Narrative review of the role of gastroenterologist in the diagnosis, treatment and palliation in gastric and gastroesophageal cancer

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Contributions: (I) Conception and design: LI Diaz, J Klapman; (II) Administrative support: None; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: LI Diaz, S Mony; (V) Data analysis and interpretation: LI Diaz, J Klapman; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Esophageal cancer (EC) and gastric cancer (GC) carry a high mortality rate. Unfortunately, a majority of patients are asymptomatic and at the time of diagnosis, the disease may invariably be in its advanced stages with limited curative options. Thus, it is imperative to recognize certain risk factors including gastroesophageal reflux disease (GERD), male gender, pre-existing Barrett's esophagus, smoking history, obesity, Helicobacter pylori infection, atrophic gastritis among others for both EC and GC, intervene on time with screening and surveillance modalities if indicated and optimize treatment plans. With advances in endoscopic techniques, early neoplastic lesions are increasingly managed by gastroenterologists, offering an alternative to surgery. The gold standard for diagnosis of EC and GC is high definition endoscopy with adequate targeted biopsies. Endoscopic ultrasound (EUS) is a key in the staging of early cancers dictating the pathway for treatment options. We also play a key role in palliation cases with the aim to reduce the symptoms like nausea, vomiting and even when possible, restore oral intake and improve nutrition in both advanced GC and EC. This review article discusses the risk factors, diagnostic and endoscopic treatment modalities of early EC and GC and palliation of advanced cancer where gastroenterologists play a key role.

Keywords: Esophageal; gastric; cancer; endoscopic ultrasound (EUS)

Submitted May 25, 2020. Accepted for publication Aug 12, 2020.
doi: 10.21037/atm-20-4143
View this article at: http://dx.doi.org/10.21037/atm-20-4143

Introduction

Despite significant advances in diagnosis and treatment, esophageal cancer (EC) and gastric cancer (GC) remain largely fatal in most parts of the world.

EC is the 6th leading cause of death from cancer with a 5-year survival around 15–25% (1). The prevalent histological type of EC worldwide is esophageal squamous cell carcinoma (SCC). However, in places like Australia, United Kingdom, United States and Western Europe, a predominance of adenocarcinoma subtype is noted. Esophagogastric junction (EGJ) and esophagus adenocarcinomas, especially Barrett's adenocarcinomas, have been on the rise in Western countries, whereas that of squamous cell cancer has been relatively stable in the same geographical location (2).

On the contrary, the incidence of GC in the United States continues to decline but remains the 5th most commonly diagnosed cancer in the world (3). GC is more prevalent in underdeveloped countries with about half of all cases in Eastern Asia, particularly China (4). In Europe and the United States, the five-year survival rate is about 25 to 28 percent, increasing to about 63 percent if the cancer is diagnosed at an early stage. However, these survival rates are lower in underdeveloped countries where GC is typically detected at its advanced stage (4).

The gastroenterologist continues to play an important role in gastric and esophageal tumors with focus on early detection, proper surveillance of high-risk patients and

accurate staging methods with the aim to prolong survival and improve the quality of life. Endoscopy and endoscopic ultrasound (EUS) have become an important tool in the diagnosis, staging, treatment, and palliation of patients with these cancers. We review the risk factors, diagnosis, staging, treatment and palliation of gastric and esophageal adenocarcinoma, with focus on early-stage disease and endoscopic therapy.

We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx.doi.org/10.21037/atm-20-4143).

Definition and classification

The universally accepted classification is the tumor, node, metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) for EC and GC.

EC

The oldest and most widely used classification system is that by Siewert *et al.* (5) in 1987. This classification separates esophageal-gastric tumors based on the location of the epicenter of the tumor in relation to the location of the EGJ. Type I tumors are those with an epicenter 2–5 cm above the EGJ, they are also known as distal esophageal tumors. They usually arise from an area of Barrett's metaplasia in the lower esophagus and infiltrate the EGJ distally. Type II tumors are located within 2 cm (above or below) of the EGJ and type III are those 2–5 cm distal to the EGJ, also known as subcardial tumors (5).

