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MINIREVIEWS

Practical approach to linear endoscopic ultrasound examination of the gallbladder

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Abstract

The gallbladder (GB) is a susceptible organ, prone to various pathologies that can be identified using different imaging techniques. Transabdominal ultrasound (TUS) is typically the initial diagnostic method due to its numerous well-established advantages. However, in cases of uncertainty or when a definitive diagnosis cannot be established, computed tomography (CT) or magnetic resonance imaging may be employed to provide more detailed information. Nevertheless, CT scans may sometimes offer inadequate spatial resolution, which can limit the differentiation of GB lesions, particularly when smaller yet clinically relevant abnormalities are involved. Conversely, endoscopic ultrasound (EUS) provides higher frequency compared to TUS, superior spatial resolution, and the option for contrast-enhanced harmonic imaging, enabling a more comprehensive examination. Thus, EUS can serve as a supplementary tool when conventional imaging methods are insufficient. This review will describe the standard EUS examination of the GB, focusing on its endosonographic characteristics in various GB pathologies.

Key Words: Endoscopic ultrasound; Linear endoscopic ultrasound; Gallbladder anatomy; Gallbladder pathologies; Therapeutic endoscopic ultrasound

Core Tip: Gallbladder pathologies can pose a health challenge to clinicians and patients when poorly examined. Linear endoscopic ultrasound has clinical and therapeutic significance when examining the gallbladder.

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INTRODUCTION

Endoscopic ultrasound (EUS) assessment of the biliary system plays a critical role as it offers a non-invasive and safe mechanism to evaluate biliary tract disorders[1]. The two types of EUS scopes are linear array and radial scanning. Both scopes combine two endoscopic modalities visualization with high frequency enabling imaging of the gastrointestinal tract wall and into vessels and organs in proximity[2]. Radial EUS – first to be advanced – offers a 360-degree view in a perpendicular plane to the scope, similar to the computed tomography (CT) image[2]. Conversely, linear EUS offers a localized oblique image parallel to the scope and allows therapeutic intervention under ultrasound[2]. While radial EUS was the first to be developed, linear EUS has gained popularity over the years due to its ability to add other diagnostic tools such as the fine-needle aspiration (FNA)[3]. This current review discusses the role of linear EUS in gallbladder (GB) imaging and its clinical implications.

Recently, the diagnostic and therapeutic fields of linear EUS have been rapidly growing, offering a feasible and relatively safe semi-invasive modality. Despite existing non-invasive imaging modalities, in the case of very small lesions, but clinically relevant such as microlithiasis or GB wall thickening, a more detailed assessment is necessary. In that context, the advantage of EUS is related to its higher frequency than TUS (5–12 *vs* 2–5 MHGB) which allows the detection of lesions 3 mm in size and meticulously assesses the GB wall. The high EUS sensitivity and specificity for the diagnosis of GB microlithiasis was shown in multiple studies accounting for 92.6%–100% and 55.6%–91%, respectively. Of note in those studies, microlithiasis was detected when the TUS result was negative[4]. Furthermore, it is well established that EUS has a high spatial resolution in comparison to CT and allows for a more detailed examination. Finally, EUS might offer a histological diagnosis of GB lesions, when EUS-guided FNA is performed for pathological evaluation of GB tumors[5]. As EUS is a more invasive technique than standard imaging modalities, the assessment requires the possession of separate technical skills and knowledge regarding the GB anatomy, pivotal for accurate recognition of abnormalities. Compared to other imaging standards, such as radiology performed ultrasound, CT, and magnetic resonance imaging, a meta-analysis by Ross *et al*[6] in 2011, found that in the diagnosis of cholelithiasis, EUS has comparable sensitivity and specificity of [(0.90; 95%CI (0.86-0.93)] and [(0.88; 95%CI (0.84, 0.91)], respectively.

EUS EXAMINATION OF THE GALLBLADDER

Gallbladder anatomy

The GB is a pear-shaped sac with an average capacity of 30-50 mL and is 7-10 cm long. It is divided into four anatomical segments: fundus, body, infundibulum, and neck[7] (Figure 1). The rounded end of the GB represents the fundus covered by the peritoneum and reaches 0.5-1.0 cm beyond the liver border[7]. The fundus merges with the body, the primary anatomical portion of the GB. The infundibulum is a transitional area between the body and the neck. Its inferior surface may occasionally have a shallow diverticulum (Hartmann pouch)[8,9]. The neck, a brief 5-7 mm section, gradually tapers towards the cystic duct.

The GB is positioned along the visceral surface of the liver within the GB fossa, situated between the right and the quadrate lobes. It is closely attached to the liver by loose connective tissue containing small veins and lymphatics. The GB fundus is positioned over the duodenum and makes direct contact with the anterior abdominal wall at the level of the ninth costal cartilage. The body rests on the duodenum on one side, with the other intimately attached to the liver. This close contact may be responsible for the early direct spread of GB carcinoma into the liver[8]. The neck is located in the deepest part of the GB fossa, within the free border of the hepatoduodenal ligament (Figure 1).

