Clinical manifestations, diagnosis, and staging of esophageal cancer

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INTRODUCTION

Squamous cell carcinoma (SCC) and adenocarcinoma account for over 95 percent of esophageal malignant tumors. For most of the 20th century, SCC predominated. In the 1960s, SCC accounted for more than 90 percent of esophageal tumors in the United States, and adenocarcinomas were considered so uncommon that some authorities questioned their existence. However, over time, the incidence of esophageal adenocarcinoma (predominantly arising in the distal esophagus and esophagogastric junction [EGJ]) has increased dramatically in Western countries such that adenocarcinoma now accounts for >60 percent of all esophageal cancers in the United States [1]. In contrast, worldwide, SCC still predominates [2]. (See "Epidemiology and pathobiology of esophageal cancer".)

Esophageal SCCs and adenocarcinomas differ in a number of features, including tumor location and predisposing factors (table 1). Smoking and alcohol are major risk factors for SCC, while Barrett's esophagus (BE) with intestinal metaplasia (a complication of gastroesophageal reflux disease [GERD]), obesity, and smoking are the risk factors for adenocarcinoma [3]. Although there is little doubt that esophageal SCCs and adenocarcinomas represent two different diseases with characteristic pathogenesis, epidemiology, tumor biology, treatment, and outcomes, whether and how histology influence the therapeutic approach remains controversial. (See "Radiation therapy, chemoradiotherapy, neoadjuvant approaches, and

postoperative adjuvant therapy for localized cancers of the esophagus", section on 'Squamous cell versus adenocarcinoma' and "Epidemiology and pathobiology of esophageal cancer".)

The clinical manifestations, diagnosis, and staging of esophageal cancer are reviewed here. The epidemiology, risk factors, and pathobiology of SCC and adenocarcinoma are covered elsewhere. (See "Epidemiology and pathobiology of esophageal cancer".)

IMPORTANCE OF PRETREATMENT STAGING ASSESSMENT

It is vitally important that newly diagnosed esophageal cancer is accurately staged in order to select appropriate treatment:

- For patients with potentially resectable tumors, the choice of initial treatment is highly dependent on clinical stage at diagnosis (table 2):
  - A minority of patients have disease that is limited to the mucosa or submucosa (ie, T1a/bN0), which has a high cure rate from surgical or endoscopic therapy alone. (See "Management of superficial esophageal cancer".)
  - Surgery is the primary curative modality for both esophageal and esophagogastric junction (EGJ) cancers that invade through the esophageal wall or are node positive. Long-term outcomes are not satisfactory with resection alone, even if microscopically complete (R0). This poor long-term outcome prompted evaluation of multimodality approaches, which have evolved in parallel for thoracic esophagus and EGJ tumors, respectively. For most patients with T3 or node-positive tumors, combined modality therapy is preferred over surgery alone. (See "Radiation therapy, chemoradiotherapy, neoadjuvant approaches, and postoperative adjuvant therapy for localized cancers of the esophagus" and "Multimodality approaches to potentially resectable esophagogastric junction and gastric cardia adenocarcinomas".)
  - The optimal approach to clinical T2N0 disease is debated, and guidelines from expert groups differ. Some suggest initial chemoradiotherapy for SCC, and either neoadjuvant chemotherapy or chemoradiotherapy for adenocarcinomas of the distal esophagus or EGJ [4]. Others, including the National Comprehensive Cancer Network (NCCN) [5], suggest initial resection for clinical T2N0 adenocarcinomas or SCCs as long as they are <3 cm and well differentiated, but initial chemoradiotherapy for others with either histology who have high-risk disease. (See "Radiation therapy, chemoradiotherapy, neoadjuvant approaches, and postoperative adjuvant therapy for localized cancers of the esophagus", section on 'Clinical T2N0 disease' and "Multimodality approaches to

potentially resectable esophagogastric junction and gastric cardia adenocarcinomas", section on 'Patients with clinical T1/2, node-negative disease'.)

- Regardless of histology, between 50 and 80 percent of patients with esophageal and EGJ cancers present with incurable, locally advanced unresectable or metastatic disease [6]. Survival is often extended by anticancer therapy, but concurrent supportive care is essential. (See "Management of locally advanced, unresectable and inoperable esophageal cancer" and "Initial systemic therapy for locally advanced unresectable and metastatic esophageal and gastric cancer".)

Selection of patients for any of these therapies is first of all dependent upon accurate staging.

CLINICAL MANIFESTATIONS

Patients with advanced thoracic or cervical esophageal carcinoma present with progressive dysphagia and weight loss. Chronic gastrointestinal blood loss from esophageal and esophagogastric junction (EGJ) cancer is common and may result in iron deficiency anemia. Early intramucosal adenocarcinomas of the distal esophagus that are recognized at endoscopy in an area associated with Barrett's esophagus (BE) is usually not symptomatic.

Thoracic esophageal tumors — Despite differing histologies, both adenocarcinoma and squamous cell carcinoma (SCC) arising in the thoracic esophagus have similar clinical presentations.

In contemporary series, approximately 6 to 10 percent are asymptomatic at the time of diagnosis [7]. Most early (superficial) esophageal cancers in the United States are detected serendipitously or during screening for or surveillance of BE. Early intramucosal cancers are not symptomatic. (See "Management of superficial esophageal cancer".)

Dysphagia and weight loss — Among patients with locally advanced esophageal cancer, obstruction of the esophagus by the tumor causes progressive dysphagia, often accompanied by weight loss. Dysphagia usually occurs once the esophageal lumen diameter is less than 13 mm (reduction by approximately 70 percent of luminal diameter), which indicates at minimum locally advanced disease. Weight loss is due to changes in diet to accommodate the dysphagia, and tumor-related anorexia may contribute. Approximately 20 percent of patients experience odynophagia (painful swallowing).

Early symptoms of esophageal cancer may be subtle and nonspecific. Transient "sticking" of solid food, which may easily be overcome by careful chewing and slower eating, may precede

frank dysphagia. The dysphagia gradually progresses from solids to liquids. Patients may also notice retrosternal discomfort or a burning sensation.

Differential diagnosis — The differential diagnosis of dysphagia is broad and includes nonmalignant strictures, achalasia and other esophageal motility disorders, esophagitis, and esophageal webs and rings. (See "Approach to the evaluation of dysphagia in adults", section on 'Symptom-based differential diagnosis'.)

The differential diagnosis of an esophageal mass includes lesions that typically arise beneath an intact mucosa, including gastrointestinal stromal tumors, leiomyomas and leiomyosarcomas, as well as high-grade neuroendocrine neoplasms (extrapulmonary small cell cancers); all of these are rare. (See "Clinical presentation, diagnosis, and prognosis of gastrointestinal stromal tumors", section on 'Location' and "Local treatment for gastrointestinal stromal tumors, leiomyomas, and leiomyosarcomas of the gastrointestinal tract", section on 'Esophagus' and "High-grade gastroenteropancreatic neuroendocrine neoplasms".)

Other symptoms — Regurgitation of saliva or food uncontaminated by gastric secretions may also occur. Aspiration pneumonia is infrequent. Hoarseness and/or cough may occur if the recurrent laryngeal nerve is invaded by either the primary tumor or associated nodal metastases.

Chronic gastrointestinal blood loss from esophageal and EGJ cancer is common and may result in iron deficiency anemia [8]. However, patients seldom notice melena, hematemesis, or blood in regurgitated food. Acute upper gastrointestinal bleeding as a result of tumor erosion into the aorta or pulmonary or bronchial arteries is rare.

Tracheobronchial fistulas are a late complication. They are caused by direct invasion of tumor through the esophageal wall and into the mainstem bronchus. Such patients often present with intractable coughing or recurrent pneumonias. Stent placement is the treatment of choice. (See "Tracheo- and broncho-esophageal fistulas in adults" and "Endoscopic palliation of esophageal cancer".)

Signs or symptoms referable to distant metastatic disease often occur. The most common sites of distant metastases are the liver, lungs, bones, and adrenal glands [9]. Adenocarcinomas most frequently metastasize to intraabdominal sites (liver, peritoneum), while metastases from SCCs are usually intrathoracic. However, many other sites are described, including cutaneous, muscle, and brain metastases [10].

Cervical esophageal tumors — Between 5 and 6 percent of esophageal cancers arise in the cervical portion of the esophagus, which is 6 to 8 cm long and extends from the hypopharynx

(upper esophageal sphincter) to the sternal notch (table 3 and figure 1) [11]. Most patients have locally advanced disease at the time of diagnosis, sometimes with extension to the hypopharynx. In retrospective series, the most common complaints are weight loss and dysphagia, and 11 to 24 percent have hoarseness as a presenting symptom [12-14].

DIAGNOSIS

The diagnosis of esophageal cancer requires a histologic examination of tumor tissue. A diagnostic biopsy may be obtained by upper endoscopy or, if metastases are present, by image-guided biopsy of a metastatic site.

Endoscopic biopsy — Early esophageal cancers appear endoscopically as superficial plaques, nodules, or ulcerations (picture 1). Advanced lesions appear as strictures (picture 2), ulcerated masses (picture 3), circumferential masses (picture 4), or large ulcerations. (See "Overview of upper gastrointestinal endoscopy (esophagogastroduodenoscopy)".)

While endoscopic visualization of a large mucosal mass is nearly pathognomonic of esophageal cancer, biopsy must be performed to confirm the diagnosis.

