The Egyptian Journal of Hospital Medicine (July 2025) Vol. 100, Page 4019-4027

Diagnostic and Therapeutic Roles of Endoscopic Ultrasound in Gastroenterology: An Overview

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ABSTRACT

In gastroenterology and hepatopancreatobiliary medicine, endoscopic ultrasonography (EUS) has developed from a largely diagnostic modality into a vital tool with growing therapeutic potential. By combining endoscopy with high-frequency ultrasonography, EUS provides detailed visualization of the gastrointestinal wall and adjacent structures, offering superior resolution to conventional cross-sectional imaging. It remains integral for TNM staging of gastrointestinal malignancies, assessing subepithelial lesions, and evaluating pancreaticobiliary disorders. Its diagnostic yield is significantly enhanced by adjunctive techniques like contrast-enhanced EUS, elastography, and fine-needle aspiration/biopsy (EUS-FNA/FNB) which provides tissue samples for histopathological examination. Therapeutically, EUS is now indispensable for interventions including pancreatic fluid collection drainage, pancreatic duct and bile duct decompression when conventional endoscopic retrograde cholangiopancreatography (ERCP) fails due to abnormal anatomy, gastrojejunostomy in gastric outlet obstruction, tumor ablation, EUS-guide endovascular therapy for management of gastric varices and a growing number of other innovative procedures, solidifying its role in offering less invasive options and improving patient outcomes in endoscopic management of gastrointestinal diseases.

Keywords: Endoscopic ultrasound, EUS-FNA, EUS-guided drainage, diagnostic endosonography, therapeutic EUS, pancreaticobiliary diseases, interventional endoscopy.

INTRODUCTION

Endoscopic ultrasonography (EUS) creates detailed images of the structures close to the gastrointestinal wall by combining an endoscope and a high-frequency ultrasonic probe. In 1980, the first radial EUS was introduced. The technical capabilities of the device and the anatomic conditions determine the indications for EUS. Because of its high-resolution capabilities, using a wide range of ultrasonic frequencies and limited penetration depths (ranging from 1 to 6 cm, depending on the ultrasonic frequency used), EUS can create extremely detailed images of the gastrointestinal tract (GIT) wall and its anatomically related abdominal structures [(1)].

Since its introduction, EUS has become a widely accepted and indispensable diagnostic tool that enables the visualization of previously inaccessible anatomical regions. As it has advanced, a number of interventional techniques have been made possible, beginning with tissue acquisition and progressing to much more complex procedures [(2)].

There are currently three different kinds of EUS scopes [(3)]. The radial scope which produces a 360-degree image, where the axis of the scope is perpendicular to the scanning plane. It is unsuitable for interventions and is nearly always utilized for staging. The linear scope, in which the scanning plane runs parallel to the ultrasonic probe, is the most widely used scope type for EUS-guided procedures. The third type is the forward-viewing echoendoscope, which is used mainly for therapeutic interventions.

With an emphasis on the field of gastroenterology, in this review, we will try to highlight the diagnostic and therapeutic applications of EUS. We searched the PubMed and Scopus databases for relevant material using the following keyword combinations: endoscopic ultrasound, EUS-FNA, EUS-guided drainage, diagnostic EUS, therapeutic EUS, and interventional EUS. We excluded papers published in languages other than English.

Diagnostic indications of EUS:

Apart from therapeutic interventions, EUS is indicated for 2 main purposes: first, for examination of the gut wall from the esophagus down to the proximal duodenum, as well as the rectum. To correctly perform T-staging and diagnose subepithelial lesions, it is critical to identify the typical five layers of the GIT wall. Based on their unique echogenicity and layer of origin, subepithelial lesions can be identified and diagnosed [(1)].

The second indication is examination of the pancreaticobiliary system and the liver, which is typically done through three stations with specific identifiable landmarks in each station. The stations include the stomach through which, the neck, body, and tail of the pancreas, as well as major vascular structures that are crucial for cancer staging, the left kidney, left adrenal gland, spleen, and left lobe of the liver can be examined, the second part of the duodenum (D2) through which the pancreatic head, uncinate process and ampulla, bile and pancreatic ducts, and their junction at the papillary orifice can be examined, and the bulb (which displays the portal vein, common hepatic artery and its branches, bile duct, gallbladder, and head of the pancreas) [(4)].

The diagnostic indications are summarized in Table 1.

