Diagnostic Endoscopic Ultrasound

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KEYWORDS

• Endoscopic ultrasound • Subepithelial lesions • Mediastinal lesions
• Pancreatic lesions • Cytology • Fine needle aspiration • Fine needle biopsy
• Staging

KEY POINTS

- Endoscopic ultrasound (EUS) is instrumental in the staging of mucosal cancers of the gastrointestinal tract (esophageal, gastric, duodenal and rectal). EUS can identify and characterize intramural lesions of the GI tract.
- EUS can identify, sample, and stage posterior mediastinal lesions and lung cancers adjacent to the esophagus.
- EUS is crucial in identifying, staging, and sampling pancreaticobiliary lesions and pathology.
- EUS facilitates the sampling of masses in the peritoneum, which would otherwise necessitate laparoscopy.
- Most recently, there has been a growth in the field of endohepatology, and EUS can now be utilized in performing EUS-guided portal pressure gradient and liver biopsies.

INTRODUCTION

Over the past 2 decades, advancements in endoscopic technologies and techniques have enabled minimally invasive assessment and sampling of lesions both inside the gastrointestinal (GI) lumen, including esophageal , gastric, and rectal masses, as well as outside the GI lumen, including the chest, abdomen, and pelvis. Integrating these endoscopic approaches has transformed the diagnosis and staging of both luminal and extraluminal malignancies, offering more accessible and safer tissue-acquisition methods. EUS also plays an important role in characterizing benign diseases of the GI tract. Recent innovations in endohepatology have allowed endoscopists to assess

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the severity of liver disease by incorporating endoscopic ultrasound-guided portal pressure gradient (EUS-PPG) and liver biopsy. These innovations continue to expand the diagnostic capabilities of EUS. This comprehensive review discusses the role of EUS in diagnosing luminal and extraluminal malignancies, its evaluation of benign diseases, and its evolving role in endohepatology.

Esophageal

In 2024, esophageal cancer (adenocarcinoma and squamous cell cancer) will account for 1.0% of all new cancer diagnoses in the United States, with an estimated 22,370 (17,690 men, 4680 women) new cases. Moreover, there is significant mortality with esophageal cancer, with a predicted 16,130 (12,880 men, 3250) associated deaths.

Diagnostic evaluation of esophageal and esophagogastric junctional cancers requires accurate staging, given treatment protocols are largely stage-dependent. Initial workup for esophageal cancer includes a detailed history and physical, upper GI endoscopy with biopsy, and fluorodeoxyglucose-positron emission tomography (FDG-PET)/computed tomographic (CT) evaluation to evaluate for M1 disease. If FDG-PET notes no M1 disease, EUS is typically obtained for locoregional staging (**Fig. 1**).[1]

Endoscopic resection, whether by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), can be considered in T1a and T1b esophageal cancer. Per the National Comprehensive Cancer Network (NCCN) guidelines, T1a esophageal adenocarcinoma can be treated with endoscopic resection (EMR vs ESD) when there is no evidence of lymph node metastases, lymphovascular invasion, or poor differentiation grade.[1] While en bloc resection rate by ESD is high in patients with T1b esophageal cancer, R0 (curative) resection rates are low. R1 (noncurative) resection is associated with disease progression.[2] Treatment of locally advanced disease, defined as IIB through IIIC, involves neoadjuvant chemotherapy with an eventual goal of curative surgical resection following restaging. Patients with metastatic disease and who are poor surgical candidates can be offered palliative chemotherapy.

EUS for esophageal cancer staging relies on radial and linear echoendoscope platforms (typically operating at a frequency of 7.5–12 MHz).[3] The radial echoendoscope

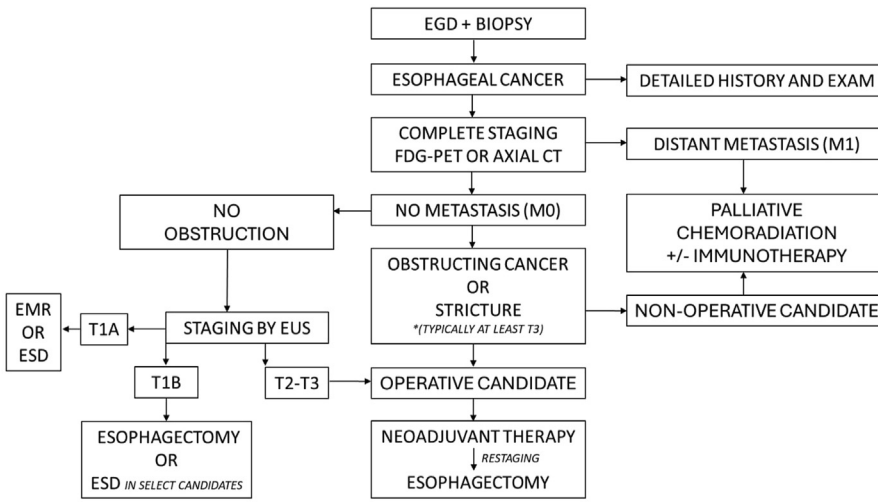

Fig. 1. Esophageal cancer evaluation.

allows for a fully circumferential, perpendicular view along the long access of the echoendoscope. This appearance is similar and complements pre-EUS staging of an axial chest CT. Often, staging starts with a radial echoendoscope, as the T-stage and N-stage are usually easier to interpret utilizing this circumferential, perpendicular view. There are 5 discrete wall layers within the esophagus, starting superficially and progressively deeper with the superficial mucosa (first layer, hyperechoic), muscularis mucosa (second layer, hypoechoic), submucosa (third layer, hyperechoic), muscularis propria (fourth layer, hypoechoic), and adventitia (fifth layer, hyperechoic).