The greater the number of biopsies (up to seven), the higher the diagnostic accuracy. As an example, in a series of 202 consecutive patients, 47 of whom had gastric or esophageal carcinoma, the percentages of correct diagnoses of esophageal carcinoma were as follows [15]:

- First biopsy – 93 percent
- Four biopsies – 95 percent
- Seven biopsies – 98 percent

For small lesions, endoscopic resection of the entire lesion may be feasible. Following histologic analysis, endoscopic resection alone may represent suitable therapy if the tumor is small and superficial (see "Overview of endoscopic resection of gastrointestinal tumors", section on 'Esophageal cancer').

Assessment and endoscopic management of superficial esophageal cancer are discussed in greater detail elsewhere. (See "Overview of endoscopic resection of gastrointestinal tumors", section on 'Esophageal cancer' and "Management of superficial esophageal cancer", section on 'Initial assessment'.)

PRETREATMENT STAGING EVALUATION

The prognosis of esophageal cancer is strongly associated with disease stage. Accurate clinical staging of both local tumor extent and the presence or absence of distant metastases is critical for estimating prognosis and selecting the appropriate treatment strategy.

Overview — Once the diagnosis of esophageal cancer is established, pretreatment staging includes an evaluation for both locoregional disease and distant metastases:

- Endoscopic ultrasound (EUS) is the preferred method for locoregional staging. For patients with a thoracic esophageal tumor at or above the carina, bronchoscopy is also indicated. For cervical squamous cell carcinomas (SCCs), flexible laryngoscopy to assess local disease spread and exclude a synchronous malignancy of the head and neck is generally recommended. (See 'Locoregional staging' below and 'Bronchoscopy and laryngoscopy' below.)

- The evaluation for distant metastases includes tomographic testing, including contrast-enhanced computed tomography (CT) of the neck, chest, and abdomen; whole-body integrated fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT; EUS; and sometimes diagnostic laparoscopy.

  - Integrated FDG-PET/CT scans are more sensitive than contrast-enhanced CT for detecting metastatic disease and are now indicated for the detection of occult metastases; if they are not detected on the initial staging CT. Use of preoperative PET/CT in the pretreatment staging evaluation results in a change in management (usually upstaging and thus avoidance of unnecessary surgery) in up to 20 percent of patients. At some institutions, PET with a diagnostic, contrast-enhanced CT is carried out with intravenous (IV) contrast, which replaces the need for a separate contrast-enhanced CT, but this practice is not widespread. (See 'CT, PET, and integrated PET/CT' below.)

  - EUS can visualize liver metastases <1 cm in the left lobe of the liver and malignant ascites; EUS-guided fine-needle aspiration (FNA) or fine needle biopsy (FNB) can get tissue from either of these sites.

  - Invasive staging (laparoscopy, thoracoscopy) may be used to enhance or replace EUS or imaging; however, no study has compared these approaches with EUS plus PET/CT, which are superior to conventional imaging for detecting distant metastases. Some clinicians advocate diagnostic laparoscopy for patients with potentially resectable clinical T3/T4 adenocarcinomas arising at the EGJ or cardia or if there is suspicion for intraperitoneal metastatic disease that cannot otherwise be confirmed. We do not

utilize thoracoscopy for patients who have access to integrated PET/CT. (See 'Laparoscopy and thoracoscopy' below.)

- Routine brain imaging is not a cost-effective or necessary evaluation unless symptoms or signs raise suspicion for brain metastases. (See 'Other tests' below.)

TNM staging criteria — The tumor, node, metastasis (TNM) staging system of the combined American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) for esophageal cancer is used universally. In the most recent (2017, eighth edition) revision [11,16], tumors involving the EGJ with the tumor epicenter no more than 2 cm into the proximal stomach are staged as esophageal cancer. In contrast, EGJ tumors with their epicenter located more than 2 cm into the proximal stomach are staged as stomach cancers, as are all cardia cancers not involving the EGJ, even if they are within 2 cm of the EGJ. Thus, regardless of histology, all esophageal tumors arising in the cervical, thoracic, or abdominal esophagus and those involving the EGJ that have an epicenter within 2 cm of the EGJ (table 3) share the same criteria for T, N, and M stage designation (table 2). However, there are separate stage groupings for SCC and adenocarcinoma regardless of site. Pathologic staging is indicated by a p designation, and pathologic staging after preoperative therapy is indicated by a yp prefix.

Histology-specific stage groupings, initially introduced in 2010, were based on an analysis of worldwide data from 4627 patients with cancer of the esophagus or EGJ who underwent surgery alone. Among patients with node-negative tumors, prognosis was dependent on not only T stage but also on histology and grade of differentiation, and for SCCs, tumor location [17]. Subsequently, investigators used updated data from the Worldwide Esophageal Cancer Collaboration to develop the following figures to illustrate risk-adjusted survival according to clinical, pathologic, and posttreatment pathologic stage for adenocarcinomas (figure 2) and SCCs (figure 3) [18-23].

Regional lymph nodes — Prior to 2010, the specific lymph node groups that were considered regional for esophageal cancer varied according to the anatomic compartment and location within the esophagus. Data suggesting the prognostic importance of the number of involved lymph nodes rather than the location (particularly in the surgical specimen after chemoradiotherapy [24-32]) led to a change in the N stage classification in the 2010 (and subsequent 2017) revision of the AJCC/UICC staging system, with an emphasis on the number of involved nodes rather than location. Regional lymph nodes for all locations in the esophagus extend from periesophageal lymph nodes to celiac nodes and are illustrated in the figure (figure 4).

Locoregional staging

EUS — EUS uses a high-frequency ultrasound transducer to provide detailed images of esophageal masses and their relationship with the five-layered structure of the esophageal wall. (See "Endoscopic ultrasound: Examination of the upper gastrointestinal tract".)

EUS is the most accurate technique for locoregional staging of invasive esophageal cancer.

T stage — The sensitivity and specificity rates of EUS for the correct evaluation of T stage are 81 to 92, and 94 to 97 percent, respectively; in general, EUS performs better with advanced (eg, T4) than with early (ie, T1) disease [33]. Briefly:

- If the EUS identifies only mucosal (T1a) disease, endoscopic mucosal resection (EMR) is usually the next step to endoscopic resection of the tumor and precisely define the depth of invasion. The pathology result from the EMR or endoscopic submucosal dissection (particularly the presence or absence of lymphovascular invasion) is used to guide therapeutic decisions. (See "Management of superficial esophageal cancer" and "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'EUS for T staging of superficial tumors'.)

- By EUS, T2, T3, and T4 tumors appear as strictures, ulcerations, or exophytic masses (picture 2 and picture 3). T2 tumors involve the muscularis propria but do not have transmural invasion through the esophageal wall. By EUS, they appear as irregular hypoechoic masses involving the esophageal wall, leaving the muscularis intact, as evidenced by a smooth contour of the mass and muscularis propria.

  T3 and T4 tumors are both intra- and extraesophageal. Masses that extend into the adventitia are stage T3. T4 masses have invaded through the muscularis propria and adventitia to involve locoregional structures such as pericardium, atrium aorta, vena cava, bronchus, diaphragm, peritoneum, or pleura.

  The finding of an irregular outer border with invasion through the wall of the esophagus may or may not indicate local unresectability. In the eighth edition TNM classification (table 2), tumors classified as T4 are divided into those that are potentially resectable (T4a: tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum) and those that are categorically unresectable (T4b: invasion of other adjacent structures, such as the aorta, vertebral body, or airway). (See "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'EUS for staging locally advanced tumors' and "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'Accuracy of EUS for determining unresectability'.)

- A caveat for EUS staging of esophageal wall penetration (T staging) is that the instrument cannot traverse a tumor-induced stenosis (which occurs in approximately 30 percent of cases). In these settings, EUS may under-stage the tumor because the entire lesion and the celiac axis as well as liver are not seen. It is controversial as to whether to dilate the esophagus for the purpose of a staging examination, since perforations may occur. This subject is discussed in detail elsewhere. (See "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'EUS for staging locally advanced tumors'.)

Regional nodes — EUS achieves nodal staging of esophageal cancer by ultrasound image characteristics and FNA or FNB tissue acquisition:

- Endosonographic criteria that are suggestive of malignant involvement of the visible lymph nodes include width >10 mm, round shape, smooth border, and echo-poor pattern (table 4 and image 1). Of these, echo-poor pattern and width >10 mm are the most specific for malignancy. When all four features are present, there is an 80 to 100 percent chance of metastatic involvement. However, only 25 percent of malignant nodes will have all of these features. These results demonstrate the limitations of EUS criteria for use in preoperative lymph node staging. (See "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'EUS for preoperative lymph node staging'.)

- EUS-guided FNA or FNB may improve the accuracy of N staging by providing cytologic confirmation of metastatic disease from accessible nodes, as long as the primary tumor is not in the pathway of the needle. Sensitivity, specificity, and accuracy of EUS-guided FNA for locoregional lymph nodes are all over 85 percent when surgical resection specimen or cytology results are considered the gold standard. (See "Endoscopic ultrasound for evaluating patients with esophageal cancer", section on 'Endoscopic ultrasound-guided fine-needle aspiration biopsy'.)

The endoscopic finding of a malignant node in the celiac area remote from the primary tumor (ie, for SCCs or for lesions in the upper or middle thoracic esophagus (figure 1)) was previously an indicator of unresectability and was staged as M1a metastatic disease. However, celiac nodal metastases are scored as regional nodal disease in the newest 2017 TNM revision (table 2) regardless of the primary tumor location or histology [11,34]. Nevertheless, prognosis is poor in such cases, even if the primary tumor is located in the distal esophagus or EGJ [35]. (See 'Regional lymph nodes' above and 'TNM staging criteria' above.)