The GB is usually supplied by a single cystic artery originating from the right hepatic artery. This artery traverses Calot's triangle, running parallel and medial to the cystic duct, and eventually divides into two branches near the GB wall [10]. One branch follows the peritoneal surface of the GB, while the other courses within the GB fossa. The origin and course of the cystic artery may exhibit variability, with the most typical arising from the right hepatic artery (95%). Less frequently, it may originate from the left hepatic artery, common hepatic artery, or aberrant right hepatic artery arising from the superior mesenteric artery[10]. Regarding drainage, the GB is connected to a network of small veins that either run toward the liver or join the cystic duct, ultimately merging with venous collaterals from the common bile duct. This network drains into the portal vein.

The GB wall is divided into four layers: Mucosa, muscularis propria, subserosa, and serosa. The serosa is absent from the GB surface, as it is in direct contact with the liver. Unlike other gastrointestinal organs, the GB lacks a muscularis mucosa layer[11]. Typically, the maximum GB wall thickness is 3 mm[12]. On EUS, the GB wall appears as two layers: Inner hypoechoic, representing the mucosa, muscularis propria, and shallow subserosal layers, and outer hyperechoic layers, representing deep subserosa and serosa layers[13] (Figure 2). The GB rests on the visceral liver surface[7]. The upper GB surface is attached by connective tissue to a shallow liver fossa located between the quadrate and right lobes.

Steps of GB assessment with EUS

EUS offers the ability to scan the GB from the stomach and the duodenum. Linear EUS, specifically, can examine GB from four stations: The fundus of the stomach, the antrum of the stomach, the bulb of the duodenum, and the descending duodenum.

Gastric fundal station: The gastric fundus extends 40-45 cm from the incisors below the gastroesophageal junction. In this station, the goal is first to identify the left lobe of the liver. Then, push the scope slightly downwards and rotate it clockwise to identify the "fish-eye appearance" of the umbilical portion of the left portal vein (PV) (Figure 3). Further rotation and slight upward tip deflection help identify the liver hilum, which is this station's landmark, where the right PV meets the left PV to form the central PV (Figure 4). At the liver hilum, the echoendoscope is pushed slightly forward with a maximum upward tip angulation of more than 90^0. Then, by torquing the scope in counterclockwise rotation, in most cases, and sometimes clockwise rotation in a small number of patients, the goal is to identify the GB, which appears on the screen between the 6 and 9 o'clock positions. Segment V of the liver might be seen in this view concerning the GB. In this view, the neck of the GB lies on the right side of the screen, while the fundus of the GB is on the left (Figure 5). From this station of GB, the right kidney and segment VI of the liver can be seen by clockwise rotation, especially in thin patients.

Gastric antral station: At the gastric antrum, the GB is situated close to the probe at 6 and 9 o'clock positions, typically achieved through counterclockwise rotation. Then, the scope tip faces the pyloric ring. At this station, the fundus of the GB lies on the right side of the screen, while the neck of the GB is on the left side. The GB may not be visualized at this station if it is contracted.

Duodenal bulb station: At the bulb of the duodenum, the scope can be intubated into the bulb of the duodenum and gently pushed into the apex of the duodenal bulb at the superior duodenal angle. A more gradual, gentler forward pushing of the probe against the superior duodenal angle creates a J-shaped position of the scope. With gentle manipulation of the scope, the PV can be identified on a long axis, which is the landmark of this station. Then, the scope is torqued in counterclockwise rotation while being withdrawn, and the tip is angled slightly downward to identify the liver. With some manipulation of the scope, upward or downward tip deflection, and push-in or pull-out movements, the GB and segment IV of the liver can be visualized below the GB (Figure 6). At this station, the fundus of the GB lies on the right side of the screen, while the neck of the GB is on the left side.

Descending duodenum station: Imaging from the descending duodenum requires entering the second part and shortening the scope. In the descending duodenum, the landmark for examination of the GB is the right kidney, which rotates clockwise. The GB can be visualized with slow scope withdrawal, anticlockwise rotation, and upward deflection. The GB fundus appears on the left side of the screen, close to the EUS probe, with the neck of the GB toward the right side (opposite to that of the antrum and D1). The GB is positioned close to the probe between the 8 and 11 o'clock positions.