T(is) is high-grade dysplasia limited to the superficial mucosa and not penetrating the lamina propria. T1a lesions invade the lamina propria or muscularis mucosa. This can be further subdivided into T1a-EP (M1—involving the epithelium), T1a-LPM (M2—involving lamina propria mucosa), and T1a-muscularis mucosa (MM) (M3—involving muscular mucosa). T1b lesions involve the submucosa and can also be further subdivided: SM1 (upper third of submucosa), SM2 (middle third of submucosa), and SM3 (lower third of submucosa).[4] T2 lesions invade into the muscularis propria (**Fig. 2**). T3 lesions invade the adventitia. T4a lesions (considered resectable) invade adjacent structures such as the pleura, pericardium, and diaphragm. T4b (considered unresectable) lesions invade adjacent structures, including the aorta, vertebral body, and trachea.

T-stage by EUS has been shown to have high sensitivity and specificity at the ends of the spectrum. Its sensitivity and specificity to diagnose T1 lesions by EUS are 81.6% and 99.4%, respectively. The sensitivity and specificity of EUS diagnosis of T4 lesions are 92.4% and 97.4%, respectively.[5] T-stage by EUS is less accurate for T2 and T3 lesions, with some studies suggesting that 32% of esophageal cancers are understaged and 47% overstaged by EUS compared to the histopathology from subsequent surgical resection.[6]

N-stage is determined by the presence or absence of regional lymph nodes, as seen by EUS. The absence of lymph nodes is N0, 1 to 2 lymph nodes is N1, 3 to 6 lymph nodes is N2, and 7 or more lymph nodes is N3. Aside from the number of lymph nodes, EUS can help identify malignant features of regional lymph nodes, including size greater than 1 cm, shape (round), sharp/demarcated borders, and hypoechoic

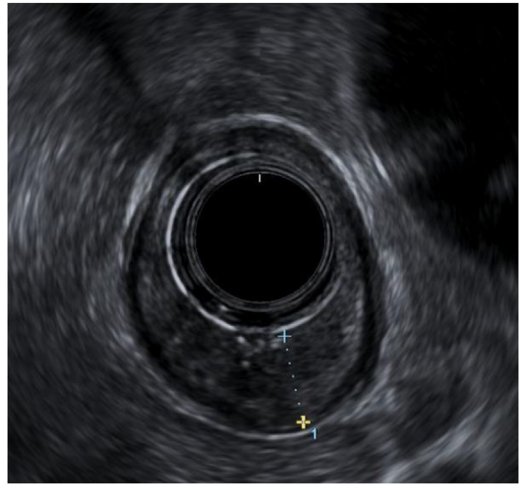

Fig. 2. Radial EUS view of a T2 esophageal adenocarcinoma involving the MP.

echogenicity. The linear echoendoscope allows for fine needle aspiration (FNA) or fine needle biopsy (FNB). This is particularly important for nodal staging or if the primary diagnosis was not obtained on upper endoscopy with standard biopsies. The sensitivity and specificity of N-staging, with FNA, are 84.7% and 96.7%, respectively.[5] An important consideration when performing FNA or FNB of a lymph node is to avoid passing through the primary tumor to avoid false-positive results. Additionally, needle passage through major blood vessels can theoretically predispose to tumor seeding.

N-stage is particularly important in patients with either T1 or T2 disease, as this can determine whether they are up-front surgical resection candidates or will benefit from neoadjuvant chemotherapy prior to surgical resection.[7] In a retrospective study of patients who received EUS and PET/CT as preoperative staging of esophageal cancer, the EUS changed the management of the patient by invoking the need for neoadjuvant chemotherapy in 34.8% of the patients. Specifically, EUS identified locoregional lymph nodes in 58.9% of cases as opposed to CT in 26.8% or PET in 37.5%.[8]

M-stage, or evaluation for metastatic disease, is usually accomplished with FDG-PET/CT, but EUS can be a complementary modality. EUS allows for a detailed evaluation and sampling of suspicious lesions in the liver, peritoneum, left adrenal gland, and distant lymph nodes.

There are several limitations of EUS when it comes to the esophagus. EUS performs relatively poorly when evaluating early and intermediate gastroesophageal junction cancers. A retrospective study of 181 patients with esophageal cancer at the gastroesophageal (GE) junction (prior to treatment) demonstrated that EUS T-staging was accurate in 48% of cases, with 23% of cases understaged and 29% of cases overstaged when compared to surgical histopathology.[9]

The T-stage of early stage esophageal cancer is limited in superficial cases (T1a vs T1b). Higher frequency EUS probes (12–30 MHz) or mini probes (through the scope) can help differentiate mucosal versus submucosal lesions, with a sensitivity of 88% and specificity of 63% (diagnostic accuracy 75%).[10]

In patients with obstructing cancers, EUS might not be feasible given the diameter of the radial and/or linear echoendoscope and the risk for perforation in the setting of a malignant esophageal stricture.[11] However, dysphagia or a malignant stricture is usually associated with at least T3 disease, limiting the overall utility of EUS in that situation (FDG-PET/CT can still be used to evaluate for metastatic involvement).[12]

Aside from diagnosing and staging esophageal cancers, EUS is also necessary for evaluating subepithelial lesions (SELs). Diagnosis is achieved by identifying the lesion's layers of origin and echogenicity and obtaining aspirate or biopsy for histopathology if necessary. SELs originating from the second layer in the muscularis mucosa (hypoechoic lesions) include leiomyomas and granular cell tumors. The fourth endosonographic layer is the hypoechoic muscular propria, which can contain leiomyomas, gastrointestinal stromal tumors (GISTs), and schwannomas (**Fig. 3**). Most (60%–80%) SELs arising from the muscularis propria (MP) in the esophagus are leiomyomas. The third endosonographic layer, or submucosa, has the largest differential of lesions. Hypoechoic lesions include carcinoid tumors, glomus tumors, fibromas, and ectopic pancreas. Anechoic lesions include cysts or lymphangiomas (**Fig. 4**). Hyperechoic lesions in the third endosonographic layer are typically lipomas.[13]