Bronchoscopy and laryngoscopy — Preoperative bronchoscopy with biopsy and brush cytology is advocated by some (including the National Cooperative Cancer Network [NCCN]) as the last investigation in the staging workup for patients with locally advanced, nonmetastatic

tumors located at or above the carina (ie, upper esophageal and cervical SCCs) [5]. In a study of 116 consecutive patients with potentially operable upper or cervical esophageal carcinoma, bronchoscopy was superior to CT and excluded 10 percent of patients from surgery because of airway invasion [36].

For cervical SCCs, which are often diagnosed by ear, nose and throat (ENT) clinicians, flexible laryngoscopy is used to assess local disease extent and to detect a synchronous malignancy of the head and neck. (See "Overview of the diagnosis and staging of head and neck cancer", section on 'Incidence of second and multiple primaries' and "Management of locally advanced, unresectable and inoperable esophageal cancer", section on 'Cervical esophageal tumors'.)

Evaluation for distant metastases — The most common sites of distant metastases in patients with esophageal cancer are the liver, lungs, bones, and adrenal glands [9]. Adenocarcinomas most frequently metastasize to intraabdominal sites (liver, peritoneum), while metastases from SCCs are typically intrathoracic. (See 'Regional lymph nodes' above.)

M staging is carried out with cross-sectional imaging (contrast-enhanced CT, PET/CT scanning), EUS, and for selected patients, diagnostic laparoscopy.

EUS — EUS can visualize liver metastases of <1 cm and malignant ascites. EUS-guided FNA or FNB can provide a tissue diagnosis for liver metastases and FNA may be performed to sample malignant ascites. (See "Endoscopic ultrasound-guided fine needle aspiration in the gastrointestinal tract", section on 'Other lesions'.)

CT, PET, and integrated PET/CT — FDG-PET and integrated PET/CT scans are useful to detect occult metastatic disease in patients who are otherwise believed to be surgical candidates after routine staging with conventional contrast-enhanced helical CT. Integrated PET/CT imaging is increasingly favored over PET alone due to better spatial resolution. It involves performance of both PET and CT sequentially during a single visit on a hybrid PET/CT scanner. However, the CT component of integrated PET/CT imaging is performed in most institutions without the use of IV contrast, which compromises the detection of small metastases both within and outside the liver. In the absence of IV contrast, an integrated PET/CT cannot substitute for a dedicated IV-contrast-enhanced CT. At some institutions, PET/CT is carried out with IV contrast. This may replace the need for a separate contrast-enhanced CT, but this practice is not widespread.

While relatively inexpensive, contrast-enhanced (oral plus IV) helical CT has a limited ability to identify locally advanced (T4 (table 2)) disease and subclinical distant metastatic disease, particularly in the peritoneal cavity [37,38].

FDG-PET is more sensitive than contrast-enhanced CT or EUS for the detection of distant metastases [37,39-44]. The addition of PET to the preoperative assessment alters management in 5 to 20 percent of cases, mainly by detecting occult metastases (ie, upstaging) that reduces the number of patients who undergo needless surgery [9,39-42,45,46]. The improved sensitivity of PET for the detection of metastatic disease makes it **potentially** the most cost-effective method of identifying patients with occult metastases for whom curative therapy should not be pursued [38,45,47,48].

A major drawback of PET for the evaluation of the primary site and nodal metastases is its poor spatial resolution that makes it difficult to localize the anatomic location of the FDG uptake. This limitation is significantly reduced by the use of integrated PET/CT imaging, a technique in which both PET and CT are performed sequentially during a single visit on a hybrid PET/CT scanner. The PET and CT images are then co-registered using fusion software, enabling the physiologic data obtained on PET to be localized according to the anatomic CT images (image 2).

Limited data suggest a greater accuracy of integrated PET/CT over PET alone in patients with cancer, including esophageal cancer [49,50], and most institutions are now performing integrated PET/CT rather than PET alone because of the better spatial resolution. At most institutions, the CT component of integrated PET/CT imaging is performed without the use of IV contrast material or in partial/complete expiration, precluding the optimal detection of small lung and liver metastases. Increasingly, PET/CT is carried out with IV contrast, but this practice is not widespread [51].

Measurement of the standardized uptake value (SUV), which reflects the metabolic activity of the tumor, may also be a prognostic factor. In a meta-analysis of seven studies that evaluated the impact of the SUV on overall survival, high SUV predicted worse survival [52]. However, in a large retrospective series that was not included in the meta-analysis, an initially high SUV did not correlate with worse survival [53]. In fact, the results suggested a better response to preoperative chemoradiotherapy in the high SUV group. The value of FDG-PET as a predictive marker of response to neoadjuvant therapy remains uncertain, however [54].

Suspicious PET findings should be confirmed with biopsy before excluding a patient from surgical consideration, given the high rate of false-positive findings [55].

As with contrast-enhanced CT scanning alone, PET/CT is of limited value for staging the extent of locoregional tumor, particularly nodal status [37]. This may be due, at least in part, to high FDG uptake in the primary esophageal malignancy, which obscures increased FDG uptake in the regional nodes, and/or low sensitivity for small involved lymph nodes. Furthermore, PET/CT is not consistently able to differentiate the depth of primary tumor invasion. EUS is more accurate

than either PET/CT or contrast-enhanced CT alone [56], and it is the locoregional tumor staging modality of choice. (See 'EUS' above.)

PET restaging after induction therapy — Integrated PET/CT may be also be useful for restaging after preoperative therapy.

Limited experience suggests that whole-body PET/CT imaging detects distant metastases in approximately 8 percent of patients following induction chemoradiotherapy with or without induction chemotherapy [57]. In many of these cases, the metastases were located in sites (eg, skeletal muscle, subcutaneous soft tissue, brain, thyroid) that are not imaged well by conventional radiographic staging techniques. Some clinicians order a post-induction-therapy PET/CT approximately four weeks after the completion of induction therapy. This is a method to assess for distant metastatic disease and potentially prevent unneeded surgery, an approach that is endorsed in the consensus-based NCCN guidelines [5]. (See "Multimodality approaches to potentially resectable esophagogastric junction and gastric cardia adenocarcinomas", section on 'PET-directed therapy'.)

In addition to detecting otherwise occult metastatic disease, post-induction-therapy FDG-PET provides information on metabolic response in the primary tumor that may be clinically useful in the selection of subsequent therapy:

- Early data from retrospective series suggest that post-chemoradiotherapy FDG-PET scanning may serve to identify those patients for whom surgery might be avoided.
- Other data suggest that responses observed on PET scans during induction chemotherapy have significant predictive and prognostic benefit [58].

These data are discussed in detail elsewhere. (See "Radiation therapy, chemoradiotherapy, neoadjuvant approaches, and postoperative adjuvant therapy for localized cancers of the esophagus", section on 'Utility of postinduction therapy PET scans' and "Multimodality approaches to potentially resectable esophagogastric junction and gastric cardia adenocarcinomas", section on 'PET-directed therapy'.)

Laparoscopy and thoracoscopy — The need for diagnostic laparoscopy for patients who appear to have potentially resectable esophageal or EGJ carcinomas is controversial, and there is no consensus on this issue from expert groups. We reserve diagnostic laparoscopy for patients who, after conventional pretreatment staging studies, appear to have potentially resectable, clinical T3 or T4 (table 2), Siewert II to III (ie, located between 1 cm proximal and 5 cm distal to the anatomical squamocolumnar junction or Z-line (figure 5)) adenocarcinomas

of the EGJ, or if there is suspicion for intraperitoneal metastatic disease that cannot otherwise be confirmed. We do not perform thoracoscopic staging in patients who have access to PET/CT.

In order to limit aggressive treatment to patients with locally advanced disease, diagnostic laparoscopy is sometimes performed to detect occult intraperitoneal metastases in patients with distal esophageal and EGJ adenocarcinomas [59-61]. Intraperitoneal metastases are notoriously difficult to diagnose noninvasively by either CT or PET.

Laparoscopic (and thoracoscopic) staging procedures have also been examined for their potential to more accurately stage regional lymph nodes (particularly celiac and intrathoracic) as compared with EUS [62-64]. As an example, in a multi-institutional study conducted by the Cancer and Leukemia Group B (CALGB), noninvasive imaging (CT, magnetic resonance imaging [MRI], and EUS) incorrectly staged (either false-negative lymph nodes or false-positive metastatic disease) 50, 40, and 30 percent of patients, respectively, as assessed by thoracoscopic or laparoscopic staging [62]. An important limitation of this study was that EUS was performed without FNA, thus limiting the accuracy of noninvasive imaging.

Although the available data support the view that invasive staging is more accurate than EUS or CT alone; however, no study has compared this approach with EUS plus integrated PET/CT scanning, which is superior to conventional imaging modalities for detecting distant metastases.

The need for diagnostic laparoscopy for patients who appear to have potentially resectable distal esophageal and EGJ adenocarcinomas is controversial, and there is no consensus on this issue from expert groups; none of these groups provides guidelines for the use of diagnostic thoracoscopy:

- Consensus-based guidelines from the NCCN consider diagnostic laparoscopy to be "optional" for patients with EGJ tumors and no evidence of metastatic disease [5].
- Guidelines from the European Society for Medical Oncology (ESMO) advocate diagnostic laparoscopy for all patients with locally advanced (T3/T4) adenocarcinomas of the EGJ infiltrating the gastric cardia [4].
- The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) states that patients who are considered to be candidates for curative resection (early stage esophageal cancer with no evidence of distant or lymph node metastases on high-quality preoperative imaging) may benefit from staging laparoscopy (grade B).