Received: 30/04/2025
Accepted: 30/06/2025

Table 1: Diagnostic indication of EUS in GIT

Luminal	• Gastric cancer. • Esophageal cancer. • Ampullary and non-ampullary duodenal tumors. • Rectal tumors. • Submucosal tumors (SMTs) in the esophagus, stomach, and duodenum. • Diffuse mural thickening of the esophagus and stomach.
Extraluminal	• Solid and cystic benign and malignant lesions of the pancreas. • Selected liver tumors. • Gallbladder and biliary tumors. • Extraluminal lymph nodes. • Retroperitoneal tumors.

Role of EUS in diagnosis and staging of luminal tumours: The EUS offers a very precise assessment of T-staging of gut wall tumors since it can view the various wall layers. It's critical to differentiate between superficial (T1) and advanced (T2 or greater) lesions due to the variations in prognosis and available treatments. For esophageal and gastroesophageal tumors, T1a stage (esophageal cancer confined to the lamina propria and muscularis mucosa) was distinguished from T1b (esophageal cancer confined to the submucosa, which is further divided into SM1, SM2, and SM3 according to invasion depth into the submucosa) in the 2017 UICC/AJCC TNM classification system [(5)]. This distinction is important because T1a and T1b SM1 cancers only have a 3–6% risk of lymph node metastasis, but T1b SM2 and SM3 tumors have a 21–24% risk [(6)]. It was reported that T staging accuracy with EUS is higher than 80% [(7)]. This can assist in determining which patients will not benefit from endoscopic minimally invasive procedures. EUS provides strong contrast resolution and can distinguish between early T1 tumors and more advanced illness, with a sensitivity of 81.6% and a specificity of 99.4%. For T1a cancers, EUS has an 85% sensitivity and 87% specificity, while for T1b tumors, the corresponding values are 86% and 86% [(8)]. According to a meta-analysis of gastric cancer, EUS was able to differentiate between tumors classified as stage T1 to T2 and stage T3 to T4 with a sensitivity of 86% (95% CI, 81 to 90) and a specificity of 90% (95% CI, 87 to 93). In identifying T1a (mucosal) and T1b (submucosal) cancers, EUS showed 87% (95% CI, 81 to 92) sensitivity and 75% (95% CI, 62 to 84) specificity [(9)].

Role of EUS in the diagnosis of submucosal tumors:

EUS is the most reliable imaging method for assessing GI tract submucosal tumors (SMTs) because it can differentiate between various histologic layers and, consequently, the most likely site of tumor formation (Table 2). There are five main ultrasonic layers that can be seen on an EUS: mucosa (including muscularis mucosa) in layers one and two, submucosa in layer three, muscularis propria in layer four, and serosa or adventitia in layer five (Figure 1). In terms of pathology, SMTs fall into three groups: malignant, potentially malignant, and benign. Consequently, it is critical to differentiate between the many pathogenic forms of gastrointestinal SMTs. In addition to determining the layer of origin, EUS allows observing the morphological structure of the lesions, the relation to the surrounding tissues, and the extent of lesion infiltration. When it comes to describing tiny (<2 cm) lesions, EUS is better than other imaging modalities (CT, MRI). Additionally, EUS enables assessment of any associated lymphadenopathy and quantification of lesion size for subsequent staging [(10)].

Table 2: EUS Characteristics of common SMTs: [(11)]

SMT	Endoscopic Appearancee	EUS layer	EUS appearance
GI stromal tumor - low risk	No particular features, absence of ulcerations	4 (rarely 2 or 3)	Hypoechoic, mostly less than 3-5 cm, smooth margins, round, homogeneous
GI stromal tumor - potentially malignant	Presence of ulcerations	4 (rarely 2 or 3)	Hypoechoic, more than 3 cm, irregular extraluminal margins, cystic spaces, heterogeneous, echogenic foci
Leiomyoma	No specific characteristics	2, 3, or 4	Hypoechoic, well-circumscribed
Lipoma	Yellow hue, pillow sign (high specificity, low sensitivity), usually isolated	3	smooth edges, uniform echogenicity, highly hyperechoic, and maybe polypoid
Pancreatic rest	90% have umbilicated surface corresponding to a draining duct, and >90% are located in the antrum	2, 3, or 4	Hypoechoic or mixed echogenicity (acinous tissue appears heterogeneous while ducts appear anechoic), indistinct margin.
GI neuroendocrine neoplasm	No specific characteristics may be yellowish; multiple stomach carcinoid tumors are common. Duodenal and rectal are typically solitary.	2 or 3	Mildly hypoechoic or isoechoic, homogeneous, oval or round, smooth margin