Mediastinal

EUS significantly evaluates posterior and inferior mediastinal disease, including the subcarinal, periesophageal, and paratracheal regions. The anterior and upper mediastinum is usually obscured from view given air from the overlapping trachea and, thus, a more difficult area for evaluation by endosonography. The anterior and upper

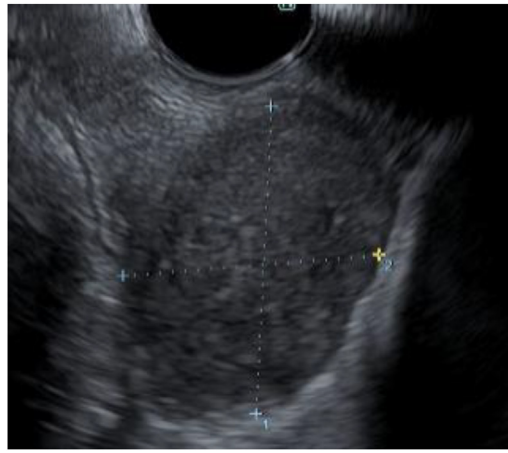

Fig. 3. Linear EUS view of a biopsy-proven leiomyoma arising from the fourth endosonographic layer/MP.

mediastinum are considered the peritracheal space and intrapulmonary regions, respectively. Positioning the echoendoscope in the esophagus to evaluate the mediastinum is typically easier than positioning it in the stomach or small bowel, given the fixed nature of the esophagus. A detailed mediastinal examination starts by placing the echoendoscope beyond the esophagogastric junction into the stomach, returning to the GE junction, and evaluating for periesophageal lymph nodes while pulling back to the upper esophageal sphincter. The subcarinal space and posterior aortopulmonary (AP) window are identified 25 to 30 cm from the incisors.[14] Lymph node stations 8 and 9 are located in the inferior mediastinum, and lymph node station 7 is located in the posterior subcarina. Station 5 and 4R nodes are only accessible depending on the lymph node size. Station 4 L is usually in view in the AP window.[15] For lymphadenopathy that is not amenable to EUS evaluation or sampling, endobronchial ultrasound can sometimes provide an alternative route for tissue diagnosis.

Benign lymph nodes are expected in the posterior mediastinum. They are typically triangular or oval, with hyperechoic centers and prominent, centrally located blood vessels (**Fig. 5**A).[14,16] Malignant lymph nodes are usually round, hypoechoic, and

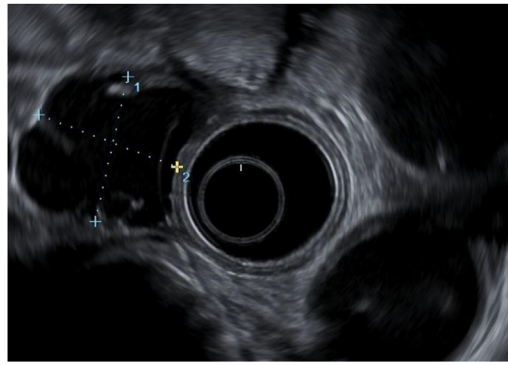

Fig. 4. Radial EUS view of a duplication cyst.

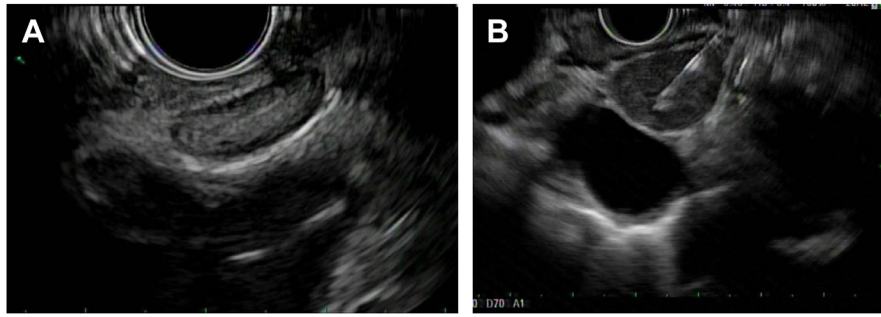

Fig. 5. Linear EUS view of (*A*) Benign lymph node. (*B*) Malignant lymph node.

do not have centrally located blood vessels interposed within the lymph nodes, as these are thought to be obscured by tumor infiltration. When differentiating malignant versus benign lymph nodes, concerning characteristics by endosonography include lymph nodes that are round, hypoechoic, well-demarcated, and large with a diameter greater than 5 mm (typically, lymph nodes >1 cm are considered suspicious for malignancy; **Fig. 5**B). The presence of all 4 of these features has a positive predictive value of 80% to 100% for the diagnosis of malignant lymph nodes.[17,18] EUS-FNA has a greater than 90% sensitivity and specificity for diagnosing malignant lymph nodes with a less than 1% complication rate.[19]

EUS-FNA/FNB is also an important adjunct for lung cancer staging. Tumor infiltration to peribronchial, hilar, or intrapulmonary lymph nodes on the same side as the primary lesion is considered N1 disease. Lymph node involvement on the ipsilateral mediastinum and/or subcarinal lymph nodes denotes N2 disease. Malignant lymph nodes on the contralateral side denote N3 disease. EUS-FNA or FNB can be used to prove definitive lymph node involvement.

EUS-FNA/FNB can also be helpful for other diseases that affect the mediastinum, including lymphoma (immunophenotyping with flow cytometry), sarcoidosis (evaluation for noncaseating granuloma), and tuberculosis (acid-fast staining and fungal culture).

Gastric

EUS is essential for diagnosing and staging a variety of gastric lesions. From superficial to deep, the gastric wall is composed of the superficial mucosa (first layer, hyperechoic), deep mucosa (second layer, hypoechoic), submucosa (third layer, hyperechoic), muscularis propria (fourth layer, hypoechoic), and serosa (as opposed to adventitia in the esophagus, fifth layer, hyperechoic; **Fig. 6**).