We reserve diagnostic laparoscopy for patients who, after conventional pretreatment staging studies, appear to have potentially resectable, clinical T3 or T4 (table 2), Siewert II to III (ie, located between 1 cm proximal and 5 cm distal to the anatomical squamocolumnar junction or Z-line (figure 5)) adenocarcinomas of the EGJ, or if there is suspicion for intraperitoneal metastatic disease that cannot otherwise be confirmed. The surgical approach, diagnostic accuracy, and yield of diagnostic laparoscopy for esophageal cancer are discussed in greater detail elsewhere. (See "Diagnostic staging laparoscopy for digestive system cancers", section on 'Esophagogastric junction and gastric cancer'.)

Another approach, laparoscopic ultrasound, may provide the benefits of both locoregional and intraperitoneal staging [65-67]. In a study of 26 patients with gastric or esophageal cancers, T and N staging with laparoscopic ultrasound were comparable with results from EUS [65]. The accuracy of M staging with laparoscopic ultrasound was better than with laparoscopy alone or CT (89 versus 44 and 64 percent, respectively). No randomized trials or large reviews have been performed to determine if laparoscopic ultrasound offers a significant advantage over laparoscopy alone for detecting unresectable disease in esophageal cancer. (See "Diagnostic staging laparoscopy for digestive system cancers", section on 'Laparoscopic ultrasound'.)

Other tests — Consensus-based guidelines for staging, such as those published by the NCCN [5] and ESMO [4], do not recommend routine pretreatment brain imaging for patients with esophageal or EGJ cancers. Brain metastases have been considered uncommon in patients with esophageal cancer (published incidence <5 percent [68,69]). However, in more contemporary esophageal cancer cohorts with higher percentages of adenocarcinoma, the incidence of brain metastases may be higher (13 percent in one series [70]). Despite these data, however, routine brain imaging is not considered cost effective or necessary as part of the routine staging evaluation unless symptoms or signs raise suspicion for brain metastases.

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: Esophageal 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 topics (see "Patient education: Upper endoscopy (The Basics)" and "Patient education: Esophageal cancer (The Basics)")
- Beyond the Basics topics (see "Patient education: Upper endoscopy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical presentation** – Patients with advanced thoracic or cervical esophageal carcinoma usually present with progressive dysphagia and weight loss. (See 'Clinical manifestations' above.)
- **Establishing the diagnosis** – The diagnosis of esophageal or esophagogastric junction (EGJ) cancer is usually established by endoscopic biopsy. Early cancers may appear as superficial plaques, nodules, or ulcerations (picture 1). Advanced lesions may appear as strictures (picture 2), ulcerated masses (picture 3), circumferential masses (picture 4), or large ulcerations. The endoscopic appearance of a large mucosal mass is frequently diagnostic of esophageal cancer. Biopsies confirm the diagnosis in more than 90 percent of cases. (See 'Diagnosis' above.)
- **Staging and pretreatment assessment**
  - The tumor, node, metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) for esophageal cancer is used universally (table 2).

    In the most recent (eighth edition, 2017) version, tumors involving the EGJ with the tumor epicenter no more than 2 cm into the proximal stomach are staged as esophageal cancers. In contrast, EGJ tumors with their epicenter located more than 2 cm into the proximal stomach are staged as stomach cancers, as are all cardia cancers

not involving the EGJ, even if they are within 2 cm of the EGJ (table 3). (See 'TNM staging criteria' above.)

- Once the diagnosis of esophageal cancer is established, selection of the appropriate therapeutic approach for an esophageal cancer is highly dependent on the accuracy of pretreatment assessment. The pretreatment staging assessment includes an evaluation for both locoregional disease extent and distant metastases:

  Endoscopic ultrasound (EUS) is the preferred method for locoregional staging. Preoperative bronchoscopy with biopsy and brush cytology is indicated for patients with locally advanced, nonmetastatic tumors that are located at or above the level of the carina, and flexible laryngoscopy is generally recommended for cervical squamous cell carcinomas (SCCs). (See 'Locoregional staging' above.)

  All patients should undergo contrast-enhanced CT of the neck, chest, and abdomen to evaluate for distant metastases. For selected patients, whole-body integrated fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT, EUS, and/or diagnostic laparoscopy may be indicated:

  - FDG-PET/CT is more sensitive than contrast-enhanced CT for detecting metastases and are now widely used to detect occult metastases if metastases are not seen on the initial staging CT scans. At some institutions, PET/CT is carried out with intravenous contrast, and this might effectively replace the need for a separate contrast-enhanced CT, but this practice is not widespread. Suspicious PET/CT findings should be histologically confirmed before excluding a patient from surgical consideration. (See 'CT, PET, and integrated PET/CT' above.)

  - EUS-guided fine-needle aspiration (FNA) or fine needle biopsy can provide a tissue diagnosis for suspected liver metastases and FNA may be done to diagnose malignant ascites.

  - The role of staging laparoscopy is controversial. We reserve diagnostic laparoscopy for patients with potentially resectable clinical T3/T4 (table 2) adenocarcinomas arising within the abdominal portion of the esophagus (table 3) or if there is suspicion for intraperitoneal metastatic disease that cannot otherwise be confirmed. We do not utilize thoracoscopy for patients who have access to EUS and integrated PET/CT. (See 'Laparoscopy and thoracoscopy' above.)

  - Routine brain imaging is not indicated unless symptoms or signs raise suspicion for brain metastases. (See 'Other tests' above.)

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Topic 2502 Version 46.0

GRAPHICS

Epidemiology of esophageal cancer in the United States, 2012

	Squamous cell	Adenocarcinoma
Incidence rate, per 100,000 population	1.2	2.8
Male-to-female ratio	2.5:1	6.5:1
White-to-Black ratio	1:4	4:1
Most common locations	Middle esophagus	Distal esophagus
Major risk factors	Smoking, alcohol	Barrett's esophagus

Data from: Thrift AP. The epidemic of oesophageal carcinoma: Where are we now? Cancer Epidemiol 2016; 41:88.

Graphic 78167 Version 4.0

Esophagus and esophagogastric junction cancers TNM staging AJCC UICC 8th edition

Primary tumor (T), squamous cell carcinoma and adenocarcinoma	
T category	**T criteria**
TX	Tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade dysplasia, defined as malignant cells confined to the epithelium 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 propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum
T4b	Tumor invades other adjacent structures, such as the aorta, vertebral body, or airway
Regional lymph nodes (N), squamous cell carcinoma and adenocarcinoma	
N category	**N criteria**
NX	Regional lymph nodes 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
Distant metastasis (M), squamous cell carcinoma and adenocarcinoma	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis
Histologic grade (G), squamous cell carcinoma and adenocarcinoma	
G	**G definition**
GX	Grade cannot be assessed

G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated, undifferentiated

Location, squamous cell carcinoma

Location plays a role in the stage grouping of esophageal squamous cancers.

Location category	Location criteria
X	Location unknown
Upper	Cervical esophagus to lower border of azygos vein
Middle	Lower border of azygos vein to lower border of inferior pulmonary vein
Lower	Lower border of inferior pulmonary vein to stomach, including gastroesophageal junction

NOTE: Location is defined by the position of the epicenter of the tumor in the esophagus.

Prognostic stage groups, squamous cell carcinoma

Clinical (cTNM)

When cT is...	And cN is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0-1	M0	I
T2	N0-1	M0	II
T3	N0	M0	II
T3	N1	M0	III
T1-3	N2	M0	III
T4	N0-2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Pathological (pTNM)

When pT is...	And pN is...	And M is...	And G is...	And location is...	Then the stage group is...
Tis	N0	M0	N/A	Any	0
T1a	N0	M0	G1	Any	IA
T1a	N0	M0	G2-3	Any	IB

T1a	N0	M0	GX	Any	IA
T1b	N0	M0	G1-3	Any	IB
T1b	N0	M0	GX	Any	IB
T2	N0	M0	G1	Any	IB
T2	N0	M0	G2-3	Any	IIA
T2	N0	M0	GX	Any	IIA
T3	N0	M0	Any	Lower	IIA
T3	N0	M0	G1	Upper/middle	IIA
T3	N0	M0	G2-3	Upper/middle	IIB
T3	N0	M0	GX	Any	IIB
T3	N0	M0	Any	Location X	IIB
T1	N1	M0	Any	Any	IIB
T1	N2	M0	Any	Any	IIIA
T2	N1	M0	Any	Any	IIIA
T2	N2	M0	Any	Any	IIIB
T3	N1-2	M0	Any	Any	IIIB
T4a	N0-1	M0	Any	Any	IIIB
T4a	N2	M0	Any	Any	IVA
T4b	N0-2	M0	Any	Any	IVA
Any T	N3	M0	Any	Any	IVA
Any T	Any N	M1	Any	Any	IVB

Post-neoadjuvant therapy (ypTNM)

When ypT is…	And ypN is…	And M is…	Then the stage group is…
T0-2	N0	M0	I
T3	N0	M0	II
T0-2	N1	M0	IIIA
T3	N1	M0	IIIB
T0-3	N2	M0	IIIB
T4a	N0	M0	IIIB
T4a	N1-2	M0	IVA
T4a	NX	M0	IVA

T4b	N0-2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Prognostic stage groups, adenocarcinoma

Clinical (cTNM)

When cT is...	And cN is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	I
T1	N1	M0	IIA
T2	N0	M0	IIB
T2	N1	M0	III
T3	N0-1	M0	III
T4a	N0-1	M0	III
T1-4a	N2	M0	IVA
T4b	N0-2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Pathological (pTNM)

When pT is...	And pN is...	And M is...	And G is...	Then the stage group is...
Tis	N0	M0	N/A	0
T1a	N0	M0	G1	IA
T1a	N0	M0	GX	IA
T1a	N0	M0	G2	IB
T1b	N0	M0	G1-2	IB
T1b	N0	M0	GX	IB
T1	N0	M0	G3	IC
T2	N0	M0	G1-2	IC
T2	N0	M0	G3	IIA
T2	N0	M0	GX	IIA
T1	N1	M0	Any	IIB

T3	N0	M0	Any	IIB
T1	N2	M0	Any	IIIA
T2	N1	M0	Any	IIIA
T2	N2	M0	Any	IIIB
T3	N1-2	M0	Any	IIIB
T4a	N0-1	M0	Any	IIIB
T4a	N2	M0	Any	IVA
T4b	N0-2	M0	Any	IVA
Any T	N3	M0	Any	IVA
Any T	Any N	M1	Any	IVB

Post-neoadjuvant therapy (ypTNM)

When ypT is…	And ypN is…	And M is…	Then the stage group is…
T0-2	N0	M0	I
T3	N0	M0	II
T0-2	N1	M0	IIIA
T3	N1	M0	IIIB
T0-3	N2	M0	IIIB
T4a	N0	M0	IIIB
T4a	N1-2	M0	IVA
T4a	NX	M0	IVA
T4b	N0-2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; N/A: not applicable.

