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Review Article

Review Article

Endoscopic ultrasound in portal hypertension: navigating venous hemodynamics and treatment efficacy

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Abstract

Portal hypertension-related complications increase mortality in patients, irrespective of its etiology. Classically, endoscopic ultrasound (EUS) was used to assess the portal venous system and collaterals, considering size and hemodynamic parameters, which correlate with portal hypertension (PH) and related complications. Furthermore, therapeutic EUS guides treatment interventions, such as embolization of the gastric varices through coil placement and tissue adhesive injection, yielding encouraging clinical results. Recently, the direct measurement of portal pressure, emerging as an alternative to hepatic venous pressure gradient, has shown promise, and further research in this area is anticipated. In this review, we aimed to provide a detailed description of various possibilities for diagnosing vascular anatomy and hemodynamics in PH and actual knowledge on the EUS usefulness for PH vessel-related complications. Also, future promises for this field of endo-hepatology are discussed.

Keywords: endoscopic ultrasound; portal hypertension; esophageal varices; gastric varices; gastrointestinal hemorrhage; cirrhosis; portal pressure gradient

Introduction

Portal hypertension (PH) is a clinical syndrome associated with cirrhosis of various etiologies, but pre-sinusoidal and post-sinusoidal causes are also encountered. The consequences of PH, such as collateral circulation, variceal bleeding, ascites and hepatic encephalopathy, contribute to higher mortality rates. The median survival for patients with compensated cirrhosis is approximately 15 years, while it drops to 2 years for those with decompensated cirrhosis and further declines to just 9 months for advanced decompensated stages. A meta-analysis including 1113 patients showed that reducing PH was associated with a lower risk of death or liver transplantation (OR = 0.50 in patients without ascites and 0.47 in patients with ascites), and with a lower rate of events (OR = 0.27), such as refractory ascites, spontaneous bacterial peritonitis or hepatorenal syndrome [1]. Therefore, PH assessment is mandatory for detecting patients at risk for decompensation and bleeding.

Endoscopic ultrasound (EUS) vessel assessment was usually performed for tumor staging of biliopancreatic pathology, but more recently, it has been employed in both the minimally invasive diagnosis and treatment of PH [2]. Although EUS is not used for esophageal varices screening due to its higher costs than conventional upper digestive endoscopy, it identifies their presence earlier. In addition, its place in the armamentarium for treating gastric varices is still under evaluation with promising results [3]. This new field of endo-hepatology has progressed towards the portal venous system hemodynamics measurements, which could represent a useful guide for preventing and treating PH-related complications.

A systematic PubMed search was performed to identify relevant peer-reviewed literature published between the beginning of 1999 and the end of 2023. The search terms were: 'endosonography' OR 'endoscopic ultrasound', AND 'portal hypertension', 'esophageal varices', 'gastric varices', 'gastrointestinal hemorrhage', 'cirrhosis', 'portal pressure gradient'. The search was completed by manual inspection of the reference lists of review articles and original articles. This review aimed to emphasize the role of EUS in assessing the ultrasound semiology and hemodynamic functionality of the venous system in PH and the treatment efficacy of its complications.

Etiology and pathophysiology of PH

The etiology of PH is briefly classified into non-cirrhotic and cirrhotic categories. Liver cirrhosis can arise from various causes, including viral infections (such as hepatitis B and C), alcohol-

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Table 1. Etiology of portal hypertension

Obstacle site	Disease
Prehepatic	PVT; fistula; external compression of the portal vein
Hepatic	
Presinusoidal	PSVD, nodular regenerative hyperplasia, sarcoidosis, congenital hepatic fibrosis, Primary biliary cholangitis, hepatic amyloidosis
Sinusoidal	Cirrhosis, acute liver injury
Postsinusoidal	Budd-Chiari syndrome, sinusoidal obstruction syndrome
Posthepatic	Budd-Chiari syndrome, congestive hepatopathy

PSVD, portosinusoidal vascular disorder.

related liver disease, autoimmune or inherited disorders and metabolic dysfunction-associated steatotic liver disease [4, 5]. Non-cirrhotic PH can be classified as extrahepatic pre-sinusoidal (in cases like portal vein thrombosis [PVT]), intrahepatic pre-sinusoidal (in conditions like portal-sinusoidal vascular disorders) and post-sinusoidal (as seen in Budd-Chiari syndrome) (Table 1) [6–8].

