



# ARTICLE

# Imaging of esophageal cancer

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#### Abstract

Esophageal cancer is a relatively uncommon gastrointestinal malignancy but carries a poor prognosis unless it is of early stage and can be surgically resected for cure. Resectability is determined by the stage of disease at diagnosis and therefore accurate staging is of importance in patients diagnosed with esophageal cancer. Imaging studies that play a role in the evaluation of esophageal cancer include barium studies, computed tomography, endoscopic ultrasound and positron emission tomography. Imaging provides important information regarding the local extent and any distant spread of disease, which in turn helps in determining optimal management for these patients. This review discusses the imaging findings that may be encountered with various imaging modalities in the diagnosis, staging and follow-up of esophageal cancer.

**Keywords:** Esophageal malignancy; imaging; staging; computed tomography; endoscopic ultrasound; positron emission tomography.

## Introduction

There is significant geographic variation in the incidence of esophageal cancer, which is a relatively uncommon tumor of the gastrointestinal tract, in Western countries. However, it is a disease that accounts for significant mortality. In 2003 the estimated number of new cases in the United States was approximately 13,900 or 6% of tumors of the digestive system. The overall number of deaths from esophageal cancer in 2003 was approximately 13,000<sup>[1]</sup>.

Most esophageal cancers are epithelial in origin. The esophagus is lined by squamous epithelium and therefore the prevalent histology of esophageal tumors is squamous cell carcinoma in most parts of the world<sup>[2]</sup>. Abuse of alcohol and tobacco are the most significant risk factors for the development of squamous cell carcinoma of the esophagus in the Western hemisphere and there is a synergistic effect in those who abuse both substances<sup>[3,4]</sup>. Dietary and cultural factors such as drinking very hot beverages or eating pickled or fermented foods have also been linked to the development of squamous cell

malignancy in other parts of the world<sup>[5,6]</sup>. Other conditions that predispose to the development of squamous cell malignancy of the esophagus include achalasia, lye strictures, celiac disease, Plummer–Vinson syndrome, and tylosis<sup>[5,6]</sup>. Patients with achalasia are estimated to have a 30-fold greater likelihood of developing esophageal cancer than the normal population<sup>[7]</sup>.

Barrett's esophagus is columnar metaplasia of the squamous epithelium of the distal esophagus likely related to gastroesophageal reflux disease<sup>[8]</sup>. Barrett's esophagus is considered a pre-malignant condition, predisposing to the development of adenocarcinoma of the esophagus<sup>[2,5,6,9,10]</sup>. Barrett's esophagus increases the risk of developing adenocarcinoma and this risk has been estimated to be between 20- and 125-fold over the general population in various studies<sup>[6]</sup>. There has been a significant increase in the incidence of adenocarcinoma arising in Barrett's mucosa over the past three decades<sup>[6]</sup>. The incidence of squamous cell carcinoma has been stable or shown a decline in some populations<sup>[6,11]</sup>. Other histologic types, such as sarcomas, do occur but are extremely rare.

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This review will outline the imaging findings that may be encountered in the diagnosis, staging, and follow-up of esophageal carcinoma.



*Figure 1* Sixty-four-year-old man with a malignant stricture of the esophagus shown on esophagram.

## **Radiologic evaluation**

Most patients with esophageal cancer present with dysphagia, which is typically a symptom of advanced disease. Barium studies are often used to evaluate these patients and double contrast barium studies have been found to be a sensitive technique for the detection of carcinoma of the esophagus and esophagogastric junction with a positive predictive value of 42%<sup>[12]</sup>. When an esophageal stricture is identified by esophagography it may be classified as benign or malignant. Benign strictures typically have symmetric areas of narrowing with smooth contour and tapered proximal and distal margins. Malignant strictures typically cause asymmetric narrowing with abrupt, shelf-like margins and irregular contours with a nodular or ulcerated mucosal surface (Fig. 1)<sup>[13]</sup>. Esophageal tumors can be polypoid, infiltrative, varicoid or ulcerative when seen by esophagography (Fig. 2)<sup>[14]</sup>. Superficial spreading lesions tend to show a nodular mucosal pattern without a well-defined mass. Early esophageal cancers may have very subtle findings on barium studies and therefore endoscopic followup of any suspected abnormality should be performed (Fig. 3(a), (b))<sup>[13,14]</sup>. Esophagography has also been used to estimate invasion of the muscularis mucosae in early esophageal cancers to determine which patients may be suitable for endoscopic treatment of mucosal cancers,