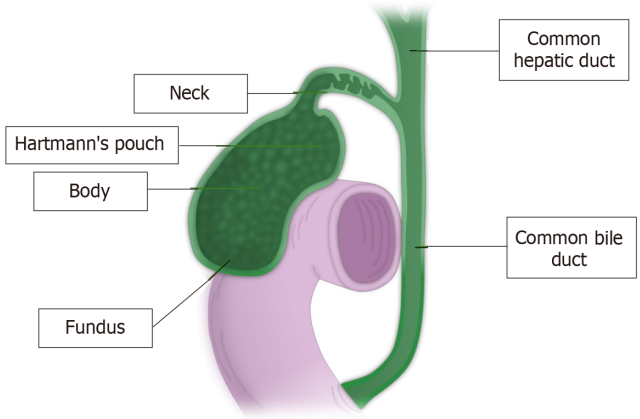

Figure 1 Gallbladder normal anatomy.

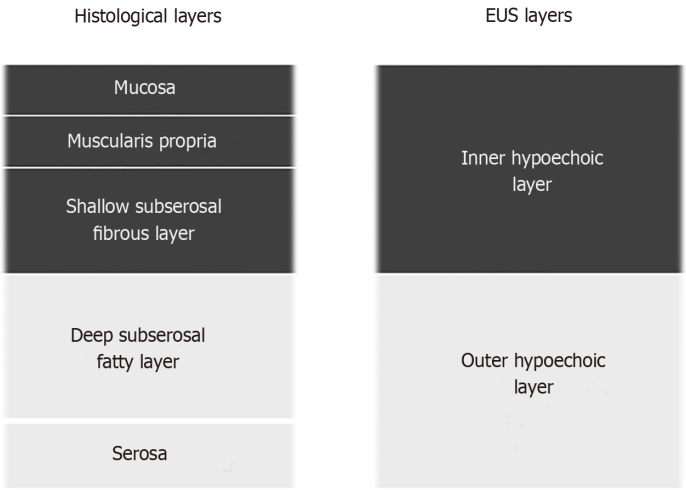

Figure 2 Comparison of gallbladder wall layers and endoscopic ultrasound findings. EUS: Endoscopic ultrasound.

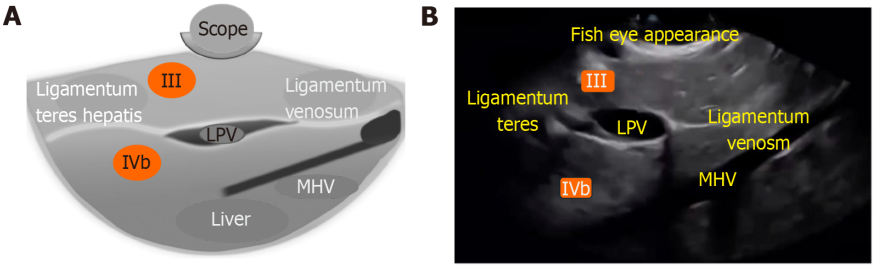

Figure 3 Fish-eye appearance of the umbilical portion of the left portal vein. A: Diagram of the umbilical portion of the left portal vein; B: Endoscopic ultrasound view which shows Fish-eye appearance of the umbilical portion of the left portal vein. LPV: Left portal vein; MHV: Middle hepatic vein; IVb: Segment 4b of the liver.

PRACTICAL APPLICATIONS OF EUS IN GB DISEASES

Diagnostic implications

The diagnostic role of EUS includes the detection of microlithiasis and GB stones, particularly in cases of idiopathic pancreatitis, differentiation of GB protuberant lesions (neoplastic or non-neoplastic), and conditions involving GB wall thickening. Protuberant GB lesions can be either non-neoplastic (cholesterol, hyperplastic, and inflammatory polyps) or neoplastic (adenoma or carcinoma). Wall-thickening disorders involve neoplastic thickening (carcinoma or lymphoma) and benign disorders such as inflammatory conditions (acute and chronic cholecystitis, xanthogranulomatous cholecystitis) and hyperplasia (adenomyomatosis and hyperplasia accompanying anomalous pancreaticobiliary junction)[14, 15].

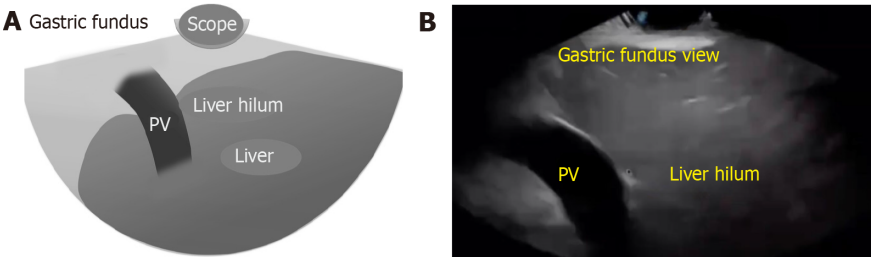

Figure 4 Liver hilum view from the gastric fundus. A: Diagram of the anatomical location of main portal vein at the liver hilum; B: Endoscopic ultrasound view of the main portal vein at the liver hilum. PV: Portal vein.