Scar tissue and regenerative nodules in the cirrhotic liver lead to vascular obliteration, constituting the structural component of PH, while endothelial dysfunction coupled with the activation of hepatic stellate cells represents the functional component [9, 10]. Increased portal pressure is caused by high intrahepatic vascular resistance due to intrahepatic fibrosis deposition and an exaggerated response to vasoconstrictors and progressive compensatory systemic changes leading to vasodilatation and a hyperdynamic circulatory status [11], followed by a progressive decrease in effective arterial blood volume and renal perfusion. Compensatory mechanisms are activated in response to the decreased circulating blood volume, stimulating angiogenesis and the formation of collaterals [12]. Another important factor in PH is bacterial translocation [13–15]. The interaction between bacterial translocation and PH is bidirectional. PH induces intestinal interstitial edema, facilitating bacterial translocation. Bacterial products, through pathogen-associated molecular patterns, stimulate the hepatic innate immune system by activating Kupffer cells and hematopoietic stem cells, ultimately leading to the worsening of PH [9, 16].

The natural history of cirrhosis includes compensated, silent phase, during which portal pressure gradually increases and liver function worsens leading to the decompensated phase, when symptoms become noticeable, commonly including ascites, bleeding, encephalopathy and jaundice [17]. Once these symptoms appear, the liver function usually deteriorates more rapidly and the course of the disease is marked by additional complications, such as rebleeding, acute kidney injury, hepato-pulmonary syndrome, portopulmonary hypertension, bacterial infections and hepatocellular carcinoma [18].

EUS assessment of static response of vessels to PH

EUS can closely visualize the entire vascular system of the portal system, allowing for detailed observation of the static response as reflected by the diameter of the component vessels. It can also detect the presence of collaterals, such as varices, as well as intravascular complications like PVT.

EUS and the portal venous system

Portosystemic collaterals form as a result of PH, aiming to divert blood from the portal circulation to the systemic circulation as a compensatory mechanism to lower pressure in the portal system. In patients with cirrhosis, varices occur in about 50% of cases, and approximately 15% to 20% of these individuals experience bleeding from esophageal varices within 1–3 years following their diagnosis [19]. Furthermore, the mortality rate within 6 weeks following variceal bleeding stands at 20% [20, 21]. The left gastric vein (LGV) primarily supplies blood to gastroesophageal varices, which run in the submucosal layer and drain into the azygos vein, establishing a connection with the territory of the superior vena cava [22]. In the retroperitoneal area, linkages with the inferior vena cava territory are established through several connections: between the splenic and pancreatic veins and the left renal vein, between the splenic and colic veins and the lumbar veins on the posterior abdominal wall, and between the hepatic veins and the diaphragmatic veins as well as the right internal thoracic vein. Other anastomoses are established with subcutaneous veins in the anterior abdominal wall through the para-umbilical vein or with the internal iliac and pudendal veins with the rectal veins [23].

Portal vein assessment

The portal vein typically measures 8 cm in length and has a diameter of up to 13 mm in normal adults. EUS identifies it from the level of the duodenal bulb and antrum, with the echoendoscope positioned upwards, by highlighting the spleno-mesenteric confluence beyond the pancreatic isthmus toward the liver hilum. Additionally, from the vertical part of the stomach, with the scope in counter-clock rotation, the part of the portal vein situated near the liver and its division into right and left branches can be visualized. This is the preferred location to be punctured for various indications, such as pressure measurement, portal liquid biopsy and thrombus biopsy. The transhepatic puncture with the fine needle aspiration (FNA) needle is preferred for lowering bleeding risks. A single study assessed time-averaged maximum velocity, as well as minimum and maximum flow velocity using Doppler ultrasound, which were correlated with the size of gastric varices but not with the size of esophageal varices [24].

