Early gastric cancer: Epidemiology, clinical manifestations, diagnosis, and staging

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INTRODUCTION

Early gastric cancer (EGC) is defined as invasive gastric cancer confined to the mucosa or submucosa, irrespective of lymph node metastasis (T1, any N). While EGC is of particular importance for patient care in Eastern Asia, its significance extends to other disciplines and patient populations:

- Globally, gastric adenocarcinoma, with nearly one million incident cases annually, is the third leading cause of global cancer mortality and the leading cause of infection-associated cancer death [1-4]. EGC accounts for 15 to 57 percent of incident gastric cancer, depending upon the geographic region, and the presence of screening programs. (See 'Epidemiology' below.)

- EGC has driven the development of imaging technologies for early neoplasia detection such as narrow band imaging and autofluorescence imaging. Subsequently, these technologies are being used for conditions throughout the gastrointestinal tract.

- The need for better approaches to the treatment of EGC has led to the development of advanced endoscopic resection techniques such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Endoscopic submucosal dissection' and "Overview of endoscopic resection of gastrointestinal tumors".)

- As highlighted in the global cancer survival surveillance data (CONCORD-3), survival rates from gastric cancer vary widely, from 10 percent in low-resource settings, to 30 percent in high-resource, low incidence nations, and to nearly 70 percent in eastern Asian countries (Korea, Japan) with gastric cancer screening programs and advanced endoscopic treatment techniques [5].

Gastric adenocarcinoma, and the major intestinal subtype in particular, progresses through a series of histopathologic stages, from normal mucosa, to chronic gastritis, multifocal atrophic gastritis, intestinal metaplasia, and finally dysplasia and adenocarcinoma. The principal cause of early pan-gastric mucosal inflammation and of chronic gastritis is *Helicobacter pylori* infection, with modulation by host genetics and the host response, diet, and other environmental factors. (See "Risk factors for gastric cancer" and "Association between Helicobacter pylori infection and gastrointestinal malignancy" and "Gastric cancer: Pathology and molecular pathogenesis".)

This topic will review the clinical manifestations, diagnosis, and staging of early gastric cancer. The treatment and prognosis of patients with early gastric cancer and the management of patients with advanced gastric cancer are discussed elsewhere. (See "Early gastric cancer: Treatment, natural history, and prognosis" and "Initial systemic therapy for locally advanced unresectable and metastatic esophageal and gastric cancer" and "Surgical management of invasive gastric cancer" and "Local palliation for advanced gastric cancer" and "Overview of endoscopic resection of gastrointestinal tumors".)

DEFINITION

The concept of early gastric cancer (EGC) originated in Japan in 1962. At that time, EGC was defined as a neoplasm that could be successfully treated with surgery. EGC is now defined more specifically as an adenocarcinoma that is restricted to the mucosa or submucosa, irrespective of lymph node metastasis (T1, any N) (table 1). These cancers have a significantly better prognosis (approximately 90 percent five-year survival rate) than do more advanced stages of gastric cancer. (See "Surgical management of invasive gastric cancer".)

Importantly, this definition, which has been adopted by the Japan Gastric Cancer Association, the Japan Gastroenterological Endoscopy Society and other international groups, acknowledges that there are a small percentage of patients with EGC who have lymph node involvement [6-8]. These cancers should still be considered EGC, even if they have nodal metastases, as is supported by decades of investigation and data from screening programs [9].

However, nodal metastases can affect treatment in two ways:

- Patients who have proven nodal metastases, patients whose pretreatment local staging evaluation indicates a high likelihood of nodal metastases, and patients with T1 disease who are at high risk for nodal metastases (because of tumor size, configuration, or depth of invasion) may not be appropriate candidates for endoscopic resection. Gastrectomy with removal of the regional nodes is the appropriate treatment strategy for such patients. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Endoscopic therapies'.)

- Patients with node-positive resected EGC are candidates for adjuvant therapy. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Adjuvant therapies'.)

EPIDEMIOLOGY

Gastric cancer demonstrates marked geographic variability, both regionally and within countries. High-incidence regions include East Asia, mountainous Latin America, and areas in Eastern Europe and Russia [2]. In the United States, the overall incidence rates are modest, and remain greater than those of esophageal cancer. When compared with White Americans, the incidence is higher in all other ethnic and racial groups including Hispanic Americans, Asian Americans, and African Americans [10]. Immigrants from high incidence regions who reside in low incidence regions maintain a higher risk for gastric cancer [11]. For unclear reasons, a rising incidence of gastric cancer has been observed among young adults in the United States [12,13].

The incidence of early gastric cancer (EGC), as well as the proportion of gastric adenocarcinomas that are EGCs, vary depending on the population:

- In Japan and Eastern Asia, up to one-half of resections for gastric adenocarcinoma represent EGC. In Japan, the proportion rose from 15 to as high as 57 percent with the introduction of screening programs [14-16].

- In Korea, 25 to 30 percent of gastric adenocarcinomas are EGCs [17,18].

- In the United States and Europe, EGCs account for 15 to 21 percent of gastric adenocarcinomas [16,19-21].

There are several explanations for the higher incidence of EGC in East Asian versus Western countries: the 5- 10-fold higher incidence rates of gastric cancer in East Asia; the longstanding screening programs, with EGC diagnostic expertise; and lastly, the well-described difference in the interpretation of gastric histology in Eastern versus non-Asian centers. (See 'Histologic classification' below.)