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Graphic 111221 Version 9.0

Anatomy of esophageal cancer primary site by ICD-O-3 topography codes

Anatomic name	Compartment ICD-O-3	Esophageal location		Anatomic boundaries	Typical esophagectomy (cm)
		ICD-O-3	Name		
Cervical	C15.0	C15.3	Upper	Hypopharynx to sternal notch	15 to <20
Thoracic	C15.1	C15.3	Upper	Sternal notch to azygos vein	20 to <25
		C15.4	Middle	Lower border of azygos vein to inferior pulmonary vein	25 to <30
		C15.5	Lower	Lower border of inferior pulmonary vein to esophagogastric junction	30 to <40
Abdominal	C15.2	C15.5	Lower	Esophagogastric junction to 2 cm below esophagogastric junction	40 to 45
		C16.0	Esophagogastric junction/cardia	Esophagogastric junction to 2 cm below esophagogastric junction	40 to 45

ICD-O-3: International Classification of Diseases for Oncology, 3rd Edition.

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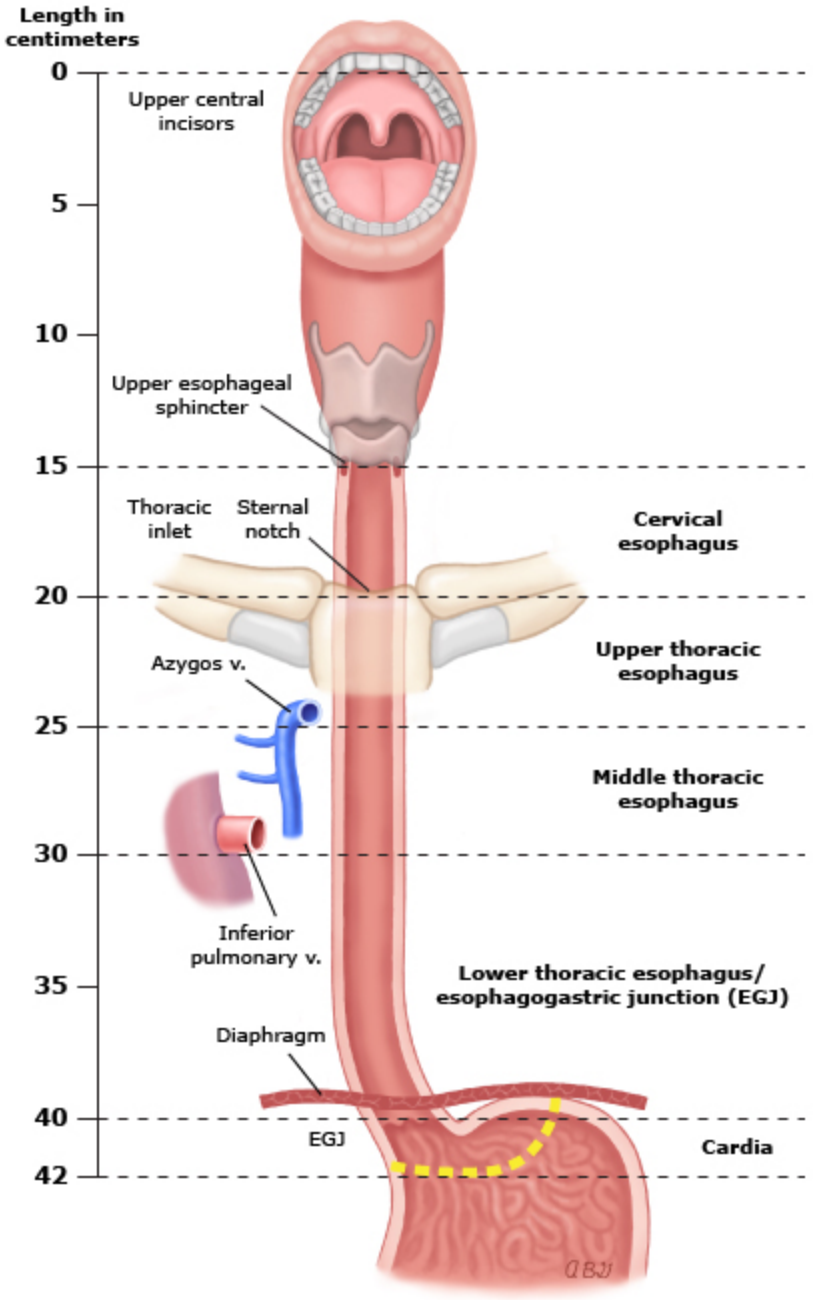
Graphic 111351 Version 7.0

AJCC 8th edition regions of the esophagus



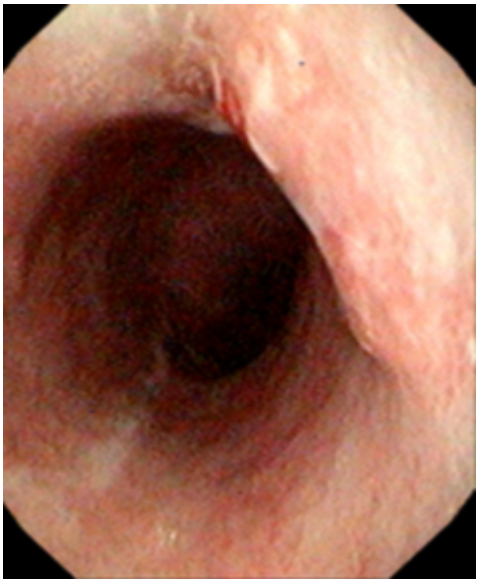
Anatomy of esophageal cancer primary site, including typical endoscopic measurements of each region measured from the incisors. Exact measurements depend on body size and height. For tumors of the EGJ and cardia, location of cancer primary site (ie, esophagus, stomach) is defined by cancer epicenter.

AJCC: American Joint Committee on Cancer; v: vein.

Modified from: Rice TW, Kelsen D, Blackstone EH, et al. Esophagus and esophagogastric junction. In: AJCC Cancer Staging Manual, 8th Ed, Amin MB (ed), Springer Science+Business Media, LLC, New York, 2017.

Graphic 111260 Version 8.0

Early, superficial esophageal cancer

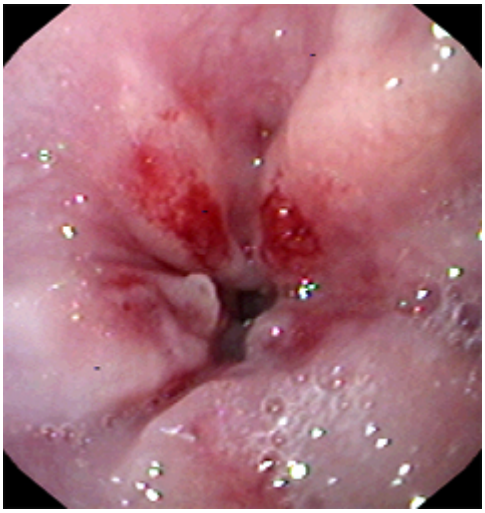


Early, superficial esophageal cancer seen on endoscopy.

Courtesy of William Brugge, MD.

Graphic 55091 Version 1.0

Malignant stricture of the esophagus

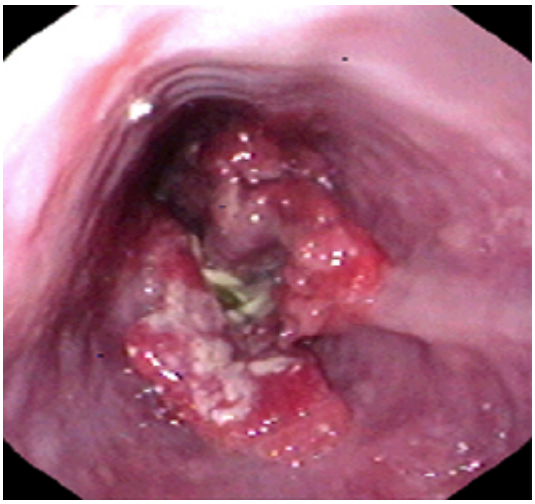


The tumor mass is not readily evident because it is predominantly infiltrating the esophageal wall.

Courtesy of William Brugge, MD.