Splenic vein assessment

The normal diameter of the splenic vein is typically less than 9 mm. EUS provides optimal visualization of the splenic vein at the gastric body/fundus, and allows for tracking it from the splenic hilum to its confluence with the portal vein. Although an enlarged splenic vein can be a sign of PH, its diameter often remains normal in Child A cirrhosis [25], but limited data exist on its association with PH. One study described the correlations between the splenic vein flow and the size of gastric varices [24]. Splenic vein thrombosis has been associated with collateral circulation, particularly following acute pancreatitis episodes or in the presence of malignancies, and it can be targeted for tissue acquisition if needed [26]. There have been reports of incidental splenic vein aneurysms detected by EUS during other investigations [27, 28].

Superior mesenteric vein assessment

The superior mesenteric vein (SMV) can be effectively visualized using EUS from the second part of the duodenum and duodenal bulb, extending beyond the pancreatic parenchyma. Its normal diameter ranges from 6 to 7 mm. It can be followed until the splenic-mesenteric confluence, posteriorly from the pancreatic isthmus. SMV visualization has been described in the context of pancreatic tumor staging [29], and less frequently in cases of PH-related vascular malformations [30]. However, as far as we know,

the implications of EUS in detecting SMV changes for predicting PH are yet to be established.

Left gastric vein assessment

The LGV usually originates at the midpoint of the lesser curvature of the stomach, courses posterior to the lesser sac and terminates at the portal-splenic vein junction [31]. Among phrenic veins and gastrorenal shunts, the LGV and posterior/short gastric vein represent afferent/efferent vessels for fundic gastric varices [32]. It forms an anastomosis with the lower esophageal veins belonging to the superior vena cava system. Its flow velocity together with the MELD score was considered useful for predicting variceal bleeding occurrence [33]. The pressure of LGV measured by direct puncture was strongly correlated with portal vein pressure [34] and the association between LGV velocity and variceal size has also been reported [35]. In a study with 30 participants, the effectiveness of direct EUS-guided treatment (involving cyanoacrylate injection and coil deployment) on the feeding vessels of gastric varices (identified from the cardia to 3 cm above) was examined. LGV was identified as the feeding vessel in 70% of the cases. The treatment had an 86% success rate, and variceal obliteration was accomplished in 96.6% of the patients [36].

After the endoscopic treatment of varices and EUS splenic embolization the diameter of the LGV decreased [37]. In a study of 306 patients who underwent endoscopic treatment, similar EUS flow parameters were observed in both the LGV and the paraesophageal vessels [38]. Additionally, Doppler-EUS measurements revealed significantly lower flow velocity in the LGV trunk among patients who responded to endoscopic therapy compared to non-responders (9.9 cm/sec vs. 13.9 cm/s, $P = 0.02$) [39]. Patients with an LGV velocity exceeding 12 cm/s and a dominant anterior branch pattern tended to experience variceal recurrence more quickly than the others [40]. Moreover, the anterior branch, which directly feeds varices, disappeared through long-term follow-up under repeated variceal endoscopic treatments, while the posterior branch acted as an extravariceal shunt [41].

Azygos vein assessment

The azygos vein is visualized as an anechoic structure of 3–5 mm in diameter, between the descending abdominal aorta and spine. In the case of PH, it ensures the blood flow through gastroesophageal collateral vessels and varices; thus, it was considered an indirect tool for assessing the PH. Color Doppler EUS has been useful for assessing the azygos vein after the injection of terlipressin or somatostatine [42] or octreotide [43]. However, another study on 34 patients proved no correlation between hepatic venous pressure gradient (HVPG) and the azygos vein flow [44].

EUS diagnosis of varices

EUS can visualize varices as anechoic vascular structures situated in the submucosa of the esophagus or stomach, and can sometimes identify ectopic varices situated in the duodenum, in a gastro-duodenal anastomosis, or in the biliary tree. Paraesophageal vessels are seen in the adventitia, outside the muscle layer and they establish the connection with the superior vena cava via the azygos vein. Perforating vessels establish the connection between esophageal varices and para-esophageal veins, and they have been proven to correlate with PH, variceal recurrence and bleeding occurrence [45]. Portal gastropathy can also be visualized as a diffuse thickened submucosal and mucosal layer featuring multiple small, round, anechoic structures, with Doppler signal in the submucosal layer being a useful tool for differentiating it from diffuse adenocarcinoma and Menetrier disease [46–48].