Gastric cancer screening in Japan began in the 1960s with photofluorography, and continues as gastric cancer is a leading cause of cancer mortality [22]. This transitioned to magnification chromoendoscopy with indigo carmine in experienced centers in eastern Asia [23]. Image-enhanced endoscopy (IEE) technology is rapidly evolving, and along with artificial intelligence (AI), will further enhance the ability to detect advanced lesions [24,25]. Notably, there is variation in screening practices by country and region. Methods used to screen for gastric cancer include endoscopy, radiology, and non-invasive testing (eg, *H. pylori* serology, and serum pepsinogen testing) [22]. (See "Chromoendoscopy" and "Gastric cancer screening", section on 'Screening modalities'.)

There has been a transition to magnification chromoendoscopy with indigo carmine spray in experienced centers in eastern Asia [23]. In addition, there is variation in screening practices by country and region. Methods used to screen for gastric cancer include endoscopy, radiology, *H. pylori* serology, and serum pepsinogen testing [22]. Of note, indigo carmine is currently in limited supply in many areas due to a shortage of the raw materials used in its production. (See "Chromoendoscopy" and "Gastric cancer screening", section on 'Screening modalities'.)

There do not appear to be significant differences in the demographic features of patients with EGC between Asian and non-Asian countries [19,20]. The sex and age distributions of EGC are similar in Japan, Europe, and America. The average age at diagnosis is approximately 60 years, and males are more commonly affected than females [20,26,27].

SCREENING FOR GASTRIC CANCER

Issues related to screening for gastric cancer are discussed in detail elsewhere. (See "Gastric cancer screening".)

CLASSIFICATION

Gastric cancers are classified by several systems, according to both histologic and endoscopic findings. In addition, molecular markers may in the future help better define the classification of these tumors, and precision medicine could influence treatment choices and better delineate a patient's prognosis.

Histologic classification — Differences in gastric histologic interpretation between East Asian and Western pathologists contributes to the higher proportion of early gastric cancers (EGCs) in Asia (see 'Epidemiology' above). The disagreement centers on the characterization of high-grade dysplasia and intramucosal adenocarcinoma [28]. Western pathologists have typically

required invasion of the lamina propria for the diagnosis of cancer, whereas Japanese pathologists have based the diagnosis on cytologic and architectural changes alone, without requiring invasion of the lamina propria. As a result, lesions classified as high-grade dysplasia by Western pathologists may be classified as intramucosal carcinoma by Japanese pathologists. (See "Gastric cancer: Pathology and molecular pathogenesis", section on 'Histologic classification'.)

The extent of the discrepancy is illustrated by one study, in which four Japanese and four Western pathologists examined 17 gastric biopsies and 18 endoscopic mucosal resection (EMR) specimens from 17 Japanese patients, with findings ranging from reactive atypia to early gastric cancer [29]. There was overall histologic agreement in only 11 of 35 cases (31 percent).

However, these differences in classification do not have a significant impact on clinical practice:

- Patients with severe dysplasia or EGC are usually managed with endoscopic resection, since both diagnoses are associated with a low risk of lymph node metastases. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Endoscopic submucosal dissection'.)

- Invasion of the lamina propria, which is the threshold for diagnosing cancer among Western pathologists, may be difficult to identify on histology [9].

In an attempt to close the gap between the Japanese and Western views and reporting schemes, consensus groups have formulated the Vienna classification of gastrointestinal epithelial neoplasia and the Padova international classification of dysplasia [28,30]. The Vienna classification recognizes the following categories:

- Category 1: Negative for neoplasia/dysplasia
- Category 2: Indefinite for neoplasia/dysplasia
- Category 3: Noninvasive low-grade neoplasia (low-grade adenoma/dysplasia)
- Category 4: Noninvasive high-grade neoplasia
    - 4.1: High-grade adenoma/dysplasia
    - 4.2: Noninvasive carcinoma (carcinoma in situ)
    - 4.3: Suspicion of invasive carcinoma
- Category 5: Invasive neoplasia
    - 5.1: Intramucosal carcinoma (invasion into the lamina propria or muscularis mucosae)
    - 5.2: Submucosal carcinoma or beyond

The World Health Organization proposed a classification of intraepithelial gastric neoplasias using different terms (negative for dysplasia, indefinite for dysplasia, low-grade and high-grade dysplasia, and carcinoma [invasion into the lamina propria or beyond]) [31]. The various classifications that have been proposed over the years are outlined in the table (table 2) [31].

Despite these classification systems, the terminology of adenoma (raised lesions) and dysplasia (flat lesions) remains widely used in Western literature and in clinical practice.

Lauren classification — Histologically, gastric cancers are classified as intestinal (well-, moderately-, poorly-differentiated) or diffuse (undifferentiated, with or without signet ring cells) subtypes based upon the Lauren classification [32,33]. These two types of gastric cancer have distinct morphologic appearances, epidemiology, pathogenesis, and genetic profiles. (See "Gastric cancer: Pathology and molecular pathogenesis", section on 'Intestinal versus diffuse types'.)

Macroscopic classification — Various macroscopic classification systems have been developed for gastric adenocarcinoma. One of the more common is the Borrmann system, with classifications of types I-IV for polypoid, fungating, ulcerated, and diffusely infiltrating tumors, respectively (figure 1).

Early gastric cancer — Classification systems have also been developed specifically for early gastric cancers. While used in Eastern Asia, they are rarely used in the United States and Europe. In particular, the Japanese Macroscopic Classification of Superficial Gastric Carcinoma is widely used in Eastern Asia [34]. The system is based upon visual and endosonographic features and was developed in an attempt to codify the indications and outcomes related to endoscopic mucosal resection [35]. (See "Overview of endoscopic resection of gastrointestinal tumors".)