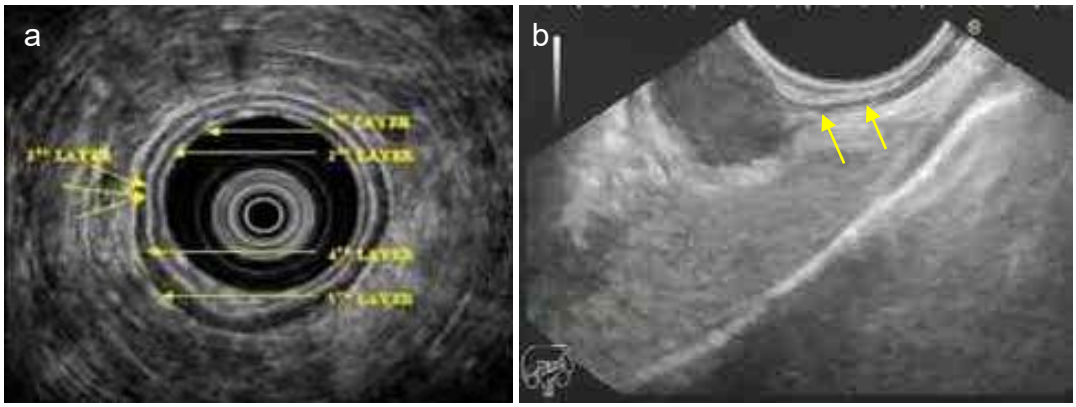

Figure 1: EUS in the diagnosis of submucosal tumours.

The five major ultrasonic layers visible on an EUS image, including the mucosa and muscularis mucosa in layers one and two, the submucosa in layers three, the muscularis propria in layers four, and the serosa or adventitia in layers five (a); A lesion that is hypoechoic that originates from the fourth layer of the mucosa (muscularis propria) (arrows) (b).

Diagnosis of benign pancreaticobiliary diseases:

Choledocholithiasis: The gold standard for identifying bile duct stones was believed to be endoscopic retrograde cholangiopancreatography (ERCP), but it can miss the diagnosis, especially when the stones are small. EUS has proven high efficacy in the diagnosis of biliary calculi (Figure 2) especially those not detected by conventional imaging. Following non-diagnostic CT or MRCP, EUS had a 94.3% diagnostic accuracy for choledocholithiasis, a 100% sensitivity, and a 96.6% specificity [(12)]. EUS and magnetic resonance cholangiopancreatography (MRCP) are often equally effective. Both MRCP and EUS had great sensitivity (92–98%) in randomized research comparing the two procedures, involving 224 patients. The two groups did not differ significantly from one another [(13)].

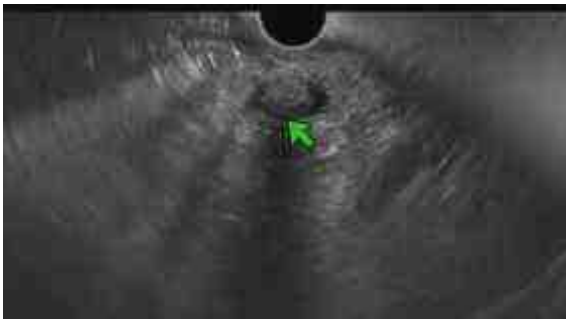

Figure 2: An EUS image of a distal CBD stone (arrow) with posterior acoustic shadow.

Gallbladder diseases:

Gallstone identification using transabdominal ultrasonography has a high sensitivity; however, it still has limitations in recognizing microlithiasis (tiny, radiologically undetectable stones, usually smaller than 3 mm). In patients with biliary colic and normal abdominal ultrasonography findings, EUS provides a high sensitivity for diagnosing microlithiasis. EUS demonstrated 98.8% and 100% sensitivity and specificity, respectively, in a prospective study for the detection of GB microlithiasis in patients who had a negative transabdominal ultrasound result [(14)].

EUS can produce high-resolution images and show the multilayer structure of the gallbladder.

Numerous studies have evaluated EUS to distinguish between GB protuberant lesions that are neoplastic and those that are non-neoplastic. Adenomas and malignant lesions are examples of neoplastic protuberant lesions (Figure 3). Localized adenomyomatosis, hyperplasia, and cholesterol and inflammatory polyps are examples of non-neoplastic protuberant lesions [(15)].

Furthermore, it has been shown that while EUS is 86.5–97% accurate in identifying neoplastic and non-neoplastic lesions, it is not very accurate at distinguishing between neoplastic and non-neoplastic polypoid lesions smaller than 10 mm [(15)].