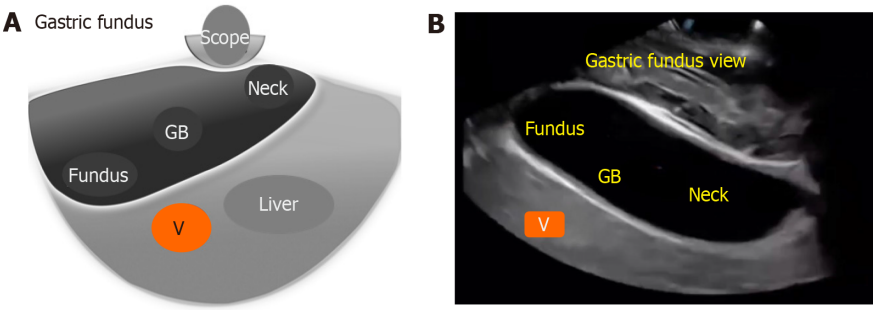

Figure 5 View of segment V of the liver and the gallbladder from the gastric fundus. A: Diagram of the gallbladder as seen from the gastric fundus; B: Endoscopic ultrasound view of the gallbladder as seen from the gastric fundus. GB: Gallbladder.

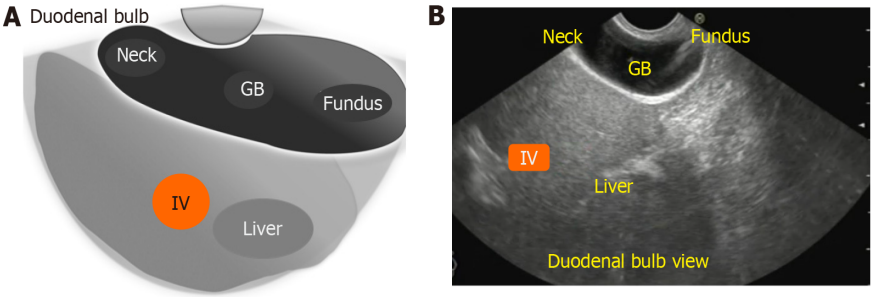

Figure 6 Biliary gravel are seen from the duodenal bulb. A: Diagram of the gallbladder view from the duodenal bulb; B: Endoscopic ultrasound view of the gallbladder gravel, less than 3 mm in diameter. GB: Gallbladder.

Gallstones: Trans-abdominal ultrasound (TUS) is the initial investigational tool for suspected GB stones. EUS has been studied for cholelithiasis detection, particularly microlithiasis, in cases of high clinical suspicion despite negative preliminary imaging tools, including TUS. Microlithiasis is defined as minute stones (less than 3 mm) in the GB and is also known as sludge, biliary gravel (Figure 6), sediment, and pseudolithiasis[16,17]. Two previous studies showed EUS's role in microlithiasis detection in more than half of patients with biliary colic with normal TUS, which implicated further management plans[18,19]. Similarly, in a case series of pediatric populations, EUS solved the suffering of three children who presented with unexplained recurrent upper quadrant pain despite negative results from other imaging tools, including TUS, CT, and magnetic resonance cholangiopancreatography (MRCP). EUS has revealed microlithiasis in GB, leading to subsequent laparoscopic cholecystectomy and intraoperative cholangiogram, ultimately alleviating post-operative pain[20]. To date, EUS has demonstrated a sensitivity of 92.6%–100% and a specificity of 55.6%–91% in diagnosing GB microlithiasis with a negative TUS test[4,18,21]. Generally, the diagnosis of minute GB stones (Figure 7) best illustrates the advantage of employing EUS over TUS.

After a cholecystectomy, a person may experience a range of signs and symptoms known as post-cholecystectomy syndrome (PCS), which can include right upper quadrant abdominal pain, dyspepsia, and/or jaundice. The biliary etiology of PCS can be related to early cholecystectomy complications, including biliary duct damage, biliary leak, retained cystic duct, or common bile duct stones[22]. In a study by Sezeur and Akel[23], cystic duct stones were found in 14.7% of patients during cholecystectomy, and these stones were not detected by pre-operative TUS or CT. EUS has been evaluated for detecting the cause of PCS in a study by Mohamadnejad *et al*[24], revealing the detection of missed stones in the remnant GB or cystic duct in 10% of the patients studied.

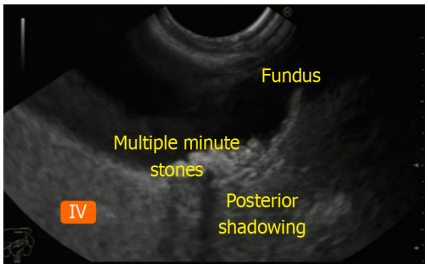

Figure 7 Gall bladder small stones with posterior shadowing, 3-5 mm in diameter.