EUS diagnosis of PVT

PVT occurs in cirrhosis in up to 25% of cases [49], and its impact on the prognosis of these patients is still a matter of debate. Patients presenting with PVT and acute variceal bleeding have higher rates of 14-day and 6-week rebleeding and higher mortality rates [50]. It is still unknown how much PVT contributes to a further increase in PH. There have been some previous attempts to evaluate the response to the non-selective beta-blocker treatment in patients with non-cirrhotic PVT, measuring the portosystemic gradient through the difference between the splenic pulp pressure (the direct puncture of the splenic pulp) and the free hepatic venous pressure [51]. However, lacking the standardization of this technique, it is difficult to draw solid conclusions. In this regard, EUS-portal pressure gradient (EUS-PPG), by being able to directly assess the portal vein hemodynamics, could make a difference in the field but no report exists on the EUS-PPG in patients with PVT.

Assessing PVT also involves determining whether the thrombus is of tumoral origin. The presence of neovascularization within the thrombus and its extent can indicate a malignant nature, which then informs subsequent treatment strategies. In cases where traditional contrast-enhanced imaging techniques (like Doppler ultrasound, CT scan or MRI) struggle to differentiate between malignant and benign thrombosis in the portal venous system, EUS-guided FNA becomes crucial. The utility of EUS in diagnosing PVT, as shown in various studies (Table 2), including the use of FNA, has been established as both safe and effective in ascertaining the nature of PVT, with no significant complications reported.

Apart from its importance in signaling the presence of hepatocellular carcinoma in patients with cirrhosis, the presence of PVT might increase the pre-sinusoidal pressure, which impedes the correct appreciation of HVPG measurements, and then only the direct PPG remains reliable.

EUS hemodynamic assessment of PH

The diagnosis of PH in cirrhosis is defined as a PPG > 5 mmHg. The concept of the gradient was adopted to minimize the risk of inaccuracy resulting from a single vessel measurement. Once the gradient exceeds 10 mmHg, the patients are at risk of PH-related complications even if the patients are completely asymptomatic and without indirect signs of PH like collateral circulation [52]. Early detection is essential for prompt intervention and prevention of further decompensation, ultimately reducing morbidity and mortality in these patients [53].

The gold standard for measuring PH is the HVPG. This method indirectly assesses PH, as it does not require direct puncture of the portal vein; instead, it uses a balloon catheter to measure pressure gradients within the hepatic veins. Defined as the difference between wedged hepatic vein pressure (WHVP, measured with the balloon inflated) and free hepatic vein pressure (FHVP, with the balloon deflated), HVPG estimates portal pressure through the gradient that the portal blood flow needs to exceed to overcome the hepatic sinusoidal resistance. It ranges between 1 and 5 mmHg in healthy individuals, and it is highly correlated with portal vein pressure as long as presinusoidal portal vein occlusion is absent. An HVPG > 10 mmHg corresponds to clinically significant PH and it is correlated with the development of esophageal varices, whereas a HVPG > 12 mmHg is associated with an increased risk of variceal bleeding [1]. Although the HVPG measurement through the transjugular route is a very good surrogate for PPG, it has its limitations. This standard procedure requires technical training and expertise and has a few inconveniences,

Table 2. EUS-FNA for PVT

Study, year	Diagnosis	No. of patients	FNA-needle	Number of FNA passes	Technical success (%)	Adverse effects
Lai *et al.*, 2004 [111]	PVT in HCC	1	22G	3	100	No
Storch *et al.*, 2007 [112]	PVT in HCC	1	22G	4	100	No
Michael *et al.*, 2011 [113]	PVT in HCC	1	25G	4	100	No
Moreno *et al.*, 2014 [114]	PVT in hidden HCC	1	22G	NA	100	No
Kayar *et al.*, 2015 [115]	PVT in HCC	3	25G	NA	100	No
Rustagi *et al.*, 2017 [116]	Remote PVT	13	22/25G	3 (mean)	100	No
Gimeno *et al.*, 2018 [117]	PVT and chronic liver disease	7	NA	NA	87.5	No
Eskandere *et al.*, 2021 [118]	PVT in cirrhosis and/or HCC	34	22G	1–2	100	No

PVT = portal vein thrombosis, HCC = hepatocellular carcinoma, FNA = fine needle aspiration.