Initial evaluation with a radial echoendoscope can provide a comprehensive evaluation by displaying a 360° axial view. Suspicious lesions can then be sampled with a linear EUS. Alternatively, an endosonographer could begin the evaluation with the linear EUS, which typically requires continual torquing to provide a composite 360° view. In contrast to the esophagus, the stomach is capacious and requires decompression, inflation of the distal EUS balloon, and use of water to improve acoustic coupling.[20]

In 2024, gastric adenocarcinoma accounts for 1.5% of all new cancer diagnoses in the United States, with an estimated 26,890 (16,160 men, 10,730 women) new cases. There is significant associated mortality with gastric adenocarcinoma, with a predicted 10,880 (6490 men, 4390 women) associated deaths.[21]

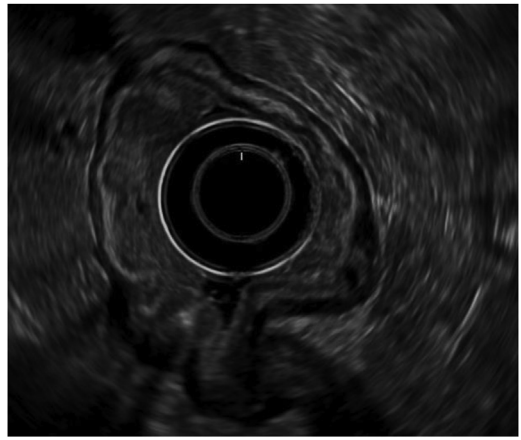

Fig. 6. Radial EUS view of the normal gastric wall layers.

EUS is helpful for locoregional staging of gastric cancer but is variable in performance. This is partially because EUS is an operator-dependent modality that requires significant training and skill to master. Other limitations to accurate staging include inflammation, fibrosis, or ulceration associated with gastric tumors, all of which may obscure wall layers, resulting in over/undercalling gastric tumors.

The depth of tumor invasion determines the T-stage into the gastric wall. T(a) denotes superficial invasion limited to the lamina propria or muscularis mucosa. T1b lesions invade the submucosa and into the muscularis propria. Again, higher frequency probes (12–30 MHz miniature probes, often through the scope) can be particularly helpful for superficial lesions. T3 lesions invade beyond the muscularis propria into the subserosa (**Fig. 7**). T4 lesions invade the serosa and/or adjacent organs or structures. T-stage, as determined by EUS, is both sensitive and specific. Differentiating T1/T2 disease (superficial) from T3/T4 (advanced) is critical for selecting definitive surgical candidates from those requiring palliative or neoadjuvant chemotherapy. EUS has a sensitivity of 86% and specificity of 91% (91% positive likelihood ratio) in differentiating T1/T2 from T3/T4 cancers.[22]

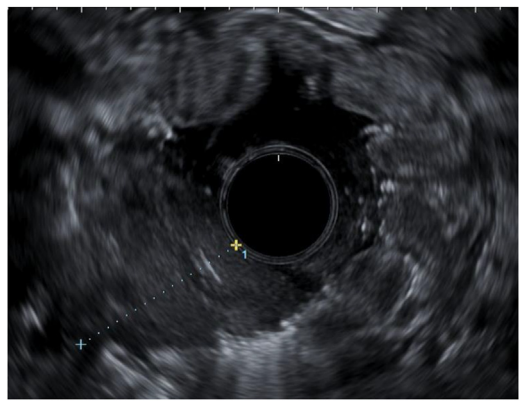

Fig. 7. Radial EUS view of a T3 gastric adenocarcinoma.

Gastric cancer's N (nodal) stage is determined by the number of positive regional lymph nodes: N1: 1 to 2, N2: 3 to 6, and N3: 7+. Overall, the pooled accuracy of EUS N-stage is 64%, with sensitivity and specificity of 74% and 80%, respectively.[23] EUS-FNA/FNB can be useful in identifying the involvement of nonregional lymph nodes and establishing a diagnosis of M1 disease requiring palliative treatment. There is one prospective study whose findings support that in patients without obvious metastatic disease prior to EUS, EUS-FNA identified lesions in 42% of patients and changed surgical management in 15% of patients.[24]

Linitis plastica, a variant of gastric adenocarcinoma, can be identified using EUS with FNA. Mucosal biopsies are often nondiagnostic (33% of cases). EUS characteristics of linitis plastica include gastric wall thickness greater than 6 mm (normal gastric wall thickness is <3 mm). Additionally, loss of defined wall layers, prominent second wall layer (MM, hypoechoic), third wall layer (submucosa, hyperechoic), or fourth wall later (MP, hypoechoic) can be seen. FNA of the gastric wall in linitis plastica can also be diagnostic.[25,26] Aside from gastric adenocarcinoma, EUS also can stage gastric lymphoma with T-stage sensitivity of 89% and 97% specificity (95% overall accuracy when assessing depth of lesion).

Gastric subepithelial tumors can be identified and diagnosed based on endosonographic characteristics and histopathologic diagnosis obtained during the EUS examination.

Lipomas (5% of gastric SELs) are benign, hyperechoic lesions found in the submucosa (third endosonographic layer; **Fig. 8**). Furthermore, on endoscopy, they usually have a yellowish appearance, and fat can be seen when performing a "bite on bite" biopsy. Pancreatic rests, another benign SEL, can often be identified endoscopically, given the location in the gastric antrum and the presence of central umbilication (**Fig. 9**A, B). By EUS, these often involve the submucosa (less often deep mucosa or muscularis propria) and will have echotexture similar to the pancreatic parenchyma (heterogeneous, hypoechoic).