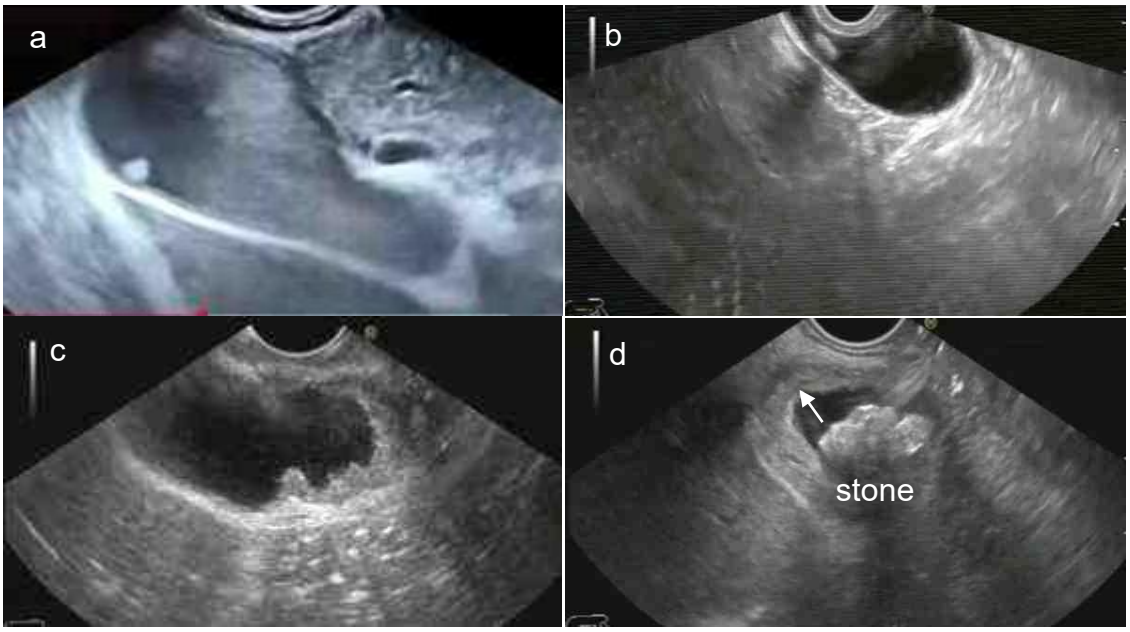

Figure 3: An EUS of the Gallbladder.

Small gallbladder adenomatous polyp appearing as homogenously echogenic subpedunculated polypoid lesion with nodular surface (a); A gallbladder stone with posterior acoustic shadowing (b); focal irregular wall thickening appearing at the gallbladder fundus with absent multilayer differentiation suggestive of gallbladder cancer (c); Gallbladder diffuse wall thickening with preserved wall layer structure with clear muscularis layer (arrow) suggesting benign nature and a large stone with posterior shadowing is seen inside the lumen (d).

Chronic pancreatitis:

EUS is considered a sensitive diagnostic method for chronic pancreatitis because it can accurately assess changes in the pancreatic duct and parenchyma. In chronic pancreatitis, the ductal features include stones, uneven contour, dilatation of the main duct and side branches, and hyperechoic duct borders; the EUS parenchymal features include hyperechoic foci, hyperechoic strands, lobularity, and cysts (Figure 4). To increase diagnostic precision, the Rosemont classification for EUS features of chronic pancreatitis assigns varying weights to the ductal and conventional parenchymal criteria of the illness [(16)].