which have a good prognosis. In depressed lesions, the presence and size of mucosal surface granules were found to correlate with the depth of invasion, as did thickened folds and esophageal wall rigidity<sup>[15,16]</sup>. It is not possible to determine the histology of esophageal tumors by their radiographic appearance, however some findings may improve specificity. The vast majority of adenocarcinomas arise from Barrett's esophagus and typically occur in the distal esophagus (Fig. 4). These tumors have a propensity to invade the gastric cardia and fundus (Fig. 5). Gastric invasion is a most unusual finding with squamous cell cancers, which largely occur in the middle third of the esophagus (Fig. 6)<sup>[17]</sup>. Complications such as tracheoesophageal fistula formation from locally advanced disease can be seen on barium studies (Fig. 7). Once a diagnosis of esophageal malignancy has been established, barium studies may be used to evaluate the morphology and size of tumors before and after treatment.





Esophageal cancers typically spread by direct extension and by means of lymphatics. Hematogenous spread is also common in those with advanced disease, and the lungs and liver are favored sites of hematogenous metastases<sup>[5]</sup>. The two most important prognostic indicators for esophageal cancer are depth of tumor penetration and nodal involvement. T1 tumors invade the lamina propria or submucosa. T2 tumors invade the muscularis propria. T3 tumors involve the adventitia and T4 tumors directly invade adjacent structures. The TNM staging of esophageal cancer is summarized in Table 1<sup>[2,5]</sup>. The 5-year survival for patients with tumors remaining within the esophageal wall is about 40%<sup>[2]</sup>. Those with tumors involving the adventitia of the esophagus have only a 4%



*Figure 3* Sixty-one-year-old man with 1 year history of dysphagia. (a) The baseline esophagram shows a subtle line (arrow) indicating a plaque-like lesion which was also seen on endoscopy. (b) The patient was lost to follow-up until 1 year later when the esophagram shows circumferential tumor (arrow) proven to be squamous cell carcinoma at the same site. The likelihood of nodal spread increases with increasing tumor (T) stage and nodal involvement also portends a very poor prognosis. When tumors are limited to the mucosa, the likelihood of nodal disease is less than 1%, increasing to 50% when there is submucosal involvement by the primary tumor. The 5-year survival for patients without nodal involvement is about 40%, diminishing to approximately 3% 5-year survival for those with nodal metastases<sup>[2]</sup>. Lymphatic drainage of the esophagus generally follows arterial pathways and so craniocaudal pathways of spread are usually seen. Generally, carcinomas arising in the upper esophagus drain to cervical or upper mediastinal nodes while those arising from the mid or lower esophagus spread to lower mediastinal or perigastric nodes. However, skip metastases are not infrequent<sup>[17]</sup>. Metastatic nodes can occur in the internal jugular, supraclavicular, paratracheal, hilar, subcarinal, paraesophageal, paraaortic, pericardial, left gastric and celiac lymph node chains<sup>[18]</sup>. Regional nodal metastases (N1) for squamous carcinoma of the esophagus includes metastasis to cervical, mediastinal, and perigastric nodes. If celiac lymph nodes are involved by squamous cell carcinoma, the disease is considered distant metastases or M1 disease. For esophageal adenocarcinoma, on the other hand, celiac adenopathy is considered N1 disease<sup>[19]</sup>.



*Figure 4* A double contrast esophagram shows adenocarcinoma (curved arrow) arising from Barrett's mucosa in the distal esophagus, proximal to a hiatal hernia in a 66-year-old male.

5-year survival. The higher mortality could relate to the fact that the esophagus lacks a serosal surface and therefore lateral spread or mediastinal invasion can occur more readily in tumors with adventitial involvement<sup>[2]</sup>.



Figure 5	An esopha	gram sho	ws aden	ocarci	noma	of
the distal	esophagus	invading	the gas	tric ca	ardia	as
evidenced	by a mass	s causing	distorti	on of	norn	ıal
gastric fol	ds (curved a	arrow).				