The Japanese system recognizes four types of early endoluminal cancers (table 3 and figure 1):

- Type I lesions are polypoid or protuberant and are subcategorized as:
  - Ip – pedunculated
  - Ips/sp – subpedunculated
  - Is – sessile
- Type II lesions are flat and are further subcategorized as:
  - IIa – superficial elevated
  - IIb – flat
  - IIc – flat depressed

- IIc+IIa lesions – elevated area within a depressed lesion
- IIa+IIc lesions – depressed area within an elevated lesion

- Type III lesions are ulcerated

- Type IV lesions are lateral spreading

The Paris system, a newer classification system, was proposed in 2002 and is similar to the Japanese classification system [36]. Superficial lesions (type 0) are classified as polypoid, nonpolypoid, or excavated (table 4 and figure 2):

- Type 0-I lesions are polypoid are subcategorized as:

  - Type 0-Ip – protruded, pedunculated
  - Type 0-Is – protruded, sessile

- Type 0-II lesions are nonpolypoid and are subcategorized as:

  - Type 0-IIa – slightly elevated
  - Type 0-IIb – flat
  - Type 0-IIc – slightly depressed

- Type 0-III lesions are excavated

Type I lesions and type IIa lesions may appear similar [36]. Type I lesions extend above the mucosa more than 2.5 mm (the width of the closed cups of a biopsy forceps). Pathologically, the height of the lesion is more than double the thickness of the adjacent mucosa. Type IIa lesions are slightly elevated, but their height is less than 2.5 mm. Type IIc and type III lesions may also appear similar. Type IIc lesions are slightly depressed with a normal epithelial layer or superficial erosions. Type III lesions are characterized by ulceration, with loss of the mucosa and possibly submucosa.

The Paris Workshop confirmed the importance of the Japanese classification for gastric cancer based upon its correlation with risk for nodal metastases [36].

Molecular classification — The NIH Cancer Genome Atlas project has redefined the molecular classification of gastric cancer into four subtypes: genomically stable tumors (GS; diffuse histology); tumors with chromosomal instability (CSI; intestinal histology); Epstein–Barr virus positive (EBV; with marked DNA hypermethylation); and microsatellite unstable tumors (MSI; with elevated mutation rates) [37]. The intestinal and diffuse subtypes were confirmed to be the major subtypes, while the EBV and MSI subtypes each accounted for about 10 percent. The improved understanding of the genetic alterations in gastric cancer may in the future also help

better define the classification of the EGC tumors, their optimal treatment, and prognosis. In addition, novel biomarkers such as microRNAs may eventually be useful for EGC screening and prognosis, but investigations remain in the early stages [38-40]. (See "Gastric cancer: Pathology and molecular pathogenesis", section on 'Molecular subtyping'.)

The molecular classification of proximal cancers at the esophageal junction and the gastric cardia is underway, and is anticipated to provide insight into the similarities and differences versus distal gastric cancer, and may also identify novel molecular targets for precision medicine treatments [41,42].

CLINICAL MANIFESTATIONS

The presenting symptoms of early gastric cancer (EGC) are nonspecific. Patients may be asymptomatic or they may present with dyspepsia, mild epigastric pain, nausea, or anorexia. Most patients in East Asia are diagnosed in the context of screening programs. A prodrome of vague upper gastrointestinal symptoms may be present for 6 to 12 months prior to the diagnosis of EGC [43] and occurs in up to 90 to 95 percent of patients who are not detected through screening [19]. Ulcerated lesions may have a longer prodrome of symptoms than protuberant lesions [27].

Warning (or alarm) signs or symptoms suggestive of invasive disease in patients with EGC, such as anemia or weight loss, occur in 5 to 15 percent and 4 to 40 percent, respectively [19]. By comparison, weight loss occurs in more than 60 percent of those with advanced gastric adenocarcinoma [44].

The nonspecific nature of symptoms in EGC and gastric cancer complicates optimal disease management strategies for patients presenting with dyspepsia [45]. While the prevalence of gastric carcinoma among patients presenting with dyspepsia is low in the United States and other Western countries, there are no reliable clinical or laboratory features to distinguish patients with benign causes of dyspepsia from those with more serious underlying disease. (See "Approach to the adult with dyspepsia".)

DIAGNOSIS

Upper endoscopy with systematic non-targeted biopsies and targeted biopsies of suspicious lesions is the diagnostic procedure of choice for patients with suspected early gastric cancer (EGC). It is more sensitive and specific for the detection of EGC than air contrast barium radiography (image 1). The sensitivity of barium studies was only 14 percent in one study

[46]; in another series, all 15 patients with surgically proven EGC had a negative barium study [47].

Upper endoscopy — Upper endoscopy is central to the diagnosis of EGC, which may appear as a subtle polypoid protrusion, a superficial plaque, mucosal discoloration, a depression, or an ulcer [7,8,48,49]. The gastric cancer miss-rate at endoscopy, or false negative rate, is significant, and can be as high as 25 percent [50]. In one meta-analysis, 26 percent of upper gastrointestinal cancers were missed on endoscopy performed within three years of the patient's diagnosis [50]. Several studies underscore the importance of careful inspection, as measured by endoscopy examination time, suggesting that a minimum duration of seven minutes may be required [51-53]. Station-based protocols (with 22 pictures) have been proposed whereby each area of the stomach is systematically viewed and photographed [48,54,55]. Additional technical aspects of upper endoscopy for patients with suspected EGC include adequate gas insufflation and mucosal cleaning as needed.