Table 3. Comparison of the EUS-PPG and HVPG

Procedure	HVPG	EUS-PPG
Route	Transvenous (transjugular most often)	Transgastric
Puncture site	Internal jugular vein	Transhepatic
Measurement site	Hepatic veins	Left or middle hepatic vein; portal vein
Measurement	Indirect	Direct
Anesthesia	Not required	Required, usually can be done with mild sedation
X-ray exposure	Yes	No
Contrast exposure	Yes	No
Side effects	Cardiac arrhythmias, hematoma at puncturing site	Abdominal pain, bleeding
Disadvantages	Underestimates PH when prehepatic portal hypertensions exists; PSVD, primary biliary cholangitis; requires special training and expertise	Need for endoscopy, mild sedation required, minimally invasive, requires special training and expertise

EUS-PPG = EUS-guided portal pressure gradient, HVPG = hepatic venous pressure gradient, PH = portal hypertension, PSVD = portosinusoidal vascular disorder.

such as the risk of cardiac arrhythmias and exposure to contrast and X-rays (Table 3). This indirect technique is not always reliable, such as in presinusoidal causes of PH where HVPG can be artificially normal and does not reflect the actual degree of PH [54]. Additionally, Baveno VII consensus highlighted that in patients with primary biliary cholangitis, an additional presinusoidal component of PH may be present, which cannot be assessed by HVPG, resulting in underestimation of the presence and severity of PH by using HVPG [53] (Table 4). Moreover, hepatic venous-to-venous collaterals were an essential factor in underestimating wedged hepatic venous pressure and HVPG, especially in the vascular liver diseases scenarios. It seems that the earlier the collateral branches appear, the greater the underestimation of PH [55].

EUS measurement of the PPG was initially described in an animal study using a 22G FNA needle and demonstrated an excellent correlation with transhepatic catheterization ($r = 0.91$) [56]. Subsequent animal studies further supported EUS-PPG as a reliable tool [57–59]. Opening a new era in the field of endohepatology in humans, EUS-PPG measurement has been successfully applied in several centers (Table 5).

Technically, the hepatic vein and the portal vein should be approached (Figure 1). The most convenient route for hepatic veins puncture is at the level of the cardia with the echoendoscope oriented clockwise towards the subdiaphragmatic part of the left liver lobe, highlighting the inferior vena cava close to its opening in the right atrium, within 2–3 cm of its confluence with the inferior vena cava. At this level, the three hepatic veins with thin walls are easily seen: the left hepatic vein divides the medial lobe from the lateral left lobe segments, while the middle hepatic vein divides the right hepatic lobe from the left hepatic lobe. For the EUS-PPG, the middle or the left hepatic vein has to be punctured, but sometimes, in case of very fibrotic hepatic tissue or in Budd Chiari syndrome, their visualization is difficult and then the inferior vena cava is to be approached. In such a situation, it can be punctured through the liver tissue in the intrahepatic/retrohepatic region or directly above the liver parenchyma and junction with the hepatic veins, although its value compared to hepatic vein pressure is unknown. In most cases, the measurements are done through the transgastric route, but the transduodenal approach has been described, with no complications reported [34, 60].

Regarding sedation, it is known that moderate to deep sedation may cause inaccurate HVPG measurements, and light sedation with 0.02 mg/kg is preferred during transjugular measurements [53]. Further assessment concerning the influence of sedation on the level of EUS-PPG measurement is awaited, given that the studies published so far have used moderate to deep sedation.

Table 4. Pressure differences depending on the location of the obstacle causing portal hypertension

Obstacle site	WHVP	FHVP	HVPG
Hepatic			
Presinusoidal	N	N	N
Sinusoidal	↑	N	↑
Extrahepatic			
Presinusoidal	N	N	N
Postsinusoidal	↑	↑	↑
Post-hepatic	↑	↑	↑ or N

WHVP = wedged hepatic vein pressure, FHVP = free hepatic vein pressure, HVPG = hepatic venous pressure gradient, N = normal, ↑ = raised.