The main purpose of cross-sectional imaging studies in patients with known esophageal carcinoma is to stage the disease as accurately as possible in order to determine which patients may be suitable for surgical resection. Computed tomography (CT) is considered complimentary to endoscopy and barium studies and is used to stage and follow esophageal tumors. CT can be used to define the local extent of tumor by showing the extent of involvement of the esophageal wall by tumor and tumor invasion of the peri-esophageal fat. CT cannot reliably delineate the individual layers of the esophageal wall and therefore cannot distinguish between T1 and T2 lesions. Infiltration of the tumor into the peri-esophageal fat as seen on CT denotes a T3 tumor and does adversely affect prognosis, although en-bloc resection for cure may still be attempted<sup>[19]</sup>. The reported accuracy of CT in diagnosing mediastinal invasion ranges between 59 and 82% <sup>[2,19]</sup>. Tumor infiltration to involve adjacent mediastinal structures such as the aorta or tracheobronchial tree denotes a T4 lesion that is considered inoperable. Contiguous invasion of adjacent structures may be difficult to predict when tumor abuts other structures in the mediastinum. Specific findings of tracheobronchial invasion include demonstration of a tracheobronchial fistula or tumor extension within the airway lumen. If the esophageal tumor indents or displaces the adjacent airway, invasion is likely. Thickening of the wall of the tracheobronchial tree also suggests invasion. Loss of fat planes between the tumor and the adjacent airway is not always a specific finding for tumor invasion and may be seen in normal individuals; however, if the loss of fat planes occurs only at the level of the esophageal mass with preservation of fat planes cranially and caudally, invasion is likely<sup>[19]</sup>. Virtual endoscopy has been attempted to determine its value in patients with esophageal cancer infiltrating the tracheobronchial tree and found to be accurate in identifying endoluminal tumors in those patients who were not amenable to endoscopy although it could not be used to replace endoscopy in all patients with tracheobronchial invasion<sup>[20]</sup>. Prediction of aortic invasion has also been evaluated with CT. The overall circumference of contact between tumor and the aortic wall was shown to be a useful predictor with an interface arc greater than 90 degrees suggesting invasion<sup>[21]</sup>. The loss of the triangular area of fat between the esophagus, aorta and spine has also been used to predict aortic invasion<sup>[22]</sup>. Magnetic resonance imaging (MRI) provides little advantage over CT in staging esophageal tumors<sup>[2]</sup>. MRI also cannot reliably distinguish the different layers of the esophageal wall, which is crucial for accurate local staging. Nodal disease and distant metastases can be shown by CT or MRI. Nodes that are larger than 1 cm in short axis dimension are considered suspect for metastatic disease although size is known to be an insensitive parameter for determining nodal spread. The overall accuracy of CT for predicting regional lymphadenopathy ranges between 50 and 70%. The accuracy in predicting lymph node metastases in the abdomen is of the order of 85%<sup>[19]</sup>. Dynamic CT may improve the overall accuracy of N staging slightly<sup>[23]</sup>. CT is useful for determining distant metastatic disease, which typically is seen in the lungs and liver. Peritoneal deposits do occur with adenocarcinoma and can be difficult to detect. Findings of distant metastatic disease would preclude surgical resection for cure. The role of helical CT in the staging of esophageal cancer remains to be better defined but a study by Romagnuolo *et al.* showed that helical CT appeared unreliable mainly because of insensitivity for identification of inoperable T4 or metastatic involvement of celiac lymph nodes in esophageal cancer<sup>[24]</sup>. In summary, CT can show advanced mediastinal invasion and can detect distant metastases primarily to the lung and liver, although it is less accurate for determining local T and N stage (Fig. 8(a)–(c)).



*Figure 6* Sixty-six-year-old man with nodular mucosal changes (arrow) of the mid esophagus shown by double contrast esophagography that proved to be squamous cell carcinoma.

Table 1 TNM staging system for esophageal cancer

Stage	Definition	
Primary tumor (T)		
TO	No evidence of primary tumor	
Tis	Carcinoma in situ	
T1	Tumor invades mucosa or submucosa	
T2	Tumor invades muscularis propria	
Т3	Tumor invades adventitia	
T4	Tumor invades adjacent structures	
Lymph nodes (N)		
N0	No regional nodes	
N1	Regional nodal metastases	
Distant metastases (M)		
M0	No distant metastases	
M1	Distant metastases	
Note: modified from [5]		

Note: modified from [5].