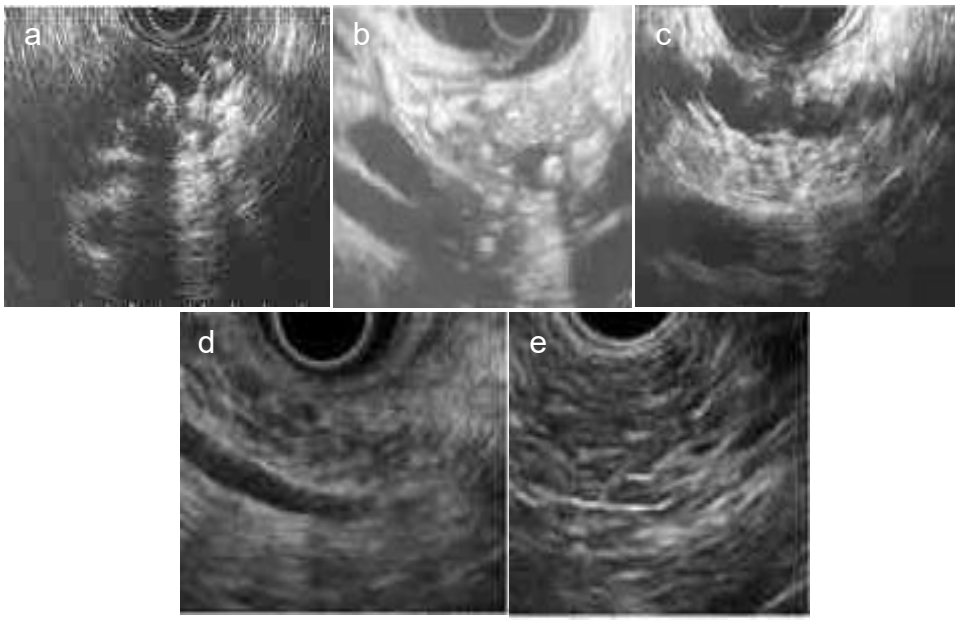

Figure 4: EUS features of chronic pancreatitis.

Hyperechoic foci with shadowing (a); pancreatic duct calculi (b) and pancreatic duct dilatation and irregularity (c); Lobularity with honey combing (d); hyperechoic strands (e).

Diagnosis of pancreatic cystic neoplasms:

For pancreatic imaging, EUS is regarded as the gold standard modality. Along with providing samples via aspiration with a tiny needle (FNA) for cytology and biochemical investigation, it delivers high-resolution pictures of pancreatic cysts for accurate characterization and diagnosis of the type of the cystic lesion [(17)].

The most prevalent forms of pancreatic cystic lesions are, pseudocysts, intraductal papillary mucinous neoplasm, mucinous cystic neoplasm, serous cystic neoplasm, and solid pseudopapillary tumor (Figure 5). EUS imaging can assess the pancreatic cystic lesions for malignancy or the possibility of malignant transformation in addition to assisting in the lesion type identification. It provides an accurate characterization of the cyst wall, helps define the size of the cyst, and helps assess for mural nodules, calcifications, or septations. It also shows how the cystic lesion and the surrounding organs and vasculature are related. Additionally, it makes it possible to estimate the main pancreatic duct (MPD) diameter and assesses whether the cyst is connected to the MPD or its branches or has no anatomic connection to the ducts [(18)].