According to the latest 8th edition revision of the AJCC staging classification, ECs are those EGJ tumors with epicenter less than 2 cm into the proximal stomach. In contrast, stomach cancers are those EGJ tumors found 2 cm or more into the proximal stomach as well as those cardia cancers not involving the EGJ, regardless of their location from the EGJ (6). This Classification guides surgical, medical and radiation oncology management.

GC

Based on the anatomic location, gastric adenocarcinomas are classified primarily as cardia and non-cardia. Gastric cardia cancers occur more adjacent to the EGJ and they share similar epidemiological qualities with esophageal adenocarcinomas. More commonly are non-cardia cancers appearing more distal in the stomach (7). GC can also be classified as diffuse (infiltrative) type or as intestinal type. One of the differences between them is that endoscopically, the intestinal type usually shows a gastric mass while the diffuse type (Linitis plastica) is more in line with a gastritis appearance and biopsies could be negative. Therefore, EUS becomes the procedure of choice as it can establish a malignant diagnosis by having the ability to perform fine needle aspiration (FNA) of the deeper gastric wall layers where the cancer may originate.

Risk factors

EC

Risk factors of esophageal adenocarcinoma cancer include chronic gastroesophageal reflux disease (GERD), male gender, pre-existing Barrett's esophagus, smoking history, high body mass index and certain drugs (8).

In men, the occurrence of esophageal adenocarcinoma is 8 times more common than those in women and 5 times more common in Caucasians than in African Americans in the United States (9). The odds ratio of developing adenocarcinoma in those with a BMI in the 25–30 rank is 1.52 when compared to those with normal BMI (9). Abdominal obesity which occurs more frequently in males, regardless of BMI rank, appears to be linked with a higher probability of acquiring esophageal adenocarcinoma but it is not associated with an increase of cardia adenocarcinoma (9,10).

There is a positive correlation in the last 30 years between higher occurrences of Barrett's esophagus and adenocarcinomas during the same time frame. Out of those patients diagnosed with GERD, 6–14% develop BE and 0.5–1% will develop adenocarcinoma (11). Finding of low-grade dysplasia was connected with an occurrence rate for adenocarcinoma of 5.1 incidents per 1,000 person-years while patients with no dysplasia saw an incidence of 1.0 case per 1,000 person-years (12).

Data regarding the protective effect of Helicobacter pylori (*H. pylori*) on the development of esophageal adenocarcinoma is conflicting. Several studies have demonstrated that *H. pylori* is not more common and does not have a different distribution in patients with Barrett's esophagus than in controls (13-18). In contrast, *H. pylori* may be a significant factor for cardia inflammation and intestinal metaplasia, a precursor lesion for cardia adenocarcinoma (19). Cardiac adenocarcinoma may be

difficult to distinguish from cancers arising in the distal esophagus, particularly when the disease is advanced.

GC

Risk factors for GC include male gender, cigarette smoking, atrophic gastritis, gastric intestinal metaplasia (GIM), *H. pylori* infection, partial gastrectomy and Ménétrier's disease (20). Several dietary factors, like a high salt, red meat, and smoked food consumption, as well as a low fruit and vegetables intake, and smoking have been incriminated as risk factors (21).

Gastric precancerous lesions such as atrophic gastritis and GIM (22), have a higher risk of GC (23) and their surveillance appears as a logical strategy to prevent advanced GC. Per AGA guidelines, surveillance should be reasonably considered in patients with GIM at higher risk for GC who have an increased value on potential but uncertain decrease in GC mortality, but add a low value on surveillance endoscopic risks. This includes incomplete and extensive GIM, family history of GC, racial/ethnic minorities and immigrants from high incidence regions. Data regarding recommendations on the ideal surveillance interval is insufficient. In patients with incidental GIM, repeated upper surveillance every 3–5 years should be considered with a cautious mucosal visualization and gastric biopsies of the antrum, body and all other lesions as long as there is a shared opinion favoring the surveillance (24).

H. pylori is a known cause of peptic ulcer disease (PUD) and is a carcinogen and should be tested and treated based on approved guidelines (25,26). According to the ACG guidelines, patients should be tested for *H. pylori* infection if they have a history of endoscopy resection of early GC, a past history of PUD, active PUD or low grade gastric mucosa-associated lymphoid tissue (MALT) and those with a positive result should be offered eradication therapy (24). By eradicating *H. pylori* infection, the rate of metachronous GC after the endoscopic resection (ER) of gastric neoplasm was reduced (27-29).