Similarly, idiopathic acute pancreatitis (IAP) could be explained by identifying microlithiasis or biliary sludge missed on standard imaging methods. In patients with IAP, EUS has demonstrated a high diagnostic accuracy (60%–80%), comparable to endoscopic retrograde cholangiopancreatography (ERCP) but with a lower complication rate[25]. A recent systematic review and meta-analysis have demonstrated greater diagnostic accuracy for EUS than MRCP (64% *vs* 34%) in the etiologic diagnosis of IAP[26]. EUS should be considered a well-established method for identifying GB sludge and small stones in patients with unexplained right upper quadrant pain and those with PCS. Likewise, in the presence of IAP, EUS is still the preferred diagnostic test to rule out any missed tiny stones, mainly when MRCP results are negative.

GB polyps: Up to 5% of adults may present with GB polyps (GBPs)[27]. Nevertheless, differentiating neoplastic GBPs, including adenomas, carcinomas, and other malignancies, from non-neoplastic (mainly cholesterol polyps or adenomyomatosis) usually represents a challenging clinical dilemma. It is known that surgical intervention is not necessary for cholesterol, inflammatory, or fibrous polyps as they do not have the potential for malignant transformation. In contrast, managing adenomatous polyps is essential, as GB carcinoma has one of the worst prognoses among digestive system cancers, and the adenoma-carcinoma sequence is well recognized in the biliary epithelium of the GB[28]. Regarding safety and affordability, TUS is considered the first-line examination tool for GBPs. However, it has relatively low accuracy for GBPs[29]. In contrast, EUS, with its high resolution and proximity to the GB wall, was reported to improve the accuracy of differentiating GBPs compared to TUS (87% for EUS *vs* 52% for TUS)[30].

Considerable efforts have been undertaken to establish sonographic characterization along with subsequent scoring systems aimed at distinguishing neoplastic GBPs. Generally, findings suggestive of a neoplastic polyp include a single lesion with a diameter of more than 10 mm, a sessile appearance, an uneven contour, loss of normal wall layer structure at the base of the polyp, and hypoechogenicity on sonography[31]. Regarding polyp size, this was found to be the most significant variable predicting the neoplastic process in a five-variable-based EUS scoring system. Polyps more significant than 15 mm were positively associated with malignancy, while those ≤ 5 mm were all non-neoplastic[32]. A more recent systematic review of 5482 GBPs concluded that risk factors associated with an increased risk of malignancy were GBP > 6 mm, single GBPs, symptomatic GBPs, age > 60 years, Indian ethnicity, gallstones, and cholecystitis[33]. Another study of 70 patients using a similar scoring system revealed that size and heterogeneous internal echogenicity were positively associated with neoplastic changes, as opposed to the presence of hyperechogenic spots related to benign polyps[34]. In another study by Ma *et al*[35] in 2022, the following preoperative scoring system was used in the differentiation of benign and malignant polyps. This system utilized the following factors: The cross sectional area, positive blood flow, age > 55.5 years, alanine transaminase (ALT) > 50 U/L, and ALT/aspartate transaminase (AST) > 0.77. This scoring system has a total score of 15, polyps with a score of > 6.5 are classified as high risk and polyps with a score of < 6.5 are classified as low risk[35].

On the other hand, while the accuracy for EUS was consistently superior to TUS in detecting neoplastic GBPs, different accuracies were observed for polyps sized less than 10 mm *vs* larger ones (44% *vs* 89%, respectively) on EUS. This difference indicates the need for an adjunct dedicated diagnostic technology to improve the EUS accuracy, particularly for smaller polyps. Contrast-enhanced harmonic EUS (CE-EUS) was utilized to improve EUS's ability to detect neoplastic GBPs. In the prospective study by Choi *et al*[16], CE-EUS improved the accuracy of conventional EUS, with a sensitivity and specificity of 93.5% and 93.2%, respectively, for CE-EUS, compared to 90.0% and 91.1% for conventional EUS. In their study, malignant GBPs could be accurately predicted by CE-EUS perfusion deficits or the presence of irregular intramural vasculature.

In another smaller retrospective study by Park *et al*[36], CE-EUS was utilized for the differentiation of adenomas *vs* cholesterol polyps, achieving a sensitivity of 75.0% and a specificity of 66.6%. Even though EUS has been shown to be effective in the diagnosis of GBPs especially malignant ones, the SRU consensus committee agreed that it should not be included in the routine evaluation of GBPs due to its invasive nature[37]. The surgical approach remains a safe and commonly used treatment option for GBPs larger than 1 cm. Nonetheless, EUS may be suggested as a surveillance method for polyps that do not meet the resection criteria, particularly those between 5 and 10 mm in size, with consideration of surgery if suspicious features are defined[24].