Graphic 55542 Version 1.0

Ulcerating malignant esophageal mass in distal esophagus

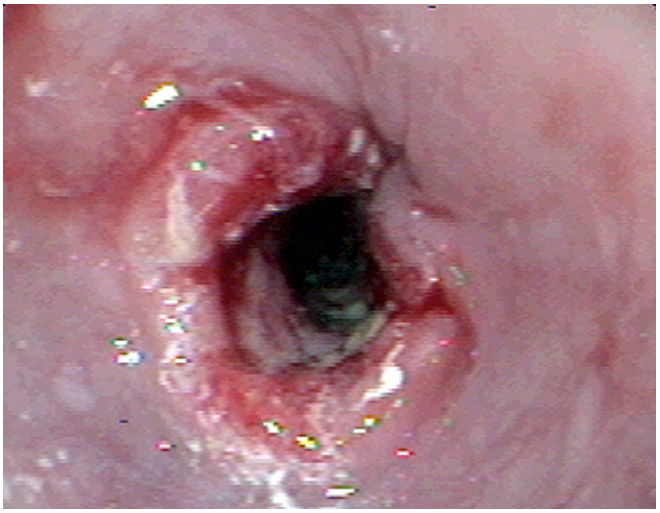


Ulcerating malignant esophageal mass in distal esophagus seen on endoscopy.

Courtesy of William Brugge, MD.

Graphic 78958 Version 1.0

Circumferential ulcerated esophageal cancer

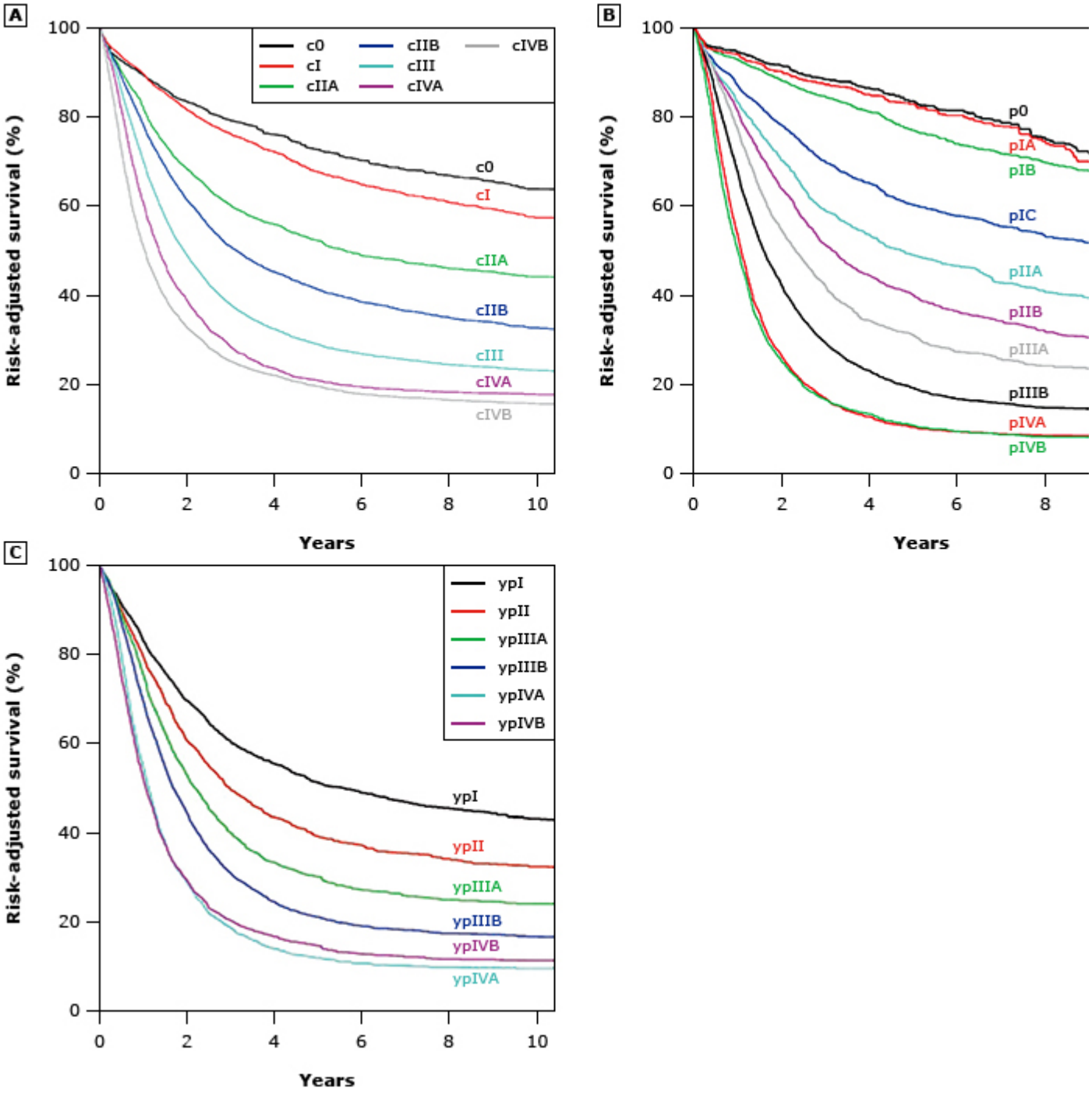


Circumferential ulcerated esophageal cancer seen on endoscopy.

Courtesy of William Brugge, MD.

Graphic 67522 Version 1.0

Risk-adjusted survival after treatment decision for clinically staged (c), patholo (p), and posttreatment pathologically staged (yp) adenocarcinoma of the esopl esophagogastric junction



(A) Risk-adjusted survival after treatment decision for clinically staged (c) adenocarcinoma of the esophagus WECC data.

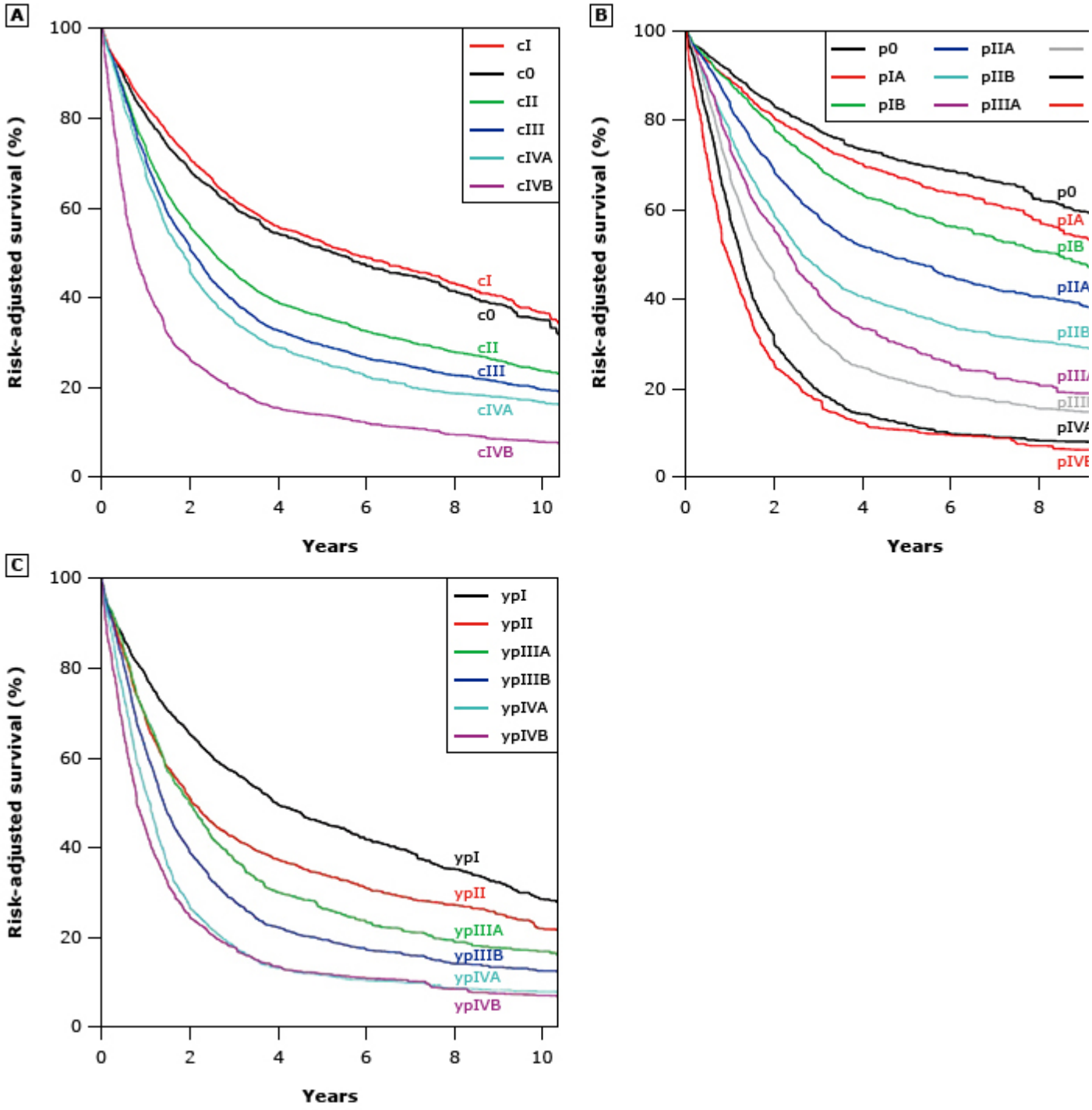
(B) Risk-adjusted survival after treatment decision for pathologically staged (p) adenocarcinoma of the esopl on WECC data.