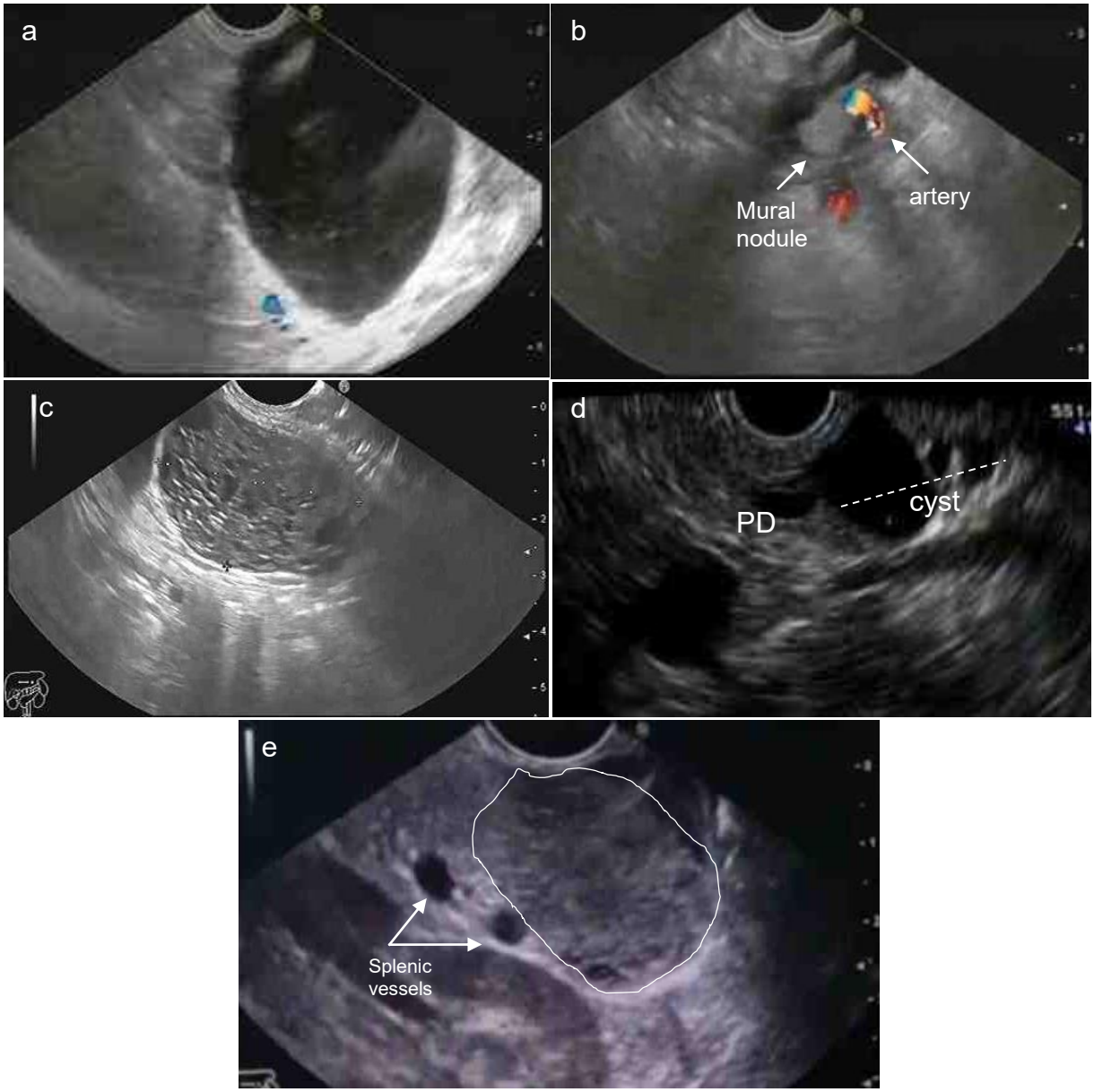

Figure 5: Pancreatic cystic neoplasms.

Pancreatic body mucinous cystic neoplasm in a 42 year-old female (a); pancreatic body mucinous cyst showing mural nodule and colour doppler showing an artery supplying it (b) EUS in a 63 year-old female patient showing pancreatic serous cystic neoplasm (microcystic type) (c); Pancreatic body intraductal papillary mucinous neoplasm appearing as multilocular cyst (dashed line) with connection to the pancreatic duct (PD) (d); A young female patient with a solid pseudopapillary tumor was found to have a pancreatic tail heterogeneous mass (delineated in white) with areas of breakdown (e).

Khashab *et al.* [19] conducted a retrospective analysis with over 150 patients, demonstrating the increased sensitivity of EUS with or without FNA. 43 (36%) and 27 (54%) more patients were identified by EUS when performed following CT and MRI, respectively. They concluded that the rate of accurate diagnosis of neoplastic cysts (confirmed by surgical excision) was improved by EUS [19].

Diagnosis of pancreatic cancer:

EUS plays a crucial role in the diagnosis and staging of pancreatic cancer as it allows detailed imaging of the pancreas and surrounding structures. Typically, pancreatic tumors are hypoechoic lesions (Figure 6) that are commonly linked to local invasion of nearby organs and signs of occlusion of the pancreatic duct. Additionally, by assessing local tumor expansion, vascular connections, and lymph node invasion, EUS enables precise staging of pancreatic cancer [20]. Furthermore, EUS enables EUS-guided fine needle biopsy (FNB) to acquire tissue samples for histological analysis and molecular profiling.

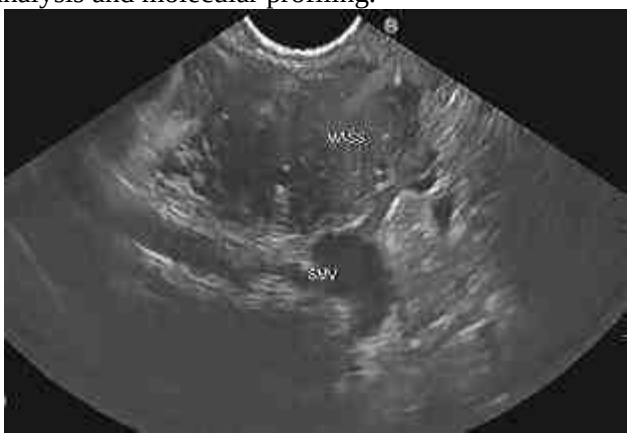

Figure 6: An EUS image of a pancreatic head hypoechoic mass abutting the superior mesenteric vein diagnosed as pancreatic ductal adenocarcinoma.