Screening

EC

Upper esophagogastroduodenoscopy (EGD) has mostly substituted contrast radiology and it is the prefer examination. EGD permits to accurately identify the site of the tumor, as well as enabling biopsies for histological diagnosis.

There are no screening guidelines for EC. However, for individuals being evaluated for GERD, most society guidelines recommend performing EGD with biopsies for endoscopically visible BE (30-32). Patients should get screened for Barrett's Esophagus if many risk factors such as male sex, Caucasian race, age older than 50, obesity, chronic reflux symptoms, and a family history of EC are identified (30-32).

The gold standard for screening and surveillance of BE is with high-resolution white-light endoscopy with forceps biopsy (FB) sampling performed according to the Seattle protocol, which consists of taking biopsies of all quadrans every 1–2 cm through the suspected area. The aim of surveillance is detection of dysplasia. Most dysplasia and intra-mucosal cancers are focal and invisible to the endoscopist; for this reason, lack of good samples or inaccurate determination of landmarks can cause misdiagnosis of Barret's (33).

An extensive range of adjunctive methods to FB have been created to increase detection of BE and improve the finding of dysplastic areas. The American Society for Gastrointestinal Endoscopy has recently included wide-area transepithelial sampling with computer-assisted three-dimensional analysis (WATS-3D) in its Standards of Practice Committee's guideline for the screening and surveillance of BE (34). It's a computer-assisted brush-biopsy method that utilizes an abrasive brush that takes a circumferential sweep of the esophagus. WATS-3D allows for the evaluation of more esophageal surface area as well as an assessment of deeper layer (35,36). This sampling is followed by a computer assisted analysis that identifies potentially abnormal cells for pathologist review. Previous studies have shown that WATS-3D as an adjunct to both targeted and random FB increase the diagnostic yield and increases the detection of HGD/EAC in a high-risk population (36,37).

GC

In Japan and Korea, where the frequency for GC is elevated in comparison to Western countries, screening for GC in the general population is common. In countries like the Unites States where incidence is low, general routine screening is not endorsed. However, there is an interest in considering screening and surveillance targeted populations based on risk factors like place of birth, race/ethnicity and other related factors for GC.

While most GCs are considered sporadic, 5–10% have a genetic component and 3–5% are related with an inherited cancer predisposition syndrome (38-43). Among these syndromes are hereditary non-polyposis colorectal cancer, familial adenomatous polyposis, hereditary diffuse GC (CDH-1 mutations), Juvenile Polyposis Syndrome and Peutz Jeghers syndrome. Each condition has different screening and surveillance guidelines than the general population (41). The most relevant it's the CDH1 mutation carriers, who elect not to undergo prophylactic gastrectomy, we offered screening every 6–12 months by upper endoscopy with multiple random biopsies as recommend by National Comprehensive Cancer Network guidelines. When patients present symptoms, this usually includes dyspepsia, weight loss, dysphagia, vomiting, iron deficiency anemia and/or early satiety (20) and this should prompt examination starting with an EGD with biopsies of any abnormal mucosa with further imaging studies depending on findings.

Diagnosis

Diagnostic and surveillance endoscopies are performed for both EC and GC with the goal of determining the presence and location of neoplastic disease and to biopsy any suspicious lesions. The gold standard for diagnosis of EC and GC is high definition endoscopy with adequate targeted biopsies. The tremendous progress in the quality of endoscopic devices has allowed a marked improvement of our capacity to detect early neoplastic lesions.

EC

During endoscopy, attention should be paid to the site of the tumor in relation to the incisors and EGJ, length and extent of circumferential involvement, and the lumen diameter at the level of obstruction should be carefully recorded. In addition, the location, length and circumferential extent of Barrett's should be categorized according to the Prague criteria if present and mucosal nodules should be documented.

In addition to adequate inspection time, multiple endoscopic methods to improve the discovery of dysplasia with minimum biopsy sampling have been studied. Narrow-band imaging (NBI) is valuable for finding esophageal squamous carcinoma but its use for EGJ adenocarcinoma detection is unknown. However, acetic acid splaying, chromoendoscopy with indigocarmine and NBI could be of use for finding such lesions (44,45).