(C) Risk-adjusted survival after treatment decision for postneoadjuvant pathologically staged (yp) adenocarc esophagus based on WECC data.

WECC: Worldwide Esophageal Cancer Collaboration.

Graphic 111241 Version 6.0

Risk-adjusted survival after treatment decision for clinically staged (c), patholo staged (p), and posttreatment pathologically staged (yp) esophageal squamous cancer



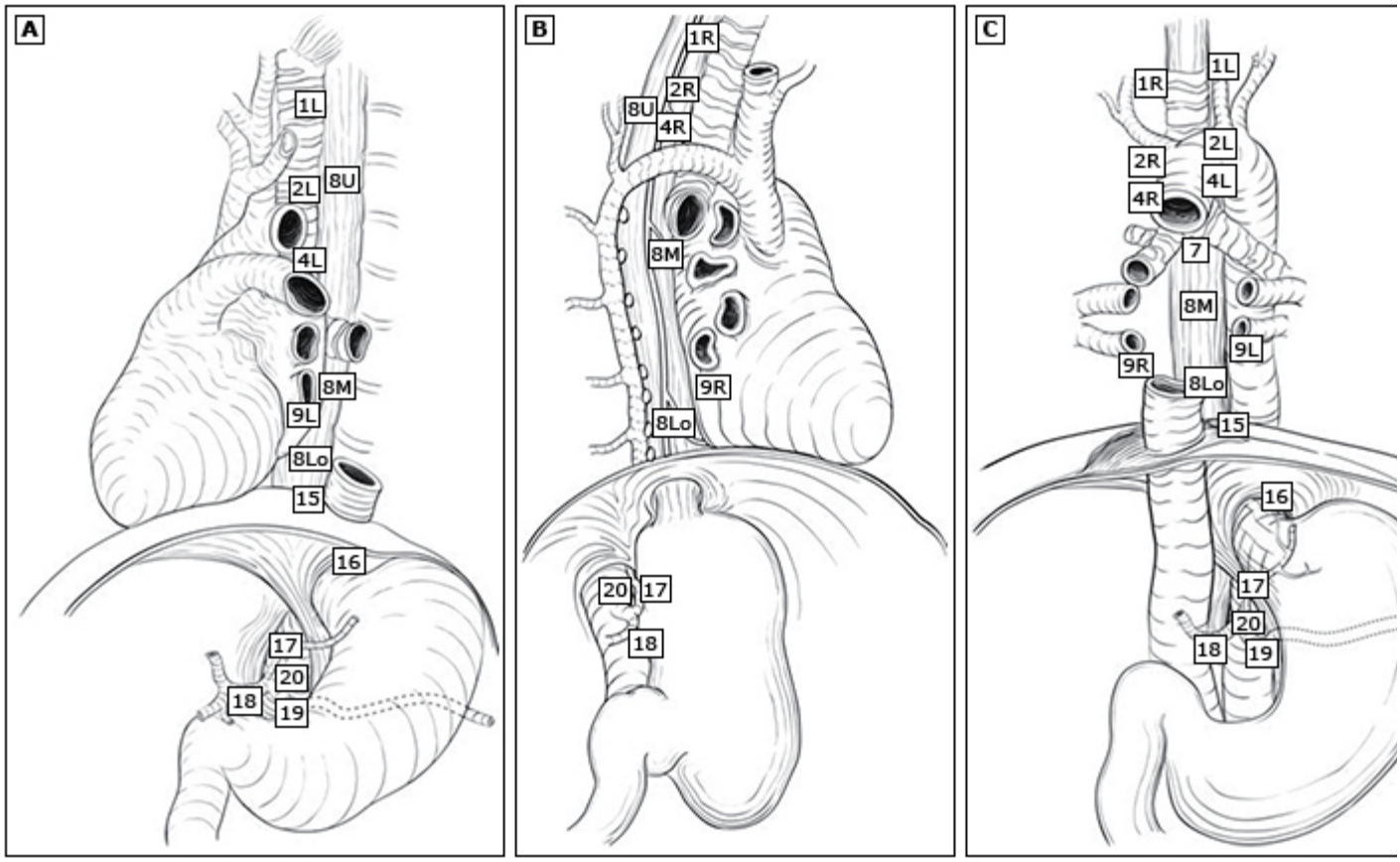
(A) Risk-adjusted survival after treatment decision for clinically staged (c) squamous cell carcinoma of the esophagus based on Worldwide Esophageal Cancer Collaboration (WECC) data.

(B) Risk-adjusted survival after treatment decision for pathologically staged (p) squamous cell carcinoma of t esophagus based on WECC data.

(C) Risk-adjusted survival after treatment decision for postneoadjuvant pathologically staged (yp) squamous carcinoma of the esophagus based on WECC data.

Graphic 111244 Version 6.0

Regional lymph node stations for staging esophageal cancer



(A-C) Lymph node maps for esophageal cancer. Regional lymph node stations for staging esophageal cance left **(A)**, right **(B)**, and anterior **(C)**.

1R: Right lower cervical paratracheal nodes, between the supraclavicular paratracheal space and apex of the **1L:** Left lower cervical paratracheal nodes, between the supraclavicular paratracheal space and apex of the l **2R:** Right upper paratracheal nodes, between the intersection of the caudal margin of the brachiocephalic a with the trachea and the apex of the lung. **2L:** Left upper paratracheal nodes, between the top of the aortic a and the apex of the lung. **4R:** Right lower paratracheal nodes, between the intersection of the caudal margir the brachiocephalic artery with the trachea and cephalic border of the azygos vein. **4L:** Left lower paratrache nodes, between the top of the aortic arch and the carina. **7:** Subcarinal nodes, caudal to the carina of the tra **8U:** Upper thoracic paraesophageal lymph nodes, from the apex of the lung to the tracheal bifurcation. **8M:** Middle thoracic paraesophageal lymph nodes, from the tracheal bifurcation to the caudal margin of the infe pulmonary vein. **8Lo:** Lower thoracic paraesophageal lymph nodes, from the caudal margin of the inferior pulmonary vein to the EGJ. **9R:** Pulmonary ligament nodes, within the right inferior pulmonary ligament. **9L:** Pulmonary ligament nodes, within the left inferior pulmonary ligament. **15:** Diaphragmatic nodes, lying on t dome of the diaphragm and adjacent to or behind its crura. **16:** Paracardial nodes, immediately adjacent to t gastroesophageal junction. **17:** Left gastric nodes, along the course of the left gastric artery. **18:** Common he nodes, immediately on the proximal common hepatic artery. **19:** Splenic nodes, immediately on the proxima splenic artery. **20:** Celiac nodes, at the base of the celiac artery.

EGJ: esophagogastric junction.

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Graphic 111319 Version 8.0

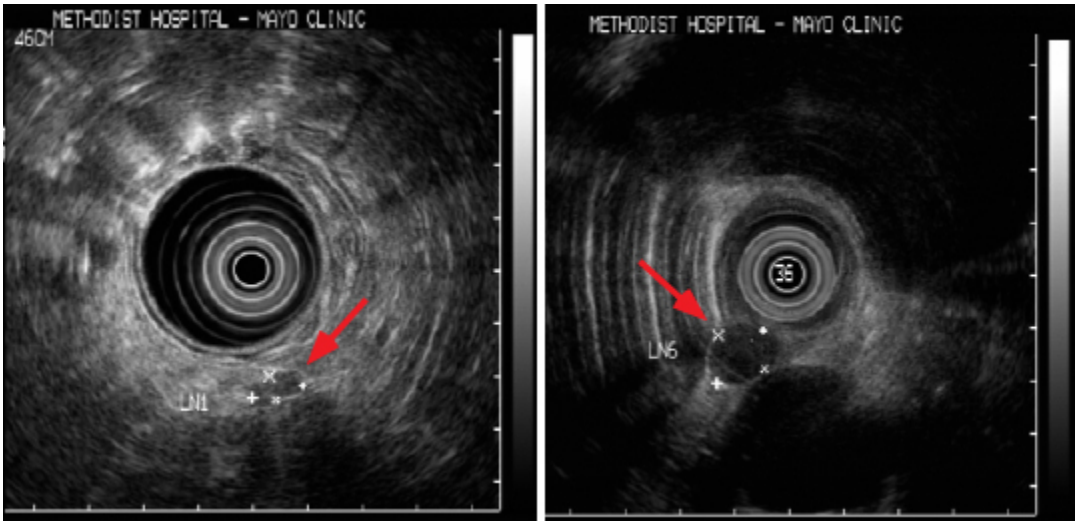
Endoscopic ultrasound (EUS) criteria for assessment of lymph nodes

	Benign	Malignant
Size (width)	<10 mm	>10 mm
Shape	Elongated	Round
Border	Irregular	Smooth
Echogenicity	Echorich	Echopoor

Data from: Catalano, MF, Sivak, MV Jr, Rice, T, et al, Gastrointest Endosc 1994; 40:442 and Bhutani, MS, Hawes, RH, Hoffman, BJ, Gastrointest Endosc 1997; 45:474.