GB carcinoma: When there is a loss of homogeneity in the inner hypoechoic layer, as illustrated in Figure 5, and there is a diffuse or localized uneven thickening of the GB wall, GB carcinoma is possible[13]. Due to its ability to show the multilayer GB wall structure, distinguish between benign and malignant polyps, and accurately delineate the degree of wall invasion, EUS provides a precise diagnosis and staging of GB carcinoma and guides the optimum surgical procedure for GB lesions, whether laparoscopic or open surgery. Indeed, EUS staging for GB carcinoma depends mainly on the

integrity of the wall layers at the base of a GBP, which continues to be the best determinant of deep invasion.

In a retrospective study with high interobserver agreement, Fujita *et al*[38] categorized GB tumors according to the depth of invasion into four categories: Type A is a pedunculated mass with a finely nodular surface, and no abnormality of the GB wall adjacent to it, indicating stage T following a comparison of EUS and histopathology. Type B is a broad-based mass with an irregular surface but no interruption of the GB wall's outer hyperechoic layer, correlating with T1 (Figure 8). Type C is an irregular outer hyperechoic layer caused by the mass echo effect and indicates T2. Type D is a disruption of the outer hyperechoic layer invading the adipose layer of the subserosa, correlating with T3 or T4[38]. The corresponding accuracies for the four types were 100%, 76%, 85%, and 93% in a subsequent trial by Sadamoto *et al*, in 41 patients with GB carcinoma[39].

Increased GB wall thickness: Many disorders are associated with GB wall thickening, including benign conditions such as inflammation (Figure 9), adenomyomatosis, or malignancy. To date, distinguishing between both disorders in these cases remains challenging, and the role of EUS in the etiological diagnosis of GB wall thickening is still poorly characterized. Intramural cystic space, the contour of the lesion, patterns of GB wall enhancement, and patterns of wall thickness are all employed as differential points[15].

GB adenomyomatosis is a relatively common benign condition, diagnosed in 2–8% of all cholecystectomies, resulting from hyperplasia of the GB wall epithelium and the development of intramural diverticula, known as Rokitansky-Aschoff sinuses (RAS), which is considered a pathognomonic finding. Adenomyomatosis is categorized according to the level of wall involvement into one of three types: fundal (a focal lesion in the GB fundus), segmental (diffuse thickening of the neck or body), or diffuse[40]. The thickened wall in GB adenomyomatosis typically has a smooth surface. However, surface irregularity, indicative of hyperplastic alterations, can rarely be seen. Confirming the existence of cystic anechoic patches reflecting RAS inside the thickened wall is crucial for diagnosis. Sometimes, comet tail artifacts are seen as a result of multipath reflection from intramural calculi or the RAS[15].

Xanthogranulomatous cholecystitis (XGC) is a rare condition characterized by chronic GB inflammation. Its clinical presentation resembles that of cholecystitis, and due to pronounced tissue-destructive alterations, the inflammation occasionally impacts nearby organs such as the liver and transverse colon, making it exceedingly challenging to identify GB carcinoma. In XGC, the subserosa layer of the GB wall thickens most prominently, and there is uneven GB wall thickening and fibrosis present. The condition may develop due to stones in the GB neck, bile leakage into the GB wall from a ruptured RAS, or mucosal ulcers[13]. XGC was found in 1.5% of a large 15-year series of cholecystectomy cases and was related to lithiasis in 85% of cases[41]. GB cancer may be a probable cause in cases without lithiasis. Occasionally, EUS can detect hyperechoic nodules in the GB wall, most likely XGC. However, it is frequently challenging to distinguish between benign and malignant conditions based just on EUS[15].

Anomalous pancreaticobiliary junction is a congenital condition in which both pancreatic and bile ducts join away from the duodenal wall, usually forming a long common channel leading to the reflux of pancreatic juice into the biliary tree[42]. As a result, the mucous membrane of the GB undergoes hyperplastic alterations, which are hypothesized to induce a pathway to dysplasia and then GB carcinoma[13]. EUS accurately diagnosed anomalous pancreaticobiliary junctions, even in asymptomatic patients with GB wall thickening and those without biliary dilatation[43].

Gallbladder carcinoma (wall-thickening type): The wall-thickening type of GB carcinoma usually exhibits uneven or papillated mucous membranes, thicker patches that are not uniform in thickness, and an unclear layered structure. Additionally, RAS-reflecting microcysts and comet tail artifacts are typically not seen[15]. The most precise EUS finding for diagnosing GB cancer in the study by Mizuguchi *et al* was the loss of multiple-layer patterns of the GB wall[44]. Additionally, wall thickening of more than 10 mm and internal echogenicity were linked to neoplastic wall thickening on multivariable analysis in a large series, including 134 patients with GB wall thickening[45]. Using contrast enhancement during harmonic EUS examination has increased its accuracy in detecting malignant GB wall thickening up to 94% compared to 73% for the standard EUS examination[46].