Lymphoscintigraphy has been attempted to try to identify sentinal lymph nodes in patients with esophageal carcinoma using technetium-99m colloidal rhenium sulfide and found to be feasible. The overall accuracy of sentinel lymph node detection in this study was approximately 91% with sensitivity of approximately 87% and a false negative rate of approximately 9% <sup>[25]</sup>.



*Figure 7* Fifty-year-old man with squamous cell carcinoma of the esophagus (arrow) complicated by tracheoesophageal fistula (arrowhead) shown on esophagram.

Endoscopic sonography provides detailed images of the esophagus and immediately surrounding structures and has been used to define the layers of the esophageal wall and thereby distinguish the depth of tumor penetration. The frequency of most endoscopic ultrasound transducers is 7.5 or 12 MHz. Endoscopic sonography is considered the most accurate estimate of locoregional disease in patients with esophageal cancer. The overall accuracy of endoscopic sonography is greater than CT and is reported to be between 85 and 90%<sup>[19,26]</sup>. Over-staging may occur because peritumoral edematous changes may be mistaken for tumor and under-staging may occur when tumor penetration is below the resolution of sonography<sup>[19]</sup>. The normal esophagus has five layers as depicted by endoscopic sonography. The innermost layer is hyperechoic and corresponds to the superficial mucosa. The next layer is hypoechoic and corresponds to the deep mucosa and muscularis mucosae. The third layer is again hyperechoic and corresponds to the submucosa and its interphase with the muscularis propria. The next layer is hypoechoic and corresponds to the muscularis propria and the final fifth layer is hyperechoic and corresponds to the adventitia<sup>[27]</sup>. Esophageal cancers appear as hypoechoic masses that can disrupt this layered pattern. Endoscopic sonography may be difficult in patients with stenotic tumors where the endoscope cannot be passed through the tumor obstructing the esophageal lumen. Endoscopic ultrasound and ultrasound guided biopsy are useful for detecting and confirming lymph node metastases in studies that have evaluated celiac lymph node metastases in patients with esophageal cancer<sup>[24,28]</sup>. Most agree that endoscopic ultrasound is the best method for locoregional staging and



*Figure 8* Sixty-eight-year-old man with esophageal adenocarcinoma. (a) CT scan of the lower chest shows thickening of the esophageal wall (arrow) with loss of surrounding fat planes along the right side compatible with invasive esophageal carcinoma. (b) Liver metastasis (arrow) and metastatic gastrohepatic ligament adenopathy (arrowhead) are seen in the abdomen. (c) Metastatic retroperitoneal adenopathy (arrowhead) is also evident.

it has also been used to determine prognosis<sup>[29]</sup>. Combining endoscopic ultrasound and CT findings

further improves accuracy for TNM staging up to 86% and therefore most recommend CT as the initial imaging study to exclude distant metastases followed by endoscopic sonography for local staging <sup>[19,23]</sup>.

Positron emission tomography (PET) using 2-F-18 fluoro-2-deoxy-D-glucose (18F-FDG) is also being used to stage patients with esophageal cancer. The primary tumor can be identified by PET scan, although the overall spatial resolution is limited and therefore the sensitivity for identifying locoregional disease is limited<sup>[2,30]</sup>. The overall accuracy for nodal staging has been reported to be between 48 and 90% <sup>[31–34]</sup>. However, PET has the advantage of total body coverage and compared with conventional imaging, PET has been shown to detect distant sites of metastatic disease at initial evaluation. Metastatic disease in distant nodes, liver, lung, bone, adrenal and others detected at initial staging can obviate surgery and affect treatment decisions. Therefore, PET can provide additional and complementary information to that obtained by CT (Fig. 9(a)–(c))<sup>[30]</sup>. <sup>18</sup>F-FDG-PET has also been used a non-invasive diagnostic technique in assessing the aggressiveness of the tumor in patients with esophageal squamous cell carcinoma. A study by Kato et al. showed that the survival rate in cases with high <sup>18</sup>F-FDG uptake was significantly lower than in cases with low <sup>18</sup>F-FDG uptake <sup>[35]</sup>.