Table 5. EUS-PPG measurement in human studies

Study, year	No. of patients	FNA-needle	Technical success rate (%)	Technical problems	Sedation	Mean pressures (mmHg)	Conclusion
Fujii-Lau *et al.*, 2014 [63]	1, case report	22G	100	None	NA	PVP = 11 HVP = 10 PPG = 1	EUS measurement proved to be safe
Huang *et al.*, 2017 [58]	28, P	25G	100	none	Moderate sedation or general anesthesia	PPG = 8.2	Excellent correlation of PH with clinical parameters
Zhang *et al.*, 2021 [60]	12, P	22G	91.7	Puncture of the inferior vena cava was not feasible due to anatomical factors	Moderate sedation	PPG = 18.82 HVPG = 8.08	PPG and HVPG correlated well (R = 0.923)
Choi *et al.*, 2022 [61]	83, R	25G	100	None	NA	PPG = 7.06	EUS-PPG correlates well with clinical markers of PH ($P < 0.05$)
Lesmana *et al.*, 2022 [62]	13, P	22G	100	None	NA	PVP = 33.46 HVP = 16.8 PPG = 16.61	High rates for detection of clinically significant portal hypertension
Romero-Castro *et al.*, 2023 [119]	21, P	25G	90	None	NA	NA	PPG measurement is safe using 25G FNA needle

PPG = portal pressure gradient, PVP = portal vein pressure, HVP = hepatic vein pressure, P = prospective, R = retrospective, EUS-PPG = EUS-guided portal pressure gradient, HVPG = hepatic venous pressure gradient, PH = portal hypertension, FNA = fine needle aspiration.

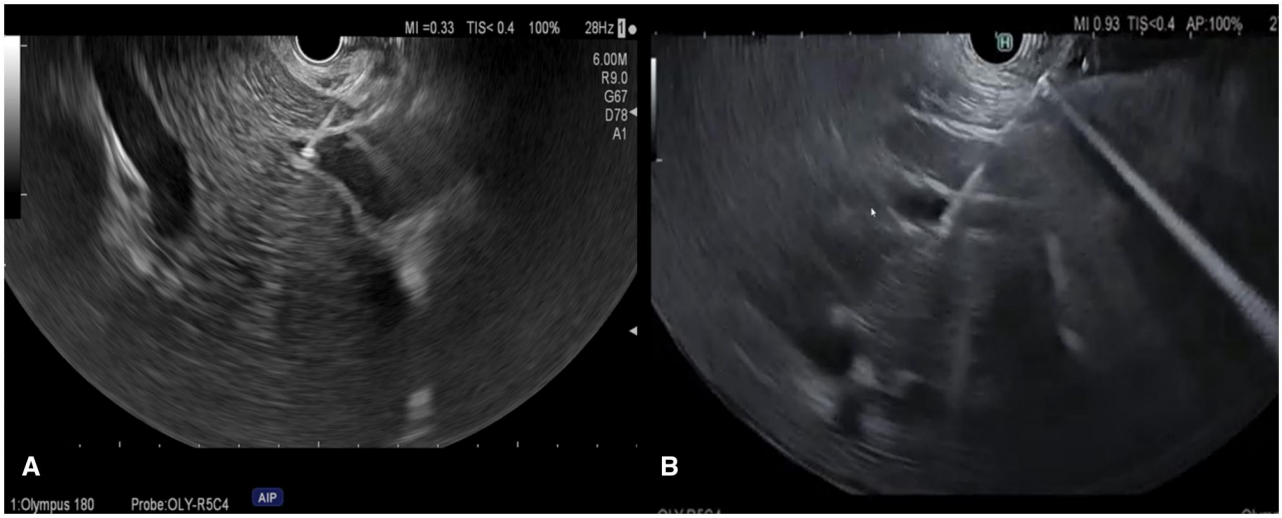

Figure 1. EUS visualization and puncturing of the middle hepatic vein (A) and portal vein (B).

Two devices for pressure measurement have been documented in the literature. One is a compact manometer attached to the 25G needle (FDA approved the EchoTip Insight®), but one study exists using a pressure sensor connected to the standard 22G needle [60] converting the measurement for display on the central pressure monitor (after establishing the zero level with the manometer placed at the level of mid axillary line). During the same EUS procedure, PH measurement, endoscopic assessment of varices, liver biopsy [61] and even gastric varices therapies [62] can be performed thereby reducing the time to