Image-enhanced endoscopy is indicated for patients at-risk for gastric premalignant lesions, EGC, and gastric cancer, and for use in combination with white-light endoscopy (WLE) [7,8]. Gastric cancer screening programs in Eastern Asia have driven the development of endoscopic imaging technologies with applications throughout the gastrointestinal tract. Image-enhanced endoscopy includes chromoendoscopy (eg, indigo carmine), optical and digital technology (eg, NBI), and magnification (eg, optical or digital zoom, near-focus) [56-58]. Magnification chromoendoscopy is routinely used in many referral centers in Eastern Asia. Narrow-band imaging (NBI), including with near-focus imaging and magnification, may have a useful role in the diagnosis of EGC, with studies underway, primarily in East Asia [59-62]. NBI has been shown to have an important role in the detection of gastric intestinal metaplasia, with key features such as the marginal turbid band, light blue crest, and white opaque substance [8,63,64]. The near-focus function, including near-focus NBI, is an emerging alternative in Western countries where magnification endoscopy is not generally available [65]. (See "Chromoendoscopy" and "Magnification endoscopy" and "Barrett's esophagus: Evaluation with optical chromoscopy".)

Gastric biopsy mapping — Systematic gastric biopsies should be considered in at-risk patients and populations. In Western regions, this approach is reasonable for: patients with a family history of gastric cancer; for immigrants from high-incidence areas; patients with known atrophy, intestinal metaplasia or dysplasia; and for patients with clinical or endoscopic parameters warranting vigilance [66,67]. Standard endoscopic biopsy mapping follows the updated Sydney protocol and includes a minimum of two non-targeted biopsies from each of the following sites: antrum (both lesser and greater curvatures), the incisura, and the corpus

(both lesser and greater curvatures) (figure 3) [68-72]. (See "Gastric intestinal metaplasia", section on 'Diagnosis'.)

Additional biopsies may be warranted from the prepyloric region, fundus, and cardia. Targeted biopsies of atypical areas of gastric mucosa are appropriate. (See "Gastric cancer screening" and "Risk factors for gastric cancer" and "Gastric intestinal metaplasia".)

In the presence of a gastric ulcer, the site and the number of biopsy specimens are important. The sensitivity for detecting a gastric cancer increases with more biopsies, but the optimal number of biopsies is uncertain. The role of follow-up endoscopy for gastric ulcers not demonstrating gastric cancer on the initial endoscopy with biopsies is in evolution and depends upon the adequacy of biopsies obtained during the initial endoscopy, the appearance of the ulcer, and patient characteristics. (See "Peptic ulcer disease: Clinical manifestations and diagnosis", section on 'Upper endoscopy'.)

TESTING FOR H. PYLORI

All patients with early gastric cancer should be evaluated for *H. pylori* infection and treated if there is evidence of infection. If the histology is negative for *H. pylori*, the serology is warranted. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Helicobacter pylori infection'.)

STAGING

Gastric cancer is staged using the tumor, node, metastasis (TNM) classification system of the American Joint Committee on Cancer (AJCC); the current (eighth edition, 2017) version is outlined in the table (table 1) [73]. Early gastric cancers (EGCs) are T1 lesions, irrespective of nodal status. (See "Clinical features, diagnosis, and staging of gastric cancer", section on 'Staging systems'.)

Lymph node metastases in EGC — The overall incidence of lymph node metastases (LNM) in clinically staged T1 EGC is 0 to 15 percent in the early literature [74-78]. Although lymph node metastases do not affect the designation of a T1 EGC tumor, they have implications for therapy. (See "Adjuvant and neoadjuvant treatment of gastric cancer".)

Tumor characteristics inform the risk of lymph node metastases and have helped refine guidelines for selecting patients for endoscopic resection [79,80]. Factors associated with lymph node metastases include larger tumor size, ulceration, diffuse (undifferentiated) or mixed

(intestinal/undifferentiated) type histology, depth of invasion, and submucosal or lymphovascular invasion [76,78,81,82]. Thus, patients with EGC who are typically appropriate for endoscopic resection include those with small (<2 cm), nonulcerated, mucosal cancers, and possibly those with submucosal tumors that are small (<2 to 3 cm), well differentiated, and lack lymphovascular invasion. Accurate endoscopic estimation of lesion size is an important factor, and underestimation of size may affect the complete and curative resection rates [83].The standard and expanded criteria for determining risk of LNM are discussed separately. (See "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Standard and expanded criteria for endoscopic resection'.)

Staging work-up — The findings on endoscopy can predict tumor stage. In one study of 2105 patients, endoscopic findings were 78 percent accurate for predicting the depth of invasion of EGC [84]. Findings associated with mucosal disease included smooth surface protrusion or depression, slight marginal elevation, and smooth tapering of converging folds. Findings suggestive of submucosal disease included an irregular surface, marked marginal elevation, and clubbing, abrupt cutting, or fusion of converging folds. (See "Clinical features, diagnosis, and staging of gastric cancer", section on 'Staging evaluation'.)

However, staging may be more accurately accomplished using a combination of endoscopic resection and endoscopic ultrasonography (EUS).

Endoscopic resection — Endoscopic resection with endoscopic submucosal dissection (ESD) is considered both a staging procedure and a treatment for EGC [7,85]. ESD is indicated for high grade dysplasia (HGD) and in some cases for low-grade dysplasia with visible abnormalities [86]. Upstaging of HGD and EGC is commonly observed with ESD en bloc resection [87,88]. En bloc resection permits T staging of the tumor and does not preclude subsequent gastrectomy if the resection is incomplete or if there are unfavorable histologic findings. The presence of unfavorable histologic findings suggests a higher incidence of lymph node metastases, and therefore, indicates that an operative approach to treatment is preferred. In referral centers in Eastern Asia and elsewhere, strict criteria are used to determine the appropriateness of endoscopic resection for EGC. (See "Overview of endoscopic resection of gastrointestinal tumors", section on 'Gastric cancer' and "Early gastric cancer: Treatment, natural history, and prognosis", section on 'Standard and expanded criteria for endoscopic resection'.)