### Treatment and follow-up

Several treatment options, including surgery, radiation, and chemotherapy, are available to patients with esophageal cancer although none has proven ideal at this time. Treatment may be aimed at palliation in those patients with advanced disease versus resection for cure in those with limited disease. Surgical resection with curative intent may include en-bloc resection of tumor and all associated nodes. This en-bloc resection may be performed through a right thoracotomy with laparotomy, such as the Ivor-Lewis esophagogastrectomy, or a left thoracotomy with a thoracoabdominal incision, or two separate abdominal and cervical incisions without a thoracotomy [5,36]. After resection of the esophageal tumor, the continuity of the upper digestive tract may be re-established by pulling the stomach into the chest and performing an anastomosis with the residual proximal esophagus. Colonic and small intestinal interpositions may also be performed although they are less common<sup>[5,36]</sup>.

Complications after esophageal resection are not uncommon. Some acute complications that may be seen with imaging include anastomotic leaks, torsion of the pulled up segment, hemorrhage, wound infections, and subphrenic abscesses. More delayed complications include anastomotic strictures, dumping syndrome, and reflux esophagitis<sup>[5]</sup>.



*Figure 9* Sixty-four-year-old man with adenocarcinoma of the esophagus. (a) An <sup>18</sup>F-FDG-PET scan shows uptake in the distal esophagus (arrow) at a site of known tumor. (b) PET scan also shows uptake in the right supraclavicular fossa (arrowhead). (c) Corresponding CT of the chest shows metastatic adenopathy (arrowhead) in the right supraclavicular fossa corresponding to the area of uptake on PET.

Neoadjuvant protocols using pre-operative chemotherapy and radiotherapy have been tried on potentially resectable candidates with more advanced disease to downstage tumors before surgery<sup>[37,38]</sup>. However, many patients are not considered candidates for resection because of tumor stage or co-morbid conditions that would preclude surgery. Palliation is therefore attempted in these patients to relieve dysphagia. Dilatation and stent placement may provide some relief to patients with severe dysphagia. Endoscopic laser ablation of obstructing intraluminal masses has also been attempted with some success<sup>[39]</sup>. Radiation therapy may also be used to palliate or definitively treat esophageal cancer in those patients who may not be surgical candidates. External-beam radiation doses of the order of 45-60 Gy are typically used<sup>[40]</sup>. Esophageal cancers that respond to radiotherapy frequently result in stricture formation that may require peroral dilation.

Imaging is often requested to follow tumors on therapy and to document response. Endoscopy is limited for identifying tumor response and in one study 41% of patients thought to have a complete pathologic response had residual tumor identified at surgery<sup>[41]</sup>. Barium studies may show the response of intraluminal tumor but are limited because they cannot show mural disease and surrounding adenopathy. CT and endoscopic sonography have also been used to document response. A decrease in wall thickness and lymph node size may be shown by endoscopic sonography, however, fibrosis may be indistinguishable from residual tumor. The role of PET scanning to document the response is not entirely clear. In a study by Downey et al., PET did not add to the estimation of locoregional resectability after induction therapy and did not detect any new distant metastases. Changes in <sup>18</sup>F-FDG-PET, however, may predict diseasefree and overall survival after induction therapy and resection in patients with esophageal cancer<sup>[42]</sup>.

The ability to detect local recurrence is variable because inflammation or fibrosis may cause esophageal wall thickening, mimicking tumor recurrence on imaging studies. Mucosal changes at the anastomosis that represent recurrence may be seen on barium studies. The overall accuracy of CT in detecting recurrence is reported to be 87% <sup>[43]</sup>. Care should be taken not to over-diagnose recurrent tumor in an under-distended intra-thoracic stomach by imaging. Endoscopic sonography is reported to have a 20% false positive rate in detection of recurrence<sup>[2]</sup>. PET may be used to image recurrent tumor as it has the advantage of not only detecting locally recurrent disease but also visualizing any distant sites of metastasis.

In summary, esophageal carcinoma, although less common than other tumors of the hollow viscera, has a high rate of mortality. Curative resection is possible in a small percentage of patients with localized disease and treatment decisions hinge upon the stage of disease at diagnosis. Imaging studies, such as endoscopic ultrasound, CT and PET are used to help stage disease and determine which patients may be suitable for surgical resection. Imaging is also used to determine treatment effectiveness after neoadjuvant therapy and for surveillance of recurrent disease.

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