Carcinoid tumors are found primarily in the submucosa (sometimes superficially) and are hypoechoic and rounded, with well-defined borders on EUS. Depending on the subtype, lesion size, presence of adenopathy, and wall layer involved, these

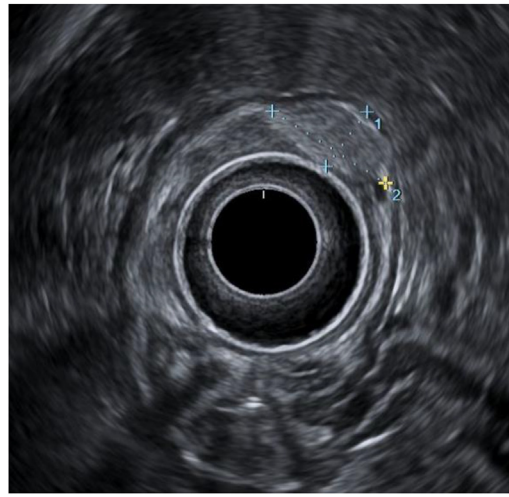

Fig. 8. Radial EUS view of a gastric lipoma.

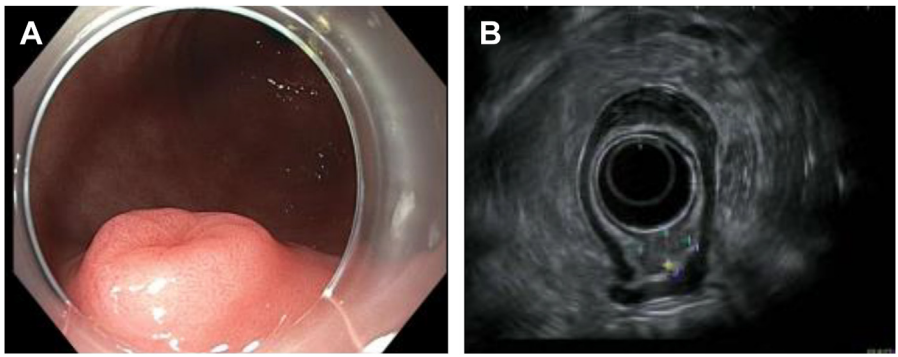

Fig. 9. Endoscopic (*A*) and radial EUS (*B*) views of a pancreatic rest.

lesions may be amenable to endoscopic resection. Granular cell tumors can also be found in the gastric submucosa (more often esophageal) and are hypoechoic by EUS (endoscopic appearance of white nodules).

Two types of cysts found in the gastric submucosa include bronchogenic and duplication cysts. Bronchogenic and duplication cysts are found more frequently in the mediastinum and esophagus but can also be found in the stomach. Bronchogenic cysts are located in the submucosa (third endosonographic layer) and have an anechoic appearance by EUS (Fig. 10). Aspiration of the cyst will often result in a yellow-mucinous appearance. Duplication cysts are also typically found in the submucosa and are hypoechoic by EUS. The wall layer of duplication cysts may include epithelium, lamina propria, submucosa, and a muscularis layer.

It is challenging to differentiate muscularis propria (stromal tumors, fourth endosonographic layer) tumors by endosonographic features alone. The differential diagnosis for stromal tumors in the stomach includes GIST, leiomyoma, leiomyosarcoma, schwannomas (and other mesenchymal tumors). By EUS, these stromal tumors are hypoechoic and typically arise from the muscularis propria but less frequently arise from the muscularis mucosa Fig. 11A, B). Only 20% to 25% of GISTs are overtly malignant on diagnosis, and certain features, including size greater than 30 mm, cystic/

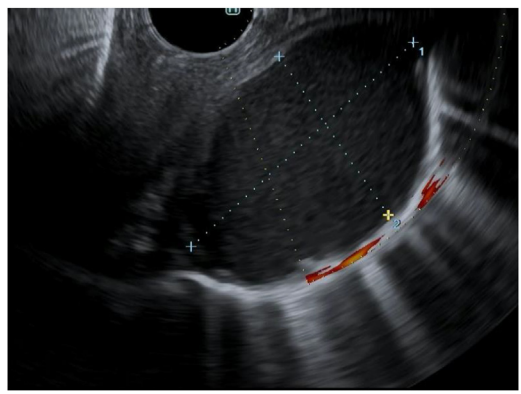

Fig. 10. Linear EUS view of a bronchogenic cyst at the level of the distal esophagogastric junction.

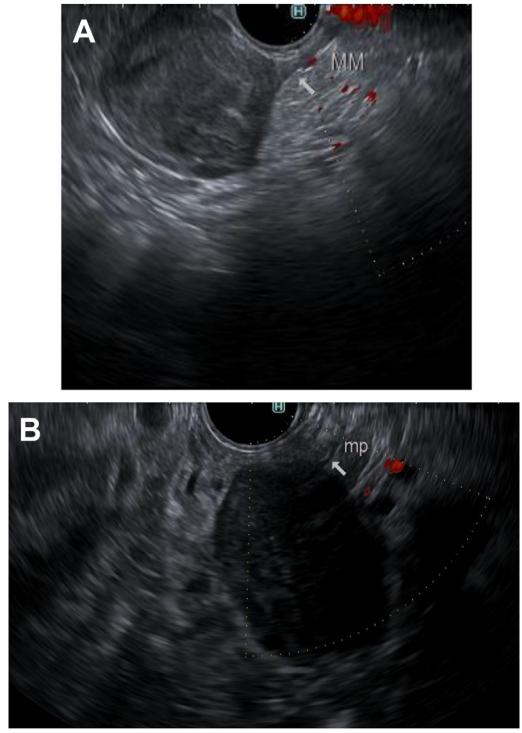

Fig. 11. (*A*, *B*) Linear EUS views of a GIST arising from fourth endosonographic layer/MP.

exophytic development, and association with lymph nodes, can be positive predictors.[20] GISTs are far more prevalent than leiomyomas in the stomach (the inverse is true in the esophagus), and the presence of a marginal halo (hyperechoic outer ring) can help differentiate GISTs from leiomyomas in some cases.