Endoscopic ultrasonography — EUS is thought to be a reliable nonsurgical method available for evaluating the depth of invasion of gastric cancer, particularly for T1 lesions [89-91]. In a study of 955 patients with suspected EGC, EUS staging accuracy was compared with surgical or endoscopic resection [92]. EUS correctly identified the T stage in 644 patients (67 percent). The accuracy of miniprobe EUS was significantly higher than radial EUS (80 versus 60 percent).

Regional lymph node involvement may also be detected by EUS. The definition of regional versus extraregional nodes for gastric cancer depends on location [93]. Regional nodes for tumors involving different parts of the stomach are depicted in the figure (figure 4). Involvement of other intraabdominal nodal groups (ie, pancreatoduodenal, retropancreatic, peripancreatic, superior mesenteric, middle colic, paraaortic, and retroperitoneal) is classified as distant metastases [73].

Although EUS may detect enlargement of regional nodes, the differentiation between benign (reactive) perigastric inflammation and nodal metastasis can be difficult. EUS-guided fine-needle aspiration of suspicious nodes and regional areas adds to the accuracy of nodal staging.

EUS has become a valuable tool for the selection of patients with EGC who are suitable for endoscopic resection [94-97]. However, certain features (eg, mid-gastric location, poorly differentiated tumors) may lead to incorrect staging [98]. For this reason, in many areas of Eastern Asia, endoscopic resection (ESD) rather than EUS is considered the primary staging procedure for EGC. By contrast, in Western countries, EUS is more commonly recommended for all patients without evidence of metastatic disease [99].

Other tests — Other staging procedures, such as CT and positron emission tomography with fluorodeoxyglucose (FDG-PET) may also be used selectively [99]. These procedures are used more commonly in Western referral centers. (See "Clinical features, diagnosis, and staging of gastric cancer", section on 'Computed tomography scan in all patients' and "Clinical features, diagnosis, and staging of gastric cancer", section on '18-fluorodeoxyglucose positron emission tomography scan'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Gastric cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading

level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Stomach cancer (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Early gastric cancer (EGC) is defined as adenocarcinoma limited to the gastric mucosa or submucosa, regardless of involvement of the regional lymph nodes (T1, any N). (See 'Introduction' above.)

  EGC is an important subset of gastric adenocarcinoma. Gastric cancer screening programs in Eastern Asia have prompted the development of advanced imaging technologies and endoscopic resection modalities, which are subsequently being used for other conditions in the gastrointestinal tract.

- The presenting symptoms of EGC are nonspecific. Patients may be asymptomatic or they may present with dyspepsia, mild epigastric pain, nausea, or anorexia. (See 'Classification' above.)

- White light endoscopy in combination with an image-enhanced endoscopic technique such as magnification chromoendoscopy or narrow band imaging is performed with a gastric mucosal biopsy protocol to make the diagnosis of EGC. (See 'Diagnosis' above.)

- Staging of EGC may be accomplished using a combination of endoscopic resection with endoscopic submucosal dissection (ESD) and endoscopic ultrasound (EUS). In clinical practice, the use of EUS is variable. (See 'Staging' above.)

- Factors associated with lymph node metastases include larger tumor size, ulceration, diffuse (undifferentiated) or mixed (intestinal/undifferentiated) type histology, depth of invasion, and submucosal or lymphovascular invasion. Although lymph node metastases do not affect the designation of a T1 EGC tumor, they have implications for therapy. (See 'Lymph node metastases in EGC' above and "Early gastric cancer: Treatment, natural history, and prognosis".)

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Topic 2520 Version 42.0

GRAPHICS

Stomach cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*: Intraepithelial tumor without invasion of the lamina propria, high-grade dysplasia
T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades the lamina propria or muscularis mucosae
T1b	Tumor invades the submucosa
T2	Tumor invades the muscularis propria*
T3	Tumor penetrates the subserosal connective tissue without invasion of the visceral peritoneum or adjacent structures¶ Δ
T4	Tumor invades the serosa (visceral peritoneum) or adjacent structures¶ Δ
T4a	Tumor invades the serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures/organs
* A tumor may penetrate the muscularis propria with extension into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures. In this case, the tumor is classified as T3. If there is perforation of the visceral peritoneum covering the gastric ligaments or the omentum, the tumor should be classified as T4. ¶ The adjacent structures of the stomach include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum. Δ Intramural extension to the duodenum or esophagus is not considered invasion of an adjacent structure, but is classified using the depth of the greatest invasion in any of these sites.	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases in 1 or 2 regional lymph nodes
N2	Metastases in 3 to 6 regional lymph nodes
N3	Metastases in 7 or more regional lymph nodes

N3a	Metastases in 7 to 15 regional lymph nodes
N3b	Metastases in 16 or more regional lymph nodes

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis
M1	Distant metastasis

Prognostic stage groups

Clinical (cTNM)

When T is…	And N is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	I
T1	N1, N2, or N3	M0	IIA
T2	N1, N2, or N3	M0	IIA
T3	N0	M0	IIB
T4a	N0	M0	IIB
T3	N1, N2, or N3	M0	III
T4a	N1, N2, or N3	M0	III
T4b	Any N	M0	IVA
Any T	Any N	M1	IVB

Pathological (pTNM)

