRNAs) are also excellent candidates for liquid biopsy. So *et al*[224] developed a serum miRNA panel to identify patients with gastric cancer from a high-risk population. A 12-miRNA panel was developed, with an area under the curve of 0.93 and 0.92 in the discovery and validation cohorts, respectively. A Markov decision model was created and showed good cost-effectiveness, indicating that the model was cost-effective for large-scale screening in current practice, at an approximate cost of 44,531 US dollars/quality-of-life years gained.

The risk of gastric cancer could be largely reduced by proper prevention strategies. As well-known, the worldwide attributable fraction of *H.pylori* in gastric cancer is higher than 85%. This CPG suggests that the eradication of *H. pylori* before the development of atrophy and/or

intestinal metaplasia is meaningful to reduce the incidence of early gastric cancer.

Upper gastrointestinal endoscopy is crucial for the diagnosis of early gastric cancer, which may present as mild polypoid protrusions, superficial plaques, mucosal discoloration, depression, or ulceration.[225] Some studies emphasize the importance of careful examination, indicated by examination time, suggesting that at least 7 minutes of examination may be required.[71] Some scholars proposed a method of site examination to systematically observe various areas of the stomach and obtain 22 photos.[71] High-definition endoscopy with virtual chromoendoscopy is superior to white light endoscopy alone. These enhanced imaging modalities allow an experienced endoscopist to accurately and robustly detect high-risk lesions in the stomach.[226] A clear endoscopic field is the prerequisite for high-quality endoscopy. Before endoscopic examination, the use of defoaming and mucus removal agents can clear bubbles and mucus in the stomach, which is conducive to the observation of lesions and improving the lesion detection rate.[227] Satisfactory pharyngeal anesthesia or intravenous anesthesia can alleviate patient discomfort during endoscopy and improve the quality of endoscopy.[37]

Treatment modalities for early gastric cancer comprise endoscopic resection, surgery (gastrectomy), antibiotic therapy for the eradication of *H. pylori*, and adjuvant therapies. Endoscopic resection is considered for tumors that have a very low possibility of lymph node metastasis and are suitable for *en bloc* resection.[187]

Endoscopic hemostasis therapy is recommended as the first choice for patients with early gastric cancer who undergo endoscopic resection and who also have acute intraoperative bleeding or delayed bleeding. Although techniques and instruments for ESD have improved, bleeding is still the most common complication. Minimizing bleeding is important because blood can interfere with subsequent procedures. Methods for reducing postprocedural bleeding comprise administration of proton-pump inhibitors or prophylactic coagulation after ESD. Hemoclipping is infrequently used during ESD because the clips interfere with subsequent resection.[228]

SLE has no obvious clinical benefit in the prevention and treatment of late postoperative bleeding, and is not currently recommended.[229] Once delayed bleeding occurs, emergency endoscopic hemostasis should be performed as soon as possible. If hemostasis during endoscopy is difficult or fails, early surgery or interventional embolization is necessary.

Endoscopic resection of early gastric cancer complicated with perforation can be successfully treated endoscopically. If endoscopic treatment is difficult or fails, surgery should be performed quickly. A meta-analysis found that the ESD perforation rate was 4.5%, while the endoscopic mucosal resection perforation rate was 1.0%.[230] Factors associated with an increased risk of ESD perforation comprise tumor location in the upper stomach and tumor size >20 mm.[231]

The recently proposed eCura scoring system predicts cancer-specific survival in patients who do not meet the curative criteria after ESD for early gastric cancer.[195] This system is expected to be a more reasonable method to evaluate the curative effect of endoscopic resection for early gastric cancer compared with previous systems. The eCura evaluation system (A/B/C-1/C-2) emphasizes the influence of the "type of differentiation, tumor size and positive horizontal resection margin" on the evaluation of cure. ESD without additional treatment may be an acceptable option for patients at low risk of recurrence.

Patients with early gastric cancer complicated with *H. pylori* infection should undergo *H. pylori* eradication after surgery. Patients with early gastric cancer who received *H. pylori* treatment had lower rates of metachronous gastric cancer and better improvement compared with baseline regarding the grade of atrophy of the gastric body compared with patients who received placebo.[109] After *H. pylori* eradication, the area affected by early gastric cancer is smaller, and the morphology tends to be flattened and depressed.[109,195] Additionally, the mucosal boundary is blurred, which affects the observation and judgment of lesions.[109,195] Therefore, eradication therapy should be performed soon after surgery in patients with early gastric cancer complicated with *H. pylori* infection.

Long-term follow-up of premalignant lesions is an important component of gastric cancer prevention. Low-grade intraepithelial neoplasia is a common premalignant lesion of gastric cancer and is considered a critical point in gastric cancer progression in the Correa cascade effect. Therefore, regular endoscopic follow-up is necessary to detect lesions early and initiate timely endoscopic treatment. After the treatment of early gastric cancer, follow-up is also critical to prevent cancer recurrence and prolong patients' survival time.

In conclusion, on the basis of recent clinical research, this CPG has been formulated to provide reference for the prevention, screening, early diagnosis, and early treatment of early gastric cancer.

## Appendix

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### Conflicts of interest

None.

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