EUS is also helpful for identifying vascular structures within the stomach, such as gastric varices. These are often anechoic, serpiginous, and with Doppler flow. Other gastric lesions include pseudoaneurysms, splenic vessels, and fistulas.

PANCREATIC NEOPLASMS

Solid Tumors

Pancreatic ductal adenocarcinoma constitutes up to 95% of all pancreatic cancers and ranks as the fourth leading cause of cancer-related deaths in the United States. Its incidence is rising, with projections indicating it will become the second leading cause of cancer-related deaths by 2030. Survival rates hinge on the stage at diagnosis and the feasibility of surgical resection.[27–30] Unfortunately, at least 80% of pancreatic cancers are diagnosed at an advanced stage, with more than half exhibiting systemic metastases at diagnosis. Accurate staging and tissue acquisition are critical for determining appropriate treatment strategies.

EUS is regarded as the most sensitive imaging modality for detecting pancreatic cancers, particularly small lesions. It allows for tissue acquisition and has a sensitivity of 89% to 100% and an accuracy of 94% to 96%.[31] The ability of the transducer to be in proximity to pancreatic tissue and surrounding structures allows for the assessment of lesion size, location, vascular involvement, lymphadenopathy, and metastatic

disease. However, cross-sectional imaging remains the method of choice for initial staging, surveillance, and determining surgical resectability.[29,31]

When performing EUS for pancreatic cancer, the endoscopist should note the mass's size, location, echogenicity borders, cystic components, ductal dilation, and relationship with major vessels (**Fig. 12**). Additionally, the presence of lymph nodes, liver metastases, ascites, and extrapancreatic lesions should be documented, with EUS-directed sampling performed for tissue confirmation.[31] Other less common pancreatic masses include neuroendocrine tumors and lymphomas. Unlike pancreatic adenocarcinoma, these lesions are less likely to cause biliary or pancreatic duct compression and have a better prognosis.

Since the introduction of EUS in the 1980s, various advancements and imaging techniques using EUS for pancreatic lesion evaluation have been made.

Cystic lesions

Pancreatic cystic neoplasms are common and classified into mucinous and nonmucinous lesions. Mucinous lesions are considered premalignant and include intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms, and solid pseudopapillary neoplasms. On the other hand, serous cystadenomas are nonmucinous, benign cysts composed of multiple smaller cysts lined with cuboidal epithelium originating from pancreatic acinar cells. Other serous pancreatic cysts include the less common solid serous adenoma and cystic lesions associated with von Hippel–Lindau syndrome.

High-resolution imaging techniques like CT and MRI offer noninvasive options for assessing and characterizing these lesions. At the same time, EUS provides a more invasive but highly sensitive method for evaluation and diagnostic sampling. EUS-FNA is particularly useful in distinguishing between serous and mucinous lesions. Mucinous fluid, known for its viscosity, often produces a positive "string sign" (a fluid string greater than 3.5 mm between glass slides or gloved fingers), which has a 95% specificity for mucinous lesions.[32–37] The columnar epithelium of mucinous lesions secretes carcinoembryonic antigen (CEA), with levels often greater than 192 ng/mL. Recent studies indicate that a low cyst fluid glucose level (<50 mg/dL) offers higher sensitivity for identifying mucinous lesions than CEA alone.[34] When cysts are sampled, most ultrasonographers send CEA and glucose to help differentiate mucinous from nonmucinous cystic lesions. Amylase is often checked as this helps distinguish IPMNs and pseudocysts from other types of cysts since they communicate with the pancreatic duct.

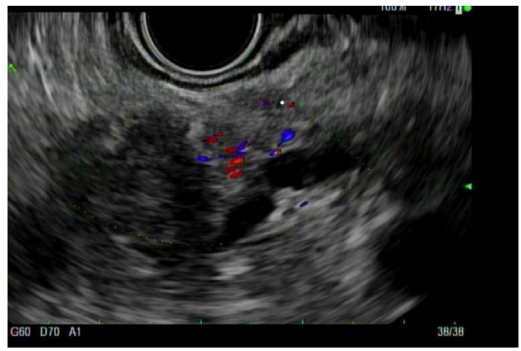

Fig. 12. Linear EUS view of an irregular, ill-defined mass in the neck of the pancreas with severe pancreatic duct dilation.

EUS-guided cyst fluid can also be analyzed through cytology and genetic testing (next-generation sequencing, NGS), aiding in identifying mutations like KRAS and GNAS associated with mucinous lesions.[38] The 2024 International Consensus guidelines on pancreatic cysts recommend using molecular DNA markers in cyst diagnostics when the diagnosis is uncertain, marking the first inclusion of NGS in major guidelines.[36] Microbiopsy forceps passed through a 19 gauge needle, can sample the cyst epithelium, increasing diagnostic accuracy with a slightly higher risk of post-procedure pancreatitis and bleeding.[33] Additionally, confocal laser endomicroscopy, performed through a 19 gauge needle following intravenous fluorescein injection, allows for detailed analysis of the cyst's epithelial lining, further enhancing diagnostic accuracy, although this is not routinely performed.[37]

While diagnostic tests for differentiating mucinous from nonmucinous pancreatic cysts have improved, better ways are still needed to predict their malignant potential.