When T is…	And N is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1	N0	M0	IA
T1	N1	M0	IB
T2	N0	M0	IB
T1	N2	M0	IIA
T2	N1	M0	IIA
T3	N0	M0	IIA
T1	N3a	M0	IIB

T2	N2	M0	IIB
T3	N1	M0	IIB
T4a	N0	M0	IIB
T2	N3a	M0	IIIA
T3	N2	M0	IIIA
T4a	N1	M0	IIIA
T4a	N2	M0	IIIA
T4b	N0	M0	IIIA
T1	N3b	M0	IIIB
T2	N3b	M0	IIIB
T3	N3a	M0	IIIB
T4a	N3a	M0	IIIB
T4b	N1	M0	IIIB
T4b	N2	M0	IIIB
T3	N3b	M0	IIIC
T4a	N3b	M0	IIIC
T4b	N3a	M0	IIIC
T4b	N3b	M0	IIIC
Any T	Any N	M1	IV

Post-neoadjuvant therapy (ypTNM)

When T is...	And N is...	And M is...	Then the stage group is...
T1	N0	M0	I
T2	N0	M0	I
T1	N1	M0	I
T3	N0	M0	II
T2	N1	M0	II
T1	N2	M0	II
T4a	N0	M0	II
T3	N1	M0	II
T2	N2	M0	II
T1	N3	M0	II

T4a	N1	M0	III
T3	N2	M0	III
T2	N3	M0	III
T4b	N0	M0	III
T4b	N1	M0	III
T4a	N2	M0	III
T3	N3	M0	III
T4b	N2	M0	III
T4b	N3	M0	III
T4a	N3	M0	III
Any T	Any N	M1	IV

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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Graphic 111190 Version 8.0

Classifications of the histological phenotypes involved in gastric carcinogenesis, each listing the categories in order of increasing risk of malignancy

Padova international	Vienna	Revised Vienna	Japanese Diagnostic Framework for Forceps Biopsy	WHO (2019)
Category 1: Negative for dysplasia	**Category 1:** Negative for dysplasia	**Category 1:** Negative for dysplasia	**Group 1:** Normal/non-neoplastic	Negative for dysplasia/IEN
Category 2: Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia	**Group 2:** Indefinite for neoplasia	Indefinite for dysplasia/IEN
Category 3.1: Low-grade dysplasia (low-grade noninvasive neoplasia)	**Category 3:** Noninvasive low-grade neoplasia (low-grade adenoma/dysplasia)	**Category 3:** Low-grade adenoma/dysplasia	**Group 3:** Adenoma	Low-grade dysplasia/IEN (low-grade adenoma/dysplasia)
Category 3.2: High-grade dysplasia (high-grade noninvasive neoplasia)	**Category 4:** High-grade neoplasia	**Category 4:** High-grade neoplasia	**Group 4:** Suspicious for carcinoma	High-grade dysplasia/IEN (high-grade adenoma/dysplasia)
	Category 4.1: High-grade adenoma/dysplasia	**Category 4.1:** High-grade adenoma/dysplasia		
	Category 4.2: Noninvasive carcinoma	**Category 4.2:** Noninvasive carcinoma		
	Category 4.3: Suspicious for invasive carcinoma	**Category 4.3:** Suspicious for invasive carcinoma		
Category 4: Suspicious for invasive carcinoma		**Category 4.4:** Intramucosal carcinoma	**Group 5:** Carcinoma (noninvasive or invasive)	
Category 5: Invasive adenocarcinoma	**Category 5:** Invasive neoplasia			Intramucosal invasive neoplasia

	Category 5.1: Intramucosal carcinoma			(intramucosal carcinoma)

WHO: World Health Organization; IEN: intraepithelial neoplasia.

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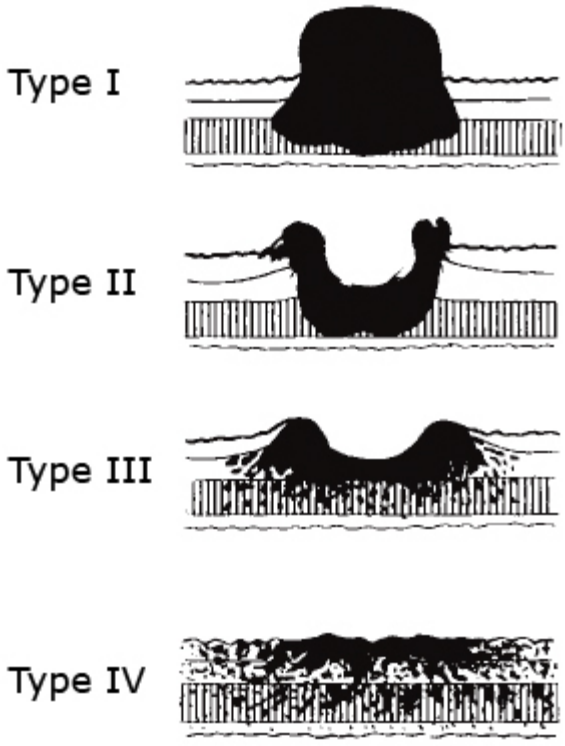
Graphic 120177 Version 8.0

Japanese Society for Gastroenterological Endoscopy classification of early endoluminal cancers



This is also known as the Borrmann Pathologic Classification of Gastric Cancer.

Reproduced from: Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma, 2nd English Edition. Gastric Cancer 1998; 1:10, with kind permission from Springer Science + Business Media B.V.