GC

Multiple (6-8) biopsies using standard size endoscopy forceps should be performed to provide adequately material for histologic interpretation, especially in the setting of an ulcerated lesion. This was shown in a prospective trial were 202 biopsy and cytology specimens were obtained from EC and GC which demonstrated that the diagnostic yield increased from 70% with one biopsy to greater than 98% when a total of seven biopsy specimens were collected (46).

Pre-treatment staging

Preoperative tumor staging is endorsed to all patients, especially those known to be surgical candidates because their disease extent will influence treatment planning.

A computed tomography scan often begins the staging by evaluating the existence of metastatic disease (i.e., to bone, lung, liver or adrenals), thus distinguishing M0 *vs.* M1 stages. However, positron emission tomography (PET) CT scanning may be more precise for the discovery of stage IV disease and may be used as an early staging evaluation (47).

EC

EUS can provide three-dimensional images of esophageal lesions and is the most sensitive test for locoregional staging of EC (34,48-51). It is also more precise than PET scanning, magnetic resonance imaging (MRI), CT scan or transabdominal ultrasound for locoregional staging of EC, with an overall accuracy of EUS for T and N staging of 90 percent (52). The universally accepted staging system—the tumor, node, metastasis staging system of the American Joint Committee on Cancer and the Union for International Cancer Control for EC (2017, eighth edition) (53) is shown in *Table 1*.

The endosonography report should include the endoscopic findings of tumor location, features (e.g., circumferential extent, skip areas, presence/absence of Barrett's), anatomic landmarks [gastroesophageal junction (GEJ), diaphragmatic hiatus, squamocolumnar junction], as well as a description incorporating the T-stage including maximal wall thickness, N-stage with specific features of identified lymph nodes (location, shape/size/border/echogenicity) and signs of distant spread, such as lesions in nearby organs (M-category). Incomplete staging due

Table 1 AJCC staging esophageal cancer—8th edition cancer staging categories for cancer of the esophagus and GE junction

Category	Criteria
T category	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High grade dysplasia, defined as malignant cells confined by the basement membrane
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 propia
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Tumor invades pleura, pericardium, azygous vein, diaphragm or peritoneum
T4b	Tumor invades other adjacent structures such as the aorta, vertebral body or trachea
N category	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases in 1–2 regional lymph nodes
N2	Metastases in 3–6 regional lymph nodes
N3	Metastases in ≥7 regional lymph nodes
M category	
M0	No distant metastasis
M1	Distant metastasis

AJCC, American Joint Committee on Cancer.

to tumoral stenosis should be described (48,52,53). The endosonographic appearance of the esophageal layers is shown in *Figure 1*.

Histologic analysis of the main tumor depth, lymphovascular invasion (LVI) and locoregional staging in superficial EC (T1 lesions, mostly <2 cm) could be achieved by using ER with EUS. Combining both procedures is a layer of preventive measure against staging errors by either histologic study or sonographic evaluation. The histology of endoscopically resected specimens could help with a more precise evaluation of superficial tumor invasion, sometimes difficult to visualize by standard radial EUS (7.5–12 MHz) (54,55). ER and EUS can also have the benefit of study of the nodes with the possibility for FNA sampling. Additionally, EUS disregards invasive deeper cancer (T2 or deeper lesions) that makes ER needless and risky.

Data suggesting the use of EUS for cancers involving the EGJ is very restricted, and a broad use of ER has been advised (54). According to this study, EUS accuracy is diminished at the EGJ *vs.* other locations of the esophagus when analyzing resected specimens; with 29% over-staged and 23% under-staged by EUS. This effect is more pronounced with smaller, early EGJ cancers that resulted in over-staging for the most part.

For patients in the beginning of the disease process, EUS can influence the treatment as a more specific consideration may be given to the depth of esophageal invasion and celiac lymph node, which is believed to be an entrance for far metastatic spread (56). According to the latest data, prognosis of malignancy-involved lymph nodes is more important than regional anatomic location, which makes the indication of EUS-FNA stronger (57,58).