CONTRAST-ENHANCED ENDOSCOPIC ULTRASOUND

The introduction of contrast-enhanced EUS (CE EUS), which uses a microbubble-based contrast agent to enhance visualization, has improved the diagnostic capabilities of EUS. This can facilitate distinguishing small lesions and differentiating chronic pancreatitis from pancreatic adenocarcinoma, both of which are challenging. Studies have shown that CE EUS significantly enhances the diagnostic yield compared to standard EUS.[29,39,40]

In a prospective tandem-controlled trial 101 patients with focal pancreas lesions (48 with masses, 28 with cysts, and 25 with pancreatitis) underwent conventional EUS followed by contrast EUS using intravenous perflutren microspheres. The diagnostic yield of conventional EUS was 64% compared to 91% with CE EUS (odds ratio [OR] 7.8, 95% confidence interval [CI], 2.7–30.2).[39]

A meta-analysis of 2644 patients from 18 studies using CE EUS to diagnose pancreatic cancer found a pooled sensitivity of 90% and specificity of 89%. The average specificity when distinguishing between neoplastic and nonneoplastic lesions was 0.95 (0.94–0.96) and 0.83 (0.77–0.87), respectively.[40]

ENDOSCOPIC ULTRASOUND WITH REAL-TIME ELASTOGRAPHY

EUS with real-time elastography (EUS RTE) measures tissue density by assessing distortion after applying predetermined pressure.[29] This technology is highly operator-dependent, and its clinical utility in determining solid pancreatic masses is still being evaluated. Studies have demonstrated high accuracy levels for EUS RTE in diagnosing pancreatic masses, although its full potential is yet to be realized. One study compared RTE EUS and CE EUS in 50 consecutive patients with focal pancreatic masses who underwent EUS FNA just prior with nondiagnostic results. The sensitivity, specificity, and accuracy of RTE EUS were 97.7%, 77.4%, and 84%, respectively. CE EUS had similar results: 89.5%, 80.7%, and 84%, respectively.[41]

FINE NEEDLE ASPIRATION VERSUS BIOPSY

EUS-guided tissue acquisition (EUS TA) can be performed using FNA or FNB with various needle sizes and shapes. FNA has limitations in retaining cellular architecture and stroma, leading to the development of FNB needles.[42] Studies comparing FNA and FNB have shown varying efficacy, with FNB often requiring fewer needle passages to obtain a pathologic confirmation.[43,44] A meta-analysis of 11 trials, including 833 total patients with solid pancreatic masses, compared the performance characteristics of

FNA versus FNB needles (271 with 22 G EUS-FNA, 239 sampled with 22 G EUS-FNB, and 323 with both needles in cross-over trials). For cases of pancreatic cancer, both were comparable for diagnostic accuracy (relative risk [RR] 1.02, 95% CI 0.97–1.08), sample adequacy (RR 1.01, 0.96–1.06; $P = .61$), and histologic core procurement (RR 1.01, 0.89–1.15; $P = .86$). Pooled sensitivity for the diagnosis of pancreatic cancer was 93.1% (87.9%–98.4%) with biopsy and 90.4% (86.3%–94.5%) with aspirate. FNB had a nonsignificant positive trend for requiring fewer needle passages to obtain pathologic confirmation (−0.32, $P = .07$) compared to FNA.[43] However, the location of the mass and the anticipated angle of needle trajectory from the transducer to the mass impact needle selection. For example, FNA needles (compared with FNB needles) are typically considered more flexible and may be better suited for lesions requiring significant scope or elevator angulation.[45] Needle selection should be tailored to the lesion's position relative to the echoendoscope, the need for tissue architecture, and the endoscopist's preference.

COMPLICATIONS OF ENDOSCOPIC ULTRASOUND-DIRECTED SAMPLING OF PANCREATIC LESIONS

EUS TA is generally safe, with low complication rates, including bleeding (1%–4%), pancreatitis (1%–2%), and perforation (<5%).[46] These risks may be higher when sampling smaller lesions, pancreatic neuroendocrine tumors, and pancreatic cystic lesions.[29,47]

RAPID ON-SITE EVALUATION

The necessity of rapid on-site evaluation (ROSE) during tissue sampling in pancreatic cancer is debated. Studies have shown comparable diagnostic accuracy with and without ROSE, suggesting that it may not be essential for all cases. A multicenter (14 centers in 8 countries), prospective, randomized, noninferiority study of 800 patients with solid pancreatic lesions assessed the diagnostic accuracy of EUS-FNB with and without ROSE and found comparable results (96.4% with ROSE vs 97.4% without ROSE, $P = .396$).[48]

GALLBLADDER

EUS can complement other imaging modalities such as abdominal ultrasound, CT, and MRI in evaluating gallbladder diseases. EUS can detect gallstones, gallbladder polyps, and tumors (**Fig. 13**A, B). For cholecystitis, EUS-guided gallbladder drainage is a treatment option for patients who are high-risk for cholecystectomy.[49,50] For gallbladder cancer, EUS can help determine invasion depth, staging, and regional metastasis.[51] High-resolution transabdominal ultrasound and EUS have shown similar diagnostic accuracy. EUS TA is not routinely performed due to the risk of complications like bile leakage and needle tract dissemination, which must be considered.

BILE DUCT

Choledocholithiasis

EUS can be used to diagnose choledocholithiasis. It is best utilized in patients with intermediate risk of choledocholithiasis (10%–50% probability of choledocholithiasis) when compared to magnetic resonance cholangiopancreatography (MRCP) and is less invasive than an intraoperative cholangiogram or endoscopic retrograde cholangiopancreatography (ERCP).[52] A metanalysis that included 5 studies and 272 patients comparing performance of EUS to MRCP supported a higher pooled sensitivity (0.97

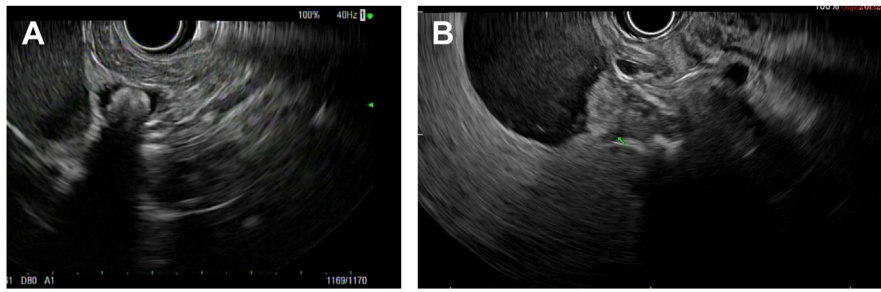

Fig. 13. Linear EUS views: (*A*) Gallstones with characteristic shadowing noted in the gallbladder neck. (*B*) Gallbladder neck mass detected via EUS.