EUS and MRI have high accuracy for pancreatic cyst detection, consequently, they serve as pancreatic cancer screening tests. EUS may be performed as a second-line diagnostic after a negative CT scan and pancreatic cancer is suspected. A meta-analysis comprising four publications that evaluated the two techniques in the context of a negative or inconclusive CT scan revealed that EUS was more accurate than CT in detecting pancreatic cancer masses [21].

Techniques to enhance diagnostic accuracy.

To increase the effectiveness of EUS diagnosis, certain techniques have been used. EUS-guided elastography and contrast-enhanced harmonic EUS (CH-EUS) have been extensively studied due to their accuracy in many clinical settings.

a) EUS-guided strain elastography:

EUS-elastography is a non-invasive technique that measures elasticity in real time by detecting and assessing the distortion of the EUS picture after light pressure is applied by the EUS probe. The strain and stress of the assessed structures can be used to compute the elasticity modulus. Elastography is based on the discovery that several pathologic conditions, such as inflammation, fibrosis, and cancer, change the stiffness of the tissue. The strain ratio (SR) (Figure 7) and strain histogram (SH) can be computed mathematically, or the strain elastography analysis can be intuitively assessed using color map distribution [22].

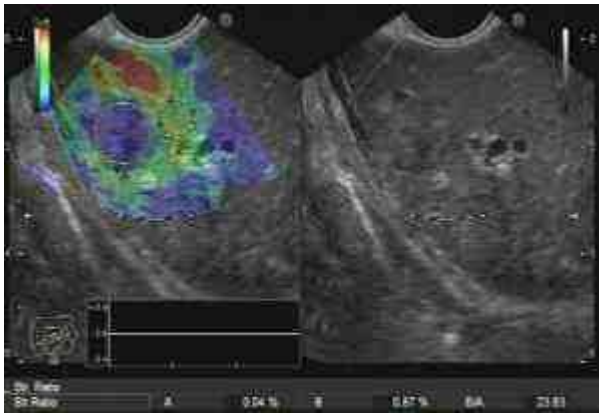

Figure 7: EUS-Elastography of a malignant metastatic liver lesion showing blue colour denoting firm consistency. The strain ratio is measured by dividing area B (the area surrounding the target lesion) by area A (the target lesion). SR is 23.83, indicating hard tissue (malignant).

b) Contrast-enhanced harmonic EUS (CH-EUS):

CH-EUS is an additional method to improve EUS-based differential diagnosis in a number of diseases. Together with advancements in ultrasound technology, the introduction of microbubble-based contrast agents has improved the capacity to scan tiny vascular structures and see microflow patterns within the lesions being studied [22]. When the contrast agent's microbubbles are exposed to an ultrasonic beam, they resonate and produce signals. The fundamental concept of CH-EUS is the ultrasonic device's selective reception of these signals. Only the signals from the contrast chemicals are amplified after the background tissue signals are automatically eliminated [23].

Lesions of interest should be recognized and recorded according to their distinct contrast enhancement. As a result, the transient effect of contrast may be assessed and compared to signals from the surrounding tissues (non-, hypo-, iso-, or hyperenhancement), and its distribution (either uniform or heterogeneous) can be ascertained [22].

Therapeutic indications of EUS:

Therapeutic EUS procedures are carried out with linear echo-endoscopes that have a large working channel. The basic idea behind therapeutic EUS is to

create an access, typically by creating a fistula or tract that joins the GI tract to a target organ or cavity.

1- EUS-guided drainage of fluid collections:

This technique is now recognized as the gold standard for managing walled-off pancreatic necrosis and symptomatic pseudocysts with precise stent placement. In addition to allowing internal drainage of the fluid accumulation, the minimally invasive method eliminates the need for percutaneous drains and reduces the possibility of pancreatic fistulas. A lumen-apposing metal stent (LAMS) or an indwelling double-pigtail plastic stent are frequently used to achieve drainage [(24)].

2- EUS-guided biliary drainage (EUS-BD):

When biliary drainage is necessary, ERCP is currently the gold standard; however, up to 10% of patients may not benefit from it. Tumor infiltration, tight strictures, and altered anatomy are some of the reasons for failure. These factors could make stent implantation difficult [(2)].