Moreover, EUS can be used to identify GB involvement in other less prevalent disorders, such as sclerosing cholangitis [47], portal biliopathy causing internal GB varices[48], GB parasites[49], Mirizzi syndrome[50], and GB papillomatosis [51].

EUS-guided FNA of gallbladder lesions: EUS-FNA from GB lesions is usually reserved for cases where a pathological diagnosis cannot be achieved even after cytological analysis of bile obtained by endoscopic transpapillary drainage[15]. EUS-FNA has been evaluated and has shown high accuracy in diagnosing malignant tumors, with sensitivity ranging from 80% to 96%[5,52] and a low rate of complications. However, acute cholecystitis[53] and biliary peritonitis[54] have been reported following FNA of a GB mass and after bile aspiration, respectively. Tamura *et al*[55] have proposed an approach considering the risk of EUS-FNA in cases of GB masses (Figure 8): Start by obtaining tissue *via* an ERCP-guided biopsy, then perform EUS-FNA from metastatic liver lesions or lymph nodes when present, and conclude with EUS-FNA from the GB mass itself. Similarly, during the FNA procedure and puncturing the GB wall, it is essential to gain stroke distance by tangentially puncturing the GB wall, avoiding puncture through the lumen.

Moreover, it is advisable to puncture the neck side of the GB to avoid sliding the GB wall during the procedure. Furthermore, it is best to target either the liver parenchyma or the GB wall that is in contact with the liver in case of liver invasion by the tumor[15]. Additionally, it was suggested to use 25-gauge EUS FNA needles when attempting FNA from GB lesions and to decrease the number of needle passes, aiming to ameliorate the risk of adverse events[28].

Contrast-enhanced EUS: The first report by Hirooka *et al*[56] declared the superiority of C-EUS using sonicated albumin over the standard EUS approach in differentiating GB lesions and evaluating the depth of tumor invasion. A study of 93

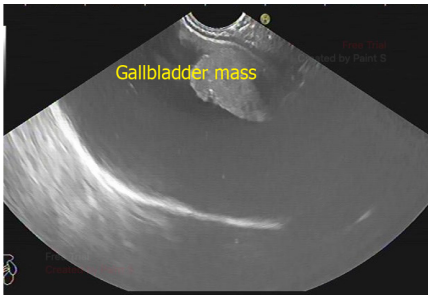

Figure 8 Gall bladder malignant mass.

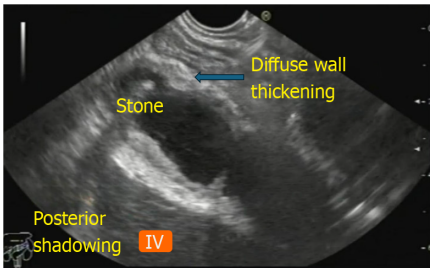

Figure 9 Inflammatory diffuse gallbladder wall thickening with well differentiated wall layers.

patients with GBPs greater than 10 mm confirmed these findings, revealing intratumoral irregular vascularization by C-EUS with a sensitivity of 93.5% and a specificity of 93.2% for malignancy[57]. C-EUS performed much better diagnostically than standard EUS in cases of GB wall thickening (94.4 *vs* 73.1%)[46]. A study by Kamata *et al*[58] found that GB carcinoma was characterized by heterogeneous enhancement in the perfusion image and irregular vessels on C-EUS, with a sensitivity, specificity, and accuracy of 90%, 98%, and 96%, respectively.

Therapeutic role of EUS in the gallbladder

EUS-guided GB drainage: According to Tokyo Guidelines 2018 (TG 2018), early surgical treatment using the laparoscopic approach is generally accepted as the treatment of choice for acute cholecystitis[59]. Patients who are poor surgical candidates due to high-risk comorbidities, including cirrhosis, ascites, coagulopathy, cancers, and cardiopulmonary conditions, are managed conservatively with percutaneous GB drainage (PGBD) or endoscopic transpapillary GB drainage (ETGBD). However, these procedures have several limitations[60].

Indications for EUS-GBD include patients with acute cholecystitis who are non-surgical candidates with or without stone extraction, as a bridge to surgical cholecystectomy, conversion from PGBD to EUS-GBD, an alternative to failed PGBD/ETGBD, and an alternative to failed EUS-guided biliary drainage, such as EUS-CDS or EUS-HGS, in patients with malignant biliary obstruction[60].