Graphic 82731 Version 7.0

Japanese Society for Gastroenterological Endoscopy classification system of early endoluminal cancers

Type	Subclasses
I: Polypoid/protuberant	Ip: Pedunculated
	Ips/sp: Subpedunculated
	Is: Sessile
II: Flat	IIa: Superficial elevated
	IIb: Flat
	IIc: Flat depressed
III: Ulcerated	
IV: Lateral spreading tumor	

Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma. 2nd English Edition. Gastric Cancer 1998; 1:10.

Graphic 71003 Version 2.0

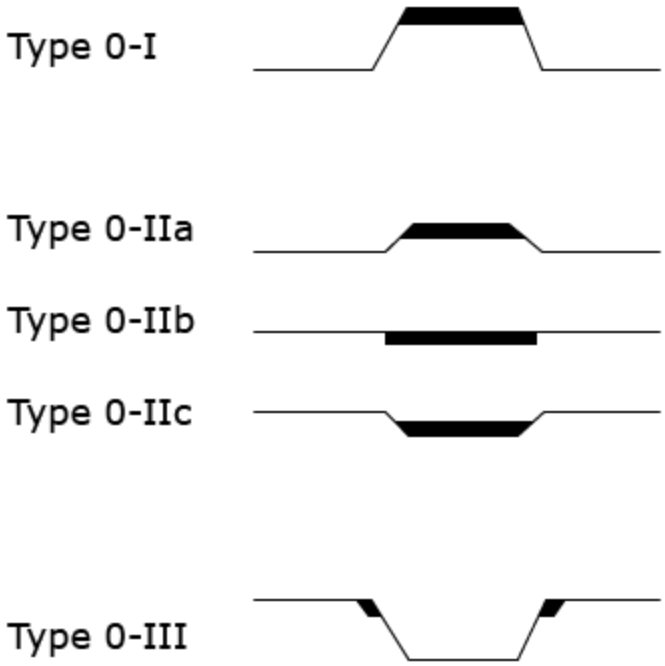
Paris classification system of superficial gastrointestinal neoplastic lesions

Type	Subclasses
0-I: Polypoid	0-Ip: Protruded, pedunculated
	0-Is: Protruded, sessile
0-II: Nonpolypoid	0-IIa: Slightly elevated
	0-IIb: Flat
	0-IIc: Slightly depressed
0-III: Excavated	

The Paris endoscopic classification of superficial neoplastic lesions: Esophagus, stomach and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58(6 suppl):S3.

Graphic 50239 Version 5.0

Paris classification system of superficial neoplastic lesions of the gastrointestinal tract

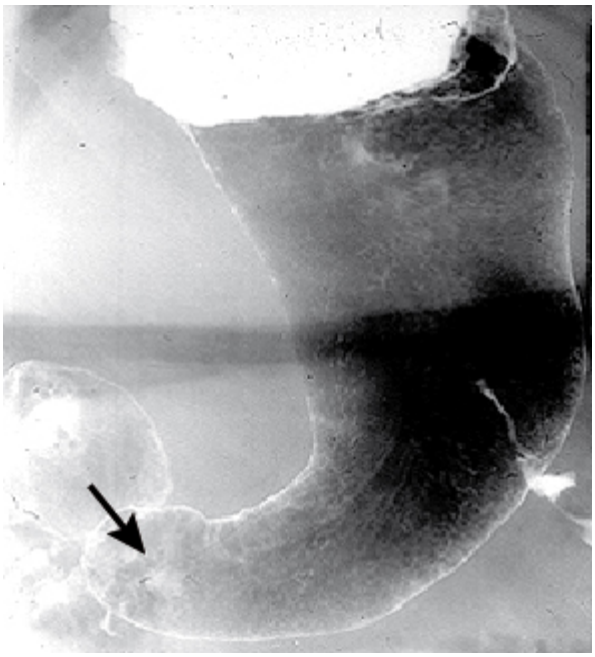


Paris classification system of superficial neoplastic lesions of the esophagus, stomach, and colon. Type 0-I lesions are polypoid (protruded or pendunculated); type 0-II lesions are nonpolypoid and may be slightly elevated (IIa), flat (IIb), or slightly depressed (IIc); type 0-III lesions are excavated.

Based on data from: The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58(6 suppl):S3.

Graphic 61277 Version 3.0

Early gastric cancer as seen on upper gastrointestinal (UGI) series

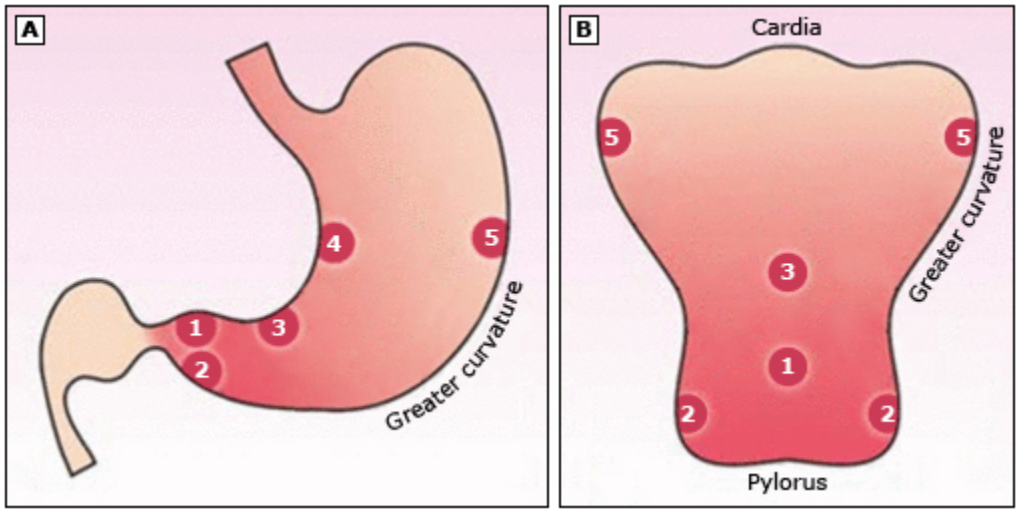


A double contrast upper gastrointestinal study shows a superficial ulcer in the gastric antrum (arrow) with thickened folds radiating towards the ulcer.