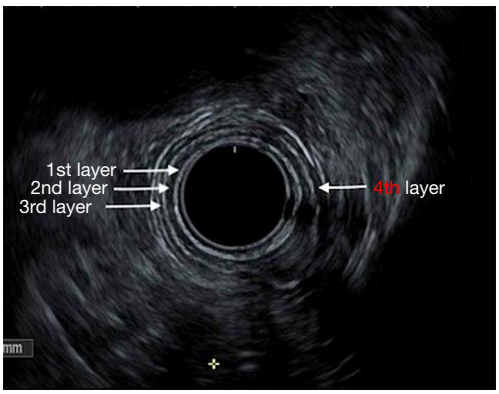

Figure 1 EUS depiction of esophageal layers. Layer 1: mucosa; layer 2: muscularis mucosa; layer 3 submucosal; layer 4: muscularis propia. EUS, endoscopic ultrasound.

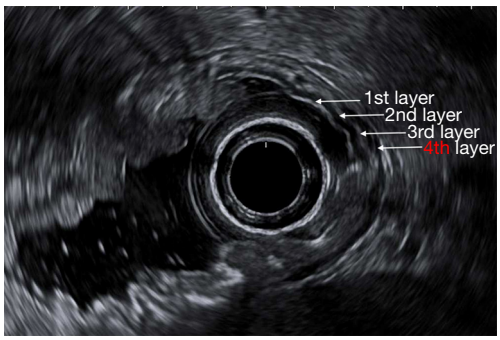

Figure 2 EUS depiction of gastric layers. Layer 1: mucosa; layer 2: muscularis mucosa; layer 3 submucosal; layer 4: muscularis propia. EUS, endoscopic ultrasound.

The accuracy of this diagnosis is significantly increased by using FNA biopsy for further cytology analysis (49). FNA of questionable lymph nodes is recommended if the procedure can be done without going through a site of primary lesion or major blood vessels, and if the study will give additional information for future treatment strategies.

Tumors that obstruct the esophagus may be at higher risk of perforation while doing staging EUS exams. The perforation risk may be diminished by using mini-probes or wire guided EUS probes. In the past, dilation was done but now it is done less frequently as the risk of perforation does not outweigh the low benefit of complete staging and finding occult M1 disease not seen on other imaging modalities.

GC staging

The choice of staging modality is dependent on the clinical scenario and local expertise. Before any treatment, the use of EUS is key in the preliminary staging of CG (59). The endosonographic appearance of the gastric layers is shown in *Figure 2*. Cautious detail to the sonographic images provides evidence of depth tumor invasion (T-category), existence of suspicious or atypical lymph nodes with a high chance to harbor cancer (N-assessment), and signs of distant spread, such as lesions in nearby organs (M-category) or the presence of ascites. The most recent revision of the AJCC/UICC TNM staging classification (eighth edition, 2017) is shown in *Table 2*. This is primarily important for patients who are being considered for endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) (60). Focal nodules less or equal than 2 cm can be better studied by gathering a larger specimen with the use of EMR or ESD. This will provide more information regarding the degree of differentiation, existence of LVI, and the depth of infiltration, further giving a more precise T-staging as detailed below (61).

Early studies have concluded that the accuracy of EUS diagnostic for T staging varies from 43% to 88% (62-66). A recent meta-analysis and systematic review showed that the sensitivity GC N staging using EUS is quite high (82%). But the specificity of EUS for the same N staging in GC was not as high (68%) (67).

A dark or hypoechoic expansion with a steady loss of the layered pattern of the normal stomach wall is the location of the tumor correspond to T-categories. A hypoechoic expansion of the first 3 layers corresponds with an infiltration of the superficial, deep mucosa and submucosa, T1 disease. A dark expansion of layers 1-4 corresponds with invasion into the muscularis propria, T2 disease, and expansion further than the muscularis propria that results in an abnormal outer border that corresponds with penetration of the subserosa, T3 disease. Fingerlike projections of tumor, termed “pseudopodia” may be seen. Loss of the serosa which is recognized by a bright line, is staged as pT4a, and expansion of the lesion into nearby organs such as the spleen, pancreas and liver is staged pT4b disease (68).