Graphic 66591 Version 5.0

Benign and malignant periesophageal lymph nodes

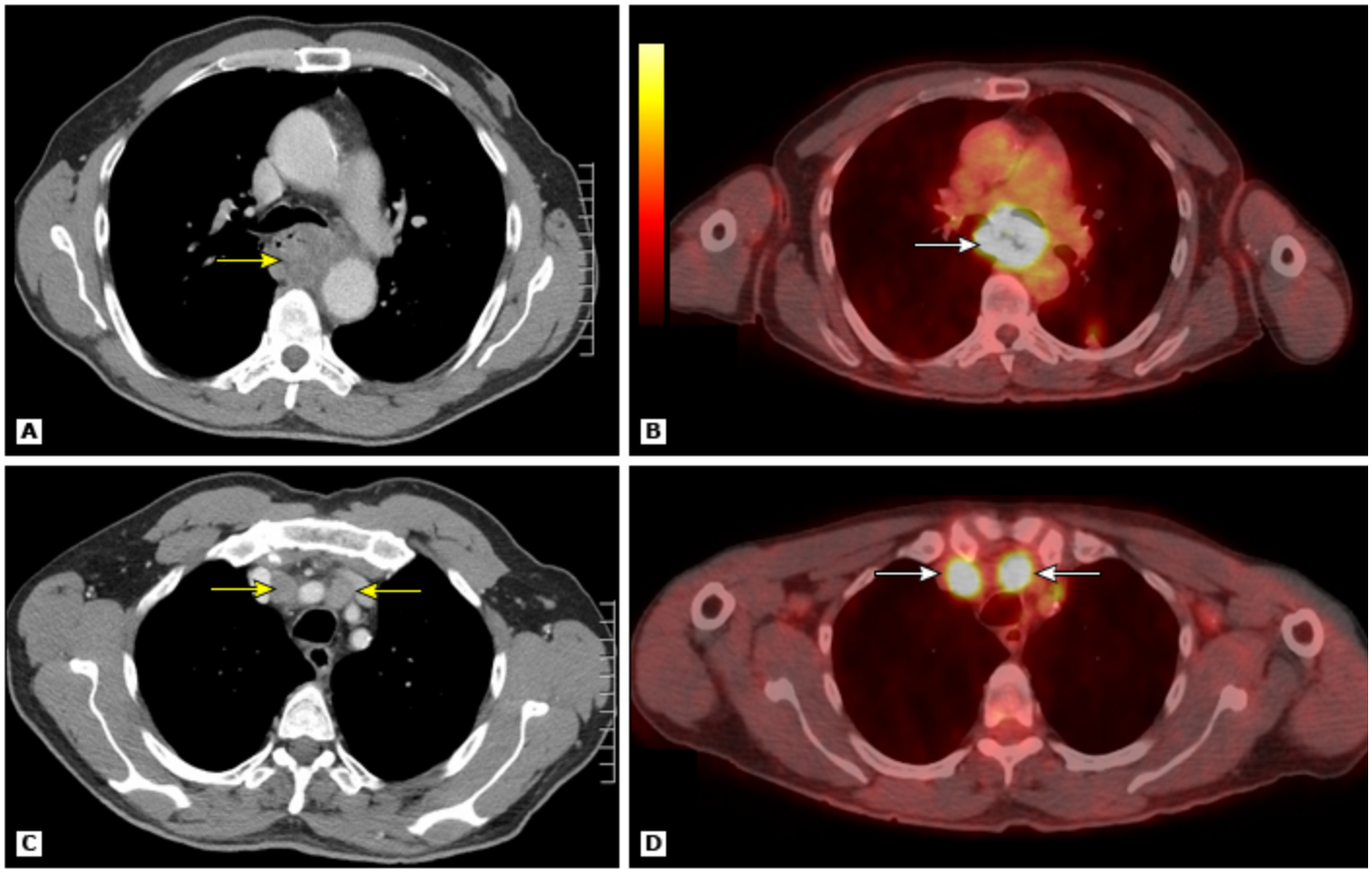


Endoscopic ultrasound images showing a benign (left panel) and malignant (right panel) appearing periesophageal lymph node in a patient with histologically proven esophageal adenocarcinoma. Characteristics of the benign lymph node are its mixed echogenicity, irregular border, elongated shape, and <10 mm width. In contrast, the malignant lymph node is echopoor, has a smooth border, has a round shape, and is >10 mm in width.

Courtesy of Enrique Vazquez-Sequeiros, MD, and Maurits J Wiersema, MD.

Graphic 57813 Version 3.0

Imaging metastatic esophageal carcinoma with CT and PET CT

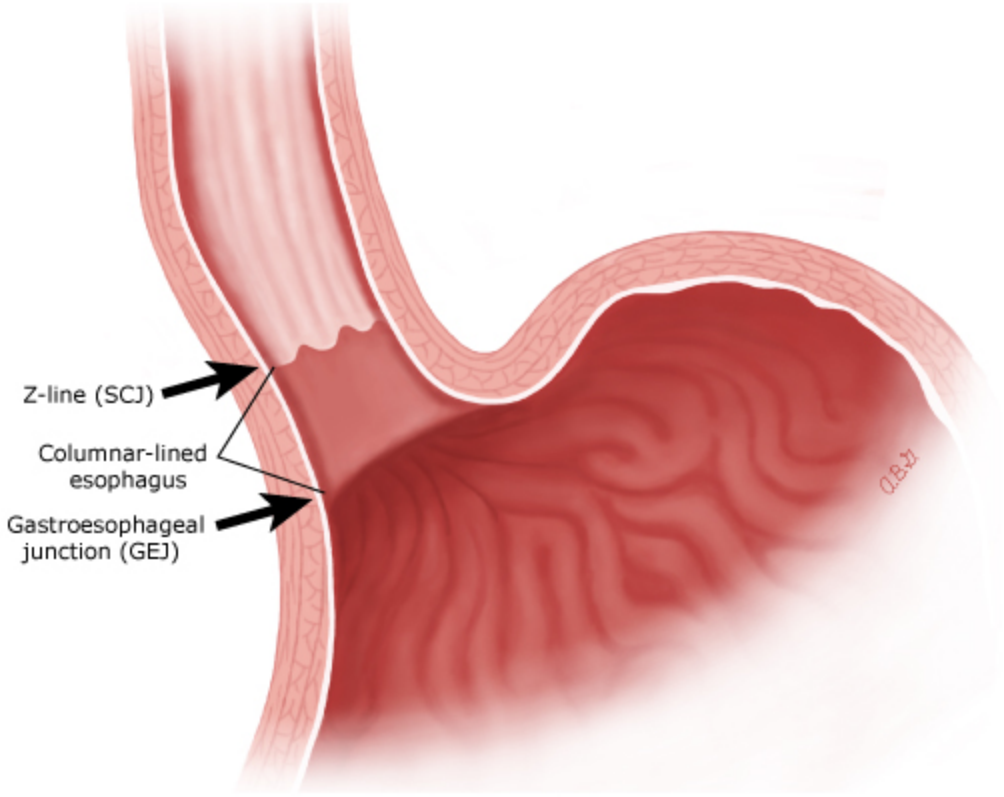


An axial CT image through the mid chest shows a large esophageal mass (arrow). Image B is a PET CT and shows a hypermetabolic mass (arrow). Image C is an axial CT image through the thoracic inlet and shows large lymph nodes alongside the brachiocephalic arteries (arrows). Image D is a PET CT showing hypermetabolic activity in the nodes indicating metastatic disease.

CT: computed tomography; PET: positron emission tomography.

Graphic 97798 Version 1.0

Anatomic landmarks for the diagnosis of Barrett's esophagus



The squamocolumnar junction (SCJ or Z-line) is the visible line formed by the juxtaposition of squamous and columnar epithelia. The gastroesophageal junction (GEJ) is the imaginary line at which the esophagus ends and the stomach begins. The GEJ corresponds to the most proximal extent of the gastric folds. When the SCJ is located proximal to the GEJ, there is a columnar-lined segment of esophagus.

Modified from: Spechler SJ. The role of gastric carditis in metaplasia and neoplasia at the gastroesophageal junction. Gastroenterology 1999; 117:218.

Graphic 76055 Version 8.0

Contributor Disclosures

John R Saltzman, MD, FACP, FACG, FASGE, AGAF No relevant financial relationship(s) with ineligible companies to disclose. **Michael K Gibson, MD, PhD, FACP** Grant/Research/Clinical Trial Support: Natera [ECOG project]; National Cancer Institute [Head and neck cancer and UGI cancer]; Papivax [IIT clinical trial]. Consultant/Advisory Boards: Amgen [Gastric cancer]; BMS [Immunotherapy]; Regeneron [Skin cancer]. Speaker's Bureau: Bristol-Myers Squibb [Immuno-oncology, not disease specific]. Other Financial Interest: AbbVie Data and Safety Monitoring Board [Phase 1 solid tumors]; Soligenix Data and Safety Monitoring Board [Head and neck cancer]. All of the relevant financial relationships listed have been mitigated. **Douglas A Howell, MD, FASGE, FACG** No relevant financial relationship(s) with ineligible companies to disclose. **Richard M Goldberg, MD** Equity Ownership/Stock Options: Advanced Chemotec Inc [Pancreatic cancer]; Compass Therapeutics [Biliary tract and colorectal cancer]. Consultant/Advisory Boards: AbbVie [GI cancers]; Advanced Chemotherapy Technologies [GI cancer]; AstraZeneca [GI cancer]; Bayer [GI cancer]; Compass Therapeutics [GI cancer]; Eisai [GI cancer]; G1 Therapeutics [GI cancer]; GSK [Colorectal cancer]; Innovative Cellular Therapeutics [Colorectal cancer]; Inspirna [Colorectal cancer]; Merck [GI cancer]; Modulation Therapeutics [Lymphoma]; Novartis [GI cancer]; Sorrento Therapeutics [GI cancer]; Taiho [GI cancer]. Other Financial Interest: Taiho [Expert testimony GI cancer]. All of the relevant financial relationships listed have been mitigated. **Sonali M Shah, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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