vs 0.87) and accuracy (OR 162.5 vs 79.0, respectively; $P = .008$) for EUS, but similar specificities (0.90 vs 0.92).[53] Patient preference, modality availability, and local expertise should be taken into account when deciding which modality to choose from. EUS and MRCP are similar in cost and are more cost-effective when compared to IOC and ERCP.[54]

Cholangiocarcinoma

Cholangiocarcinoma is a malignancy arising from biliary epithelial cells, divided into intrahepatic, hilar, and distal subtypes. EUS can be superior to endoscopic retrograde cholangiography (ERC)-directed sampling but carries a higher risk of needle tract seeding, especially in liver transplantation candidates.

ENDOHEPATOLOGY

Endoscopic Ultrasound-guided Portal Pressure Gradient

EUS-PPG measurement is a novel endosonographic technique that allows the portosystemic pressure gradient to be measured (**Fig. 14**A, B). The advantage of EUS-PPG over wedged hepatic vein pressure as a surrogate for sinusoidal pressure is that a direct portal vein pressure is obtained. Early reports suggest good validity, as EUS-PPG measurements correlate well with hepatic venous pressure gradient (HVPG) when measured concomitantly in a cohort of patients with known portal hypertension.

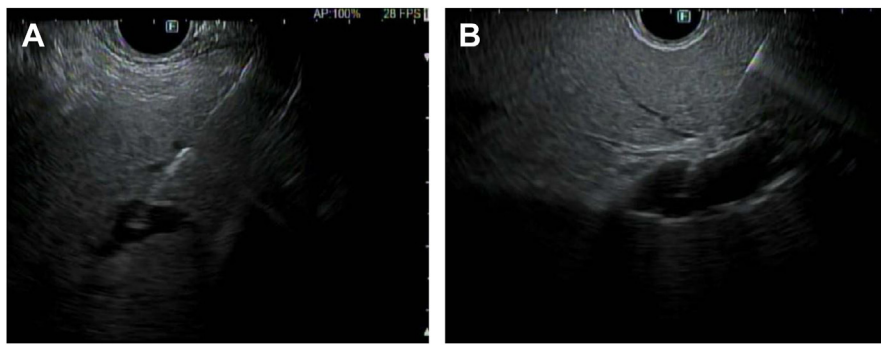

Fig. 14. Linear EUS views: (*A*) EUS-PPG: a 25 ga needle is placed in the middle hepatic vein for pressure measurement. (*B*) EUS-PPG: a 25 ga needle is placed in the central portal vein for pressure measurement.

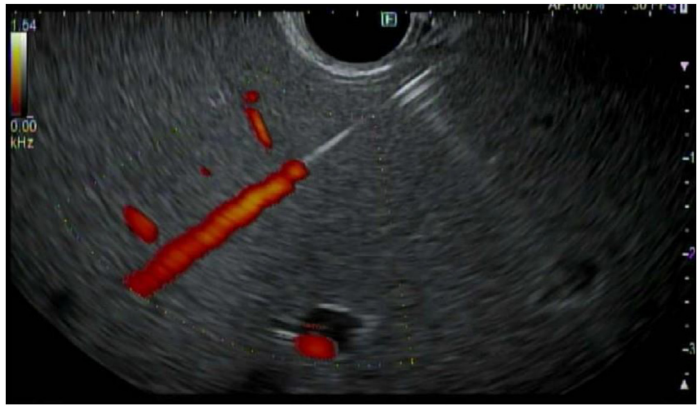

Fig. 15. Linear EUS view of EUS-FNB of the left lobe of the liver.

Performing EUS-PPG offers a 3-in-1 procedure as it allows the concurrent ability to perform EGD to assess and treat esophageal, gastric varices, and EUS-guided liver biopsy.[55–57]

Endoscopic Ultrasound-guided Liver Biopsy

A 19 gauge needle (Franseen needle using a wet suction technique is most often utilized) is used to obtain tissue from the left (transgastric approach; **Fig. 15**) and right (transduodenal approach) lobes of the liver. Data have shown that the diagnostic yield is over 90%, as well as the superiority of EUS-guided liver biopsy over the transjugular approach.[58–61]

SUMMARY

Over the past 20 years, endoscopic technologies and techniques have developed, facilitating minimally invasive methods for examining and sampling lesions both within and outside the gastrointestinal lumen, such as in the chest, abdomen, and pelvis. These advanced endoscopic strategies have transformed the diagnosis, evaluation and staging of intraluminal and extraluminal lesions and made tissue acquisition easier and safer.

CLINICS CARE POINTS

- In nonmetastatic disease, EUS plays a vital role in the locoregional (T and N) staging of GI luminal cancers.
- EUS identifies the wall layer of origin and allows for tissue sampling of GI subepithelial lesions.
- EUS plays an invaluable role in the identification, characterization, and tissue diagnosis of solid pancreatic lesions.
- EUS allows for pancreatic cyst characterization through cyst fluid aspiration and analysis.
- EUS is more accurate than cross-sectional imaging and transabdominal ultrasound in identifying bile duct and gall bladder stones.
- Endohepatology is an emerging field that allows for EGD, EUS-PPG, and liver biopsy in one setting.

DISCLOSURE

M. J. Radlinski: Cook Medical. H. B. Zaver: None. V. M. Shami: Consultant for Olympus America, Cook Medical, Boston Scientific, and Pentax Medical.

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