EUS can quickly detect perigastric lymph nodes, and the detection of well-circumscribed, homogenous, hypoechoic, enlarged, rounded lesions around the stomach corresponds with the existence of malignant or inflammatory lymph nodes. The echoendoscope should go through the antrum and the whole peri-gastric area should be scanned

Table 2 Stomach cancer TNM staging AJCC UICC 8th edition

Category	Criteria
T category	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propia, 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 propia
T3	Tumor invades the subserosal connective tissue without invasion of the visceral peritoneum or adjacent structures
T4	Tumor invades the serosa (visceral peritoneum) or adjacent structures
T4a	Tumor invades the serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures/organs
N category	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases in 1–2 regional lymph nodes
N2	Metastases in 3–6 regional lymph nodes
N3	Metastases in ≥7 regional lymph nodes
N3a	Metastases in 7 or 15 regional lymph nodes
N3b	Metastases in 16 or more regional lymph nodes
M category	
M0	No distant metastasis
M1	Distant metastasis

AJCC, American Joint Committee on Cancer; UICC, Union for International Cancer Control.

while retrieving it. FNA of questionable lymph nodes is recommended if the procedure can be done without going through a site of primary lesion or major blood vessels, and if the study will give additional information regarding treatment. Additionally, an effort should be made to detect the existence of ascites and FNA is recommended to rule out peritoneal spread of disease (69,70).

Patients who appear to have locoregional disease after preoperative testing are potentially curable; all patients with a primary tumor T2 or higher or with a high suspicion of nodal involvement on pretreatment staging studies should be referred for multidisciplinary evaluation to identify the best treatment strategy (i.e., upfront surgery versus initial chemotherapy or chemoradiotherapy).

Gastric linitis plastica (GLP) is a diffuse, infiltrating carcinoma characterized by thickening and rigidity of the stomach wall (71). Because of the predominant submucosal or muscular infiltration, the positive rate for superficial biopsies in GLP patients is low and FNA can be performed to obtain a diagnosis. EUS is helpful for GLP surveillance and staging (72,73). On EUS two findings can be seen. One is that the normal five-layer pattern is replaced by a homogenous, hypoechoic band. The second finding, the five-layer pattern appears intact, but the muscularis propria (fourth layer) is thickened and prominent, beneath a bright, hyperechoic submucosal layer. In both the gastric wall is

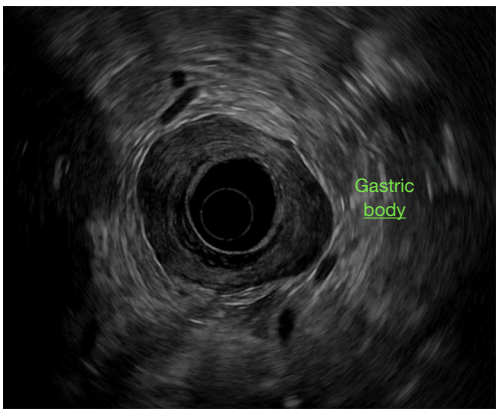

Figure 3 EUS findings in Linitis plastica. All five-layer pattern is obliterated and replaced by a homogenous band. EUS, endoscopic ultrasound.

thickened to >4 mm (73) as seen in *Figure 3*.

Treatment

EG endoscopy therapy

TNM staging and tumor location will determine the optimal treatment strategy for adenocarcinomas of the GEJ. The depth of tumor invasion into the wall of the esophagus is an important factor in selecting treatment and must first be predicted based on visual findings at endoscopy and later confirmed by diagnostic ER if it is thought that superficial invasion is probable.

Early EC is defined as invasion depths consistent with Tis, T1a, and T1b staging. The American Society for Gastrointestinal Endoscopy guidelines recommend ER (30,74) for both treating and staging suspected intra-mucosal adenocarcinoma, with the goal of eradication or complete removal of early disease. Endoscopic treatments include ablation, EMR or endoscopic mucosal dissection (ESD) (30,74).