Courtesy of Norman Joffe, MD.

Graphic 61767 Version 5.0

Gastric biopsy sampling protocol

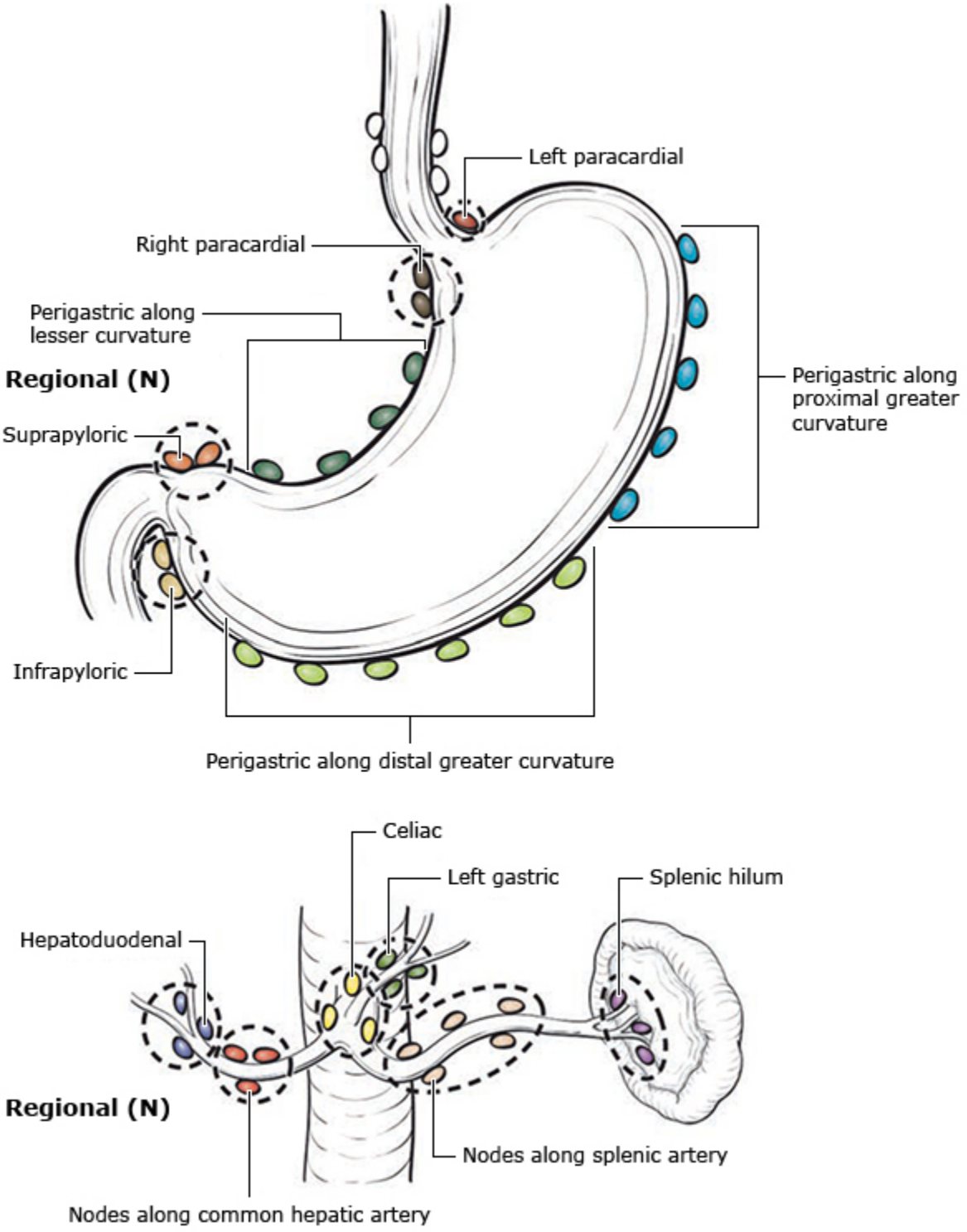


- **(Panel A)** Sydney protocol biopsy sites in the anatomic view.
- **(Panel B)** Sydney protocol biopsy sites in the opened stomach along the greater curvature.
- **Gastric biopsies should be obtained from the following sites:**
    1. Distal antrum, lesser curvature, within 3 to 5 cm of pylorus
    2. Distal antrum, greater curvature, within 3 to 5 cm of pylorus
    3. Lesser curvature of the incisura angularis
    4. Proximal corpus, lesser curvature
    5. Proximal corpus, greater curvature

Adapted from: Nieuwenburg SA, Waddingham WW, Graham D. Accuracy of endoscopic staging and targeted biopsies for routine gastric intestinal metaplasia and gastric atrophy evaluation study protocol of a prospective, cohort study: the estimate study. BMJ Open 2019; 9:e032013. Copyright © 2019 The Authors. Available at: https://bmjopen.bmj.com/content/9/9/e032013 (Accessed on February 18, 2020). Reproduced under the terms of the Creative Commons Attribution License.

Graphic 127130 Version 2.0

Regional lymph nodes of the stomach



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Contributor Disclosures

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