Through EUS, with the scope tip in the duodenum and proximal stomach, the endoscopist can puncture the common bile duct (CBD) and the intrahepatic bile ducts in segments 2 and 3 of the liver, respectively. In order to perform a rendezvous procedure or direct antegrade placement of a metal stent across a stricture, EUS-BD entails first puncturing the bile duct with a FNA needle, then moving a guidewire past the stenosis until it exits through the papilla into the duodenum, and finally switching to a traditional duodenoscope. Transmural stenting, such as EUS-guided choledochoduodenostomy or EUS-guided hepaticogastrostomy, is an alternative [(2)].

3- EUS-guided gallbladder drainage (EUS-GBD):

Laparoscopic cholecystectomy is the recommended method of treatment for acute cholecystitis. According to the 2018 Tokyo guidelines, percutaneous transhepatic gallbladder drainage (PT-GBD) is the recommended treatment for patients at high surgical risk, with EUS-GBD serving as a backup if qualified endoscopists are available [(25)]. A meta-analysis that comprised only three retrospective studies using LAMSs found that EUS-GBD outperformed PT-GBD in terms of readmissions, re-intervention requirements, and hospital stay duration [(26)].

4- EUS-guided pancreatic duct drainage (EUS-PDD):

When pancreatic duct obstruction occurs due to transpapillary or transanastomotic (pancreaticojejunal anastomosis following pancreatic surgery), endoscopic therapy is the standard management [(27)]. When the procedure is technically challenging such as inaccessible papilla or anastomosis, EUS-guided drainage offers an effective treatment option. EUS-PDD employs two main techniques: The first is called EUS-assisted rendezvous (EUS-RV) endoscopic retrograde pancreatography, and it is done with a balloon-assisted endoscope or a colonoscope, either from the anastomotic site after pancreatic surgery (transanastomotic) or when a conventional duodenoscope can reach the papilla (transpapillary). The second strategy is EUS-transmural drainage (EUS-TMD). It includes EUS-guided pancreatico-enterostomy, which inserts a stent between the PD and the stomach, duodenum, or jejunum, and transenteric antegrade stenting, which advances the stent further into the ampulla or anastomotic site [(28)].

5- EUS-guided gastrojejunostomy (EUS-GJ):

Recently, minimally invasive methods for treating benign and malignant pyloric stenosis have been established. An anastomosis is created using LAMSs to create a gastroenteroanastomosis under endosonographic guidance. After a jejunal loop or the distal part of the duodenum is punctured from the EUS site in the stomach, a stent is placed. Consequently, the stomach and either the duodenum or the jejunum form an anastomosis [(29)].

While shorter hospital stays, an earlier return to oral feeding, and fewer adverse events are linked to EUS-GJ, it seems to be of similar efficacy as open or laparoscopic surgical gastrojejunostomy [(30)].

6- EUS-guided tumor ablation:

Localized lesions could be treated thanks to specialized EUS-guided radiofrequency ablation (EUS-RFA) needles. This probe exposes a lesion to high-frequency alternating current, which results in cell necrosis. When RFA is applied, bubbles may occur and a hyperechoic zone may thereafter arise, both of which are indications that the ablation was successful [(31)]. EUS-RFA had excellent therapeutic efficacy with little adverse events, especially when it came to symptom management for small functional neuroendocrine tumors [(32)].

7- EUS-guided endovascular therapy:

Because of the adverse event of pulmonary glue embolization, standard endoscopic cyanoacrylate injection (ECI) is not the first choice for primary prophylaxis of isolated gastric varix (IGV) and gastroesophageal varix type 2 (GOV2). ECI, however, is the suggested course of treatment for bleeding GOV2 and IGV. EUS-guided coil insertion and cyanoacrylate injection (EUS-CCI) has been developed to lower the risk of pulmonary embolization. A retrospective analysis of 152 patients with GOV2/IGV1 who underwent EUS-CCI for active bleeding and secondary or primary prophylaxis is the greatest experience to date. It showed that 93 of the 100 patients who underwent follow-up EUS had complete varix obliteration, and the technical success rate was greater than 99% [(33)].

CONCLUSION

For many gastrointestinal and hepatic disorders, EUS is currently regarded as the gold standard procedure. The clinical applicability of EUS has

broadened beyond diagnostics to encompass therapeutic applications, many of which exhibit significant promise, as a result of the increasing number of indications. It is now feasible to access distant lesions that were previously difficult for histological diagnosis thanks to EUS-guided tissue acquisition. Moreover, EUS enabled endoscopists to access many adjacent organs for different therapeutic interventions, including drainage, creating an anastomosis, tumor ablation, etc.

Conflict of interest: None.
Funding: None.

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