Tis or high-grade dysplasia: This stage has to be evaluated for the presence of nodularity, lateral spread and to rule out multifocal disease. The most use therapeutic approach is a combination of ER technique associated with ablative techniques to ablate the remaining dysplastic tissue. Nodular lesions showed be resected rather than ablated. The therapeutic efficacy can be up to 98%. Potential complications include perforation, residual stenosis and bleeding (75). Other ablative methods include, cryoablation, photodynamic therapy (PDT) (76-80).

Mucosal adenocarcinomas (T1m1-m3/T1a): due to their estimated low risk of lymph node metastasis of approximately 1–2%, LVI or poor differentiation grade, T1a tumors have the strongest indication to endoscopic treatment as definitive therapy (81).

Tis or T1a residual Barrett's esophagus should be ablative following mucosal resection. A more aggressive approach with EMR or ESD can also be performed at the initial intervention to resect completely an area of superficial tumor or nodular mucosa with a maximal dimension of <2 cm (82,83).

The standard for mucosal cancer resection is band EMR, unless the target lesion is bulky or if there is suspicion of submucosal invasion, in which case ESD may be preferred to achieve en bloc resection. ESD has been accepted as a minimally invasive and curative treatment early EC (84). ESD helps with more accurate pathologic assessment that includes invasion depth, tumor margins and lymph vascular involvement. Reports on ESD efficacy for EGJ cancer have been reported but are still an area of controversy (85).

T1b cancers

These have an increased risk of nodal metastasis according to the M/SM sub-classification system, exceeding 10%, therefore definitive endoscopic therapy is generally not recommended (81,82,86).

GC endoscopy therapy

Surgeons, gastroenterologist, pathologists, medical and radiation oncologist and dieticians should be part of the multidisciplinary treatment planning.

En bloc resection is considered for tumors with low probability of lymph node metastasis. A recent meta-analysis comparing EMR *vs.* ESD for early GC found that curative and complete resection is higher with ESD with lower risk of recurrence compared with patients who undergo EMR. However, ESD has increased risk of perforation and longer operational time (84). Furthermore, ESD requires greater skills and instrumentation to perform.

Per the Japanese guidelines (61), ER, as standard of treatment is indicated for non-ulcerative differentiated-type adenocarcinoma T1a with a diameter ≤2 cm. ESD is indicated as an investigational treatment in tumors clinically diagnosed as T1a and:

- Differentiated-type without ulcerative findings but >2 cm in diameter, or;
- Ulcerative findings but ≤3 cm in diameter or;

- ❖ Undifferentiated-type, without ulcerative findings and ≤2 cm in diameter.

If all of these conditions are fulfilled, the resection is considered endoscopic curability type A: en block resection, histologically differentiated type dominant, negative vertical and horizontal margins, any tumor size and no lymph vascular infiltration. Another ESD can be done for local mucosal recurrence after EMR/ESD. However, the validity of repeat ESD should be performed as part of investigational therapy given the paucity of this evidence (61).

Poorly differentiated GCs, evidence of LVI, deep submucosal invasion, positive deep or lateral margins, metastasis to lymph nodes after ESD or EMR should be considered to be incomplete. Gastrectomy with lymphadenectomy should be considered as additional therapy (87).

Post-treatment endoscopic surveillance

After completion of treatment, endoscopic surveillance should continue after ablative therapy or resection of early EC. Biopsies needs to be taken from the neo-squamous mucosa even if there are no mucosal abnormalities as dysplasia can present beneath the squamous mucosa. We should also look for the presence of BE and four-quadrant biopsies (Seattle protocol biopsy) should be taken to detect recurrent or residual dysplasia. Cryotherapy or RFA should be considered for the residual or recurrent dysplasia. Non-dysplastic BE does not need to be ablated (53,81). For EC and GC, biopsies should be taken if any mucosal abnormalities or strictures are visualized to rule out neoplastic recurrence (53,56).

Surveillance endoscopy every 3 months for one year and then annually, is recommended post treatment of Tis or T1a EC (88).

For GC, surveillance recommendations vary according to the depth of invasion and treatment modality and includes history and physical exam, complete blood count and chemistry profile as clinically indicated. For patients who had partial or subtotal gastrectomy, surveillance may include EGD, CT chest/abdomen/pelvis with oral and IV contrast and FDG-PET/CT for suspicious lesions seen on CT scan. The exact intervals and surveillance strategy are tailored to the stage at diagnosis and treatment plan in a multidisciplinary setting as suggested by National Comprehensive Cancer Network.