Selection of the approach: The GB can be accessed from the gastrointestinal tract by both the distal gastric antrum (transgastric approach) and duodenal bulb (transduodenal approach)[61]. There is no evidence of clinical differences between the two sites. Tyberg *et al*[61] reported that the location of the stent was not a significant predictor of clinical failure (P = 0.432) or adverse events (P = 0.289). However, the transduodenal approach is technically less challenging, as the duodenum may have less mobility than the stomach, and the risk of stent migration and food reflux into the GB through the stent is lower with this approach[62].

The transgastric approach in the stomach has some benefits, especially in stent deployment, as the puncture will be through the GB, providing a larger entry point. Additionally, it is the preferred approach for patients who will ultimately undergo cholecystectomy, attributed to the simplified fistula closure. Surgery is more accessible for patients with this approach in cases of perforations and stent migration[62].

In cases of surgically altered anatomy, such as Roux-en-Y gastric bypass, the anastomotic tract may be between the GB and jejunum (cholecystojejunostomy). The decision to create a cholecystoduodenostomy, cholecystogastrostomy, or cholecystojejunostomy is based on operator preference, patient-specific anatomy, and proximity of the GB to the lumen [62].

Technique: A 19-gauge needle is used to puncture the GB, and contrast is injected to confirm the location. A 0.025-inch or 0.035-inch guidewire is then passed through the needle and coiled into the GB. The fistula can be dilated using a bougie (6F or 7F) or tapered-tip balloon dilator (4 mm), followed by the insertion of plastic double-pigtail stents[63] or fully covered self-expandable metal stents (FCSEMS), which is preferable to plastic stents due to incidences of bile leaks attributed to their small diameter and their association with potential complications such as pneumoperitoneum, bile peritonitis, and stent migration.

Using a single-step electrocautery-enhanced delivery system, the lumen-apposing metal stent (LAMS) is an excellent alternative. The main advantages of LAMS include a lower risk of stent migration, better tissue apposition, and a reduced risk of leakage and tissue ingrowth due to the silicon lining. LAMS also have a larger diameter than plastic stents or FCSEMS, which helps reduce the risk of stent obstruction and plays an excellent role in stone extraction and cholecystography. Additionally, the removal of LAMS is accessible[59]. All these advantages affect the technical success rate, especially as LAMS is a single-step procedure[59].

A retrospective study was conducted to compare the technical success rates between cold and hot AXIOS, and it showed that there were no significant differences [100% (10/10) *vs* 95.9% (47/49) respectively, $P = 1.00$]. The rate of adverse events was not significantly different[64].

Endoscopic laser lithotripsy and lithotomy through the lumen-apposing metal stent for giant GB stones: Wang *et al*[65] reported five patients who were treated using endoscopic laser lithotripsy and lithotomy through the LAMS for giant GB stones, with a 100% success rate. There was no gallstone recurrence in the mean 27.8-month follow-up (24-36 months). Endoscopic laser lithotripsy and lithotomy should be performed at least two weeks after the LAMS implantation[65]. Larghi *et al*[66] reported one video case of a 74-year-old female patient with acute calculus cholecystitis and a history of inoperable bismuth IV cholangiocarcinoma. An EUS-guided cholecystogastrostomy, using a fiber-optic cholangioscopy system (SpyGlass) assisted in the holmium laser lithotripsy of symptomatic gallstones performed *via* the lumen-apposing FCSEMS, was performed using hot AXIOS. On the second day, balloon dilatation was conducted, followed by inserting the SpyGlass scope using therapeutic gastroscopy, and the holmium laser lithotripsy was successfully performed[66].

LIMITATIONS OF LINEAR EUS USE IN THE DIAGNOSIS OF GALLBLADDER DISEASES

The major limitation of linear EUS in the diagnosis of GB diseases is its invasive nature. Furthermore, this type of EUS does not have high diagnostic ability in the early stages of GB cancer as it cannot clearly differentiate between T1 and T2 stage of GB cancer[5]. This has limited its application in the diagnosis of GB lesions. Furthermore, even though the few conducted studies have not reported major complications related to the use of this type of EUS in the diagnosis of GB pathologies, the risk of bleeding and tumor seeding are still high with the continuous use of EUS in the diagnosis of GB pathologies such as GB cancer[55,58].

CONCLUSION

The endosonographic assessment of GB has emerged as a problem-adjunct tool for assessing GB conditions when conventional imaging methods prove inadequate for diagnosis. While providing a more comprehensive evaluation, EUS is reserved for specific cases due to its invasive nature compared to non-invasive imaging techniques. In general, linear EUS evaluation of biliary tract (including the GB) is effective and feasible following the station wise mechanisms. In addition, linear EUS should be considered a sensitive mechanism for detecting gallstones and can be significant in high-and intermediate-risk patients when the gallstones are not detected by imaging techniques.

FOOTNOTES

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