EUS post chemotherapy or radiation therapy has a reduced ability to accurately determine the stage of the disease post-treatment as it was shown in Ryun Park *et al.* study where forty patients with locally advanced GC underwent preoperative EUS and computed tomography (CT) after neoadjuvant chemotherapy. The accuracy of EUS and CT was found to be 47% and 57%, respectively for T classification and 39% and 37%, respectively for N classification (50,89,90). After chemotherapy or radiation therapy, biopsies may not accurately diagnose the presence of residual disease neither. EUS should only be done in specific cases after neoadjuvant therapy when FNA of lymph node would change management

Palliation

Endoscopic lumen restoration

The goals of palliation therapy for patients with esophageal or gastric obstruction are to reduce the symptoms like nausea, vomiting and even when possible, restore oral intake and improve nutrition. Endoscopy options include placement of esophageal stent for EGJ/gastric cardia obstruction (GOO), relief of gastric outlet obstruction with enteral stent, percutaneous endoscopic gastrostomy or EUS-guided gastroenterostomy (91,92).

Self-expandable metal stents (SEMS) are used increasingly as the primary palliation in advanced EC, specifically for dysphagia, intractable vomiting from underlying malignant strictures/fistula. It achieves rapid palliation, is safer and more cost-effective than the plastic esophageal prostheses used previously (93). However, stent ingrowth and overgrowth can be a problem, warranting repeat procedures (94).

For GOO, a large multicenter trial demonstrated high short-term efficacy of palliative endoscopic stent placement (95). A Dutch multicenter randomized trial and a systematic review of randomized controlled trials demonstrated faster initial symptom relief in patients with stent placement compared with surgical gastrojejunostomy, but long-term relief was better after gastrojejunostomy. In addition, more major complications, recurrent symptoms, and need for reintervention occurred in the stent group (91,96).

EUS-guided gastrojejunostomy using lumen-apposing metal stents has also been evaluated (92,97). While efficacy was noted to be similar to surgical gastrojejunostomy, there are insufficient data to support this as an alternative to established procedures such as surgical gastrojejunostomy or duodenal stenting.

When obstruction cannot be alleviated, venting

gastrostomy tube can be placed to reduce the obstructive symptoms (98). If tumor location permits, endoscopic, percutaneous or surgical gastrostomy tube placement can be done. The decision regarding whether to select gastrojejunostomy *vs.* endoscopic stenting should depend on the life expectancy, condition and performance status of patients.

Endoscopic therapy for bleeding

The treatment of EC and GC may differ depending on the tumor characteristics. The data is limited however if bleeding appears to be primarily from tumor surface, then available therapeutic options include mechanical therapy, ablative therapy (cryotherapy, argon plasma coagulation, hemospray), injection therapy or a mixed of methods. When endoscopy methods are not helpful, angiography embolization could be useful in this situation (89,99).

Other palliative therapies

External Beam radiation, PDT and brachytherapy may be considered in conjunction with endoscopic treatment or chemotherapy for control of bleeding or obstruction.

Conclusions

As endoscopic technologies and techniques evolve, the role of the gastroenterologist has shifted from being purely a diagnostician to now becoming an integral part of the multidisciplinary management of EGJ and GC patients. EUS provides accurate staging and guides management while ER for early lesions may be curative and obviate the need for more high-risk and invasive procedures and treatments. As we continue to work with the oncologic surgeons, medical and radiation oncologists, patients will continue to benefit from personalized treatments which will hopefully translate into better outcomes and long-term survival which is the ultimate goal.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Dr. Khaldoun Almhanna) for the series "Gastroesophageal Cancer 2020" published in *Annals of Translational Medicine*. The article was sent for external peer review organized by the Guest Editor and the editorial office.

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-4143

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-4143). The series "Gastroesophageal Cancer 2020" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Diaz LI, Mony S, Klapman J. Narrative review of the role of gastroenterologist in the diagnosis, treatment and palliation in gastric and gastroesophageal cancer. Ann Transl Med 2020;8(17):1106. doi: 10.21037/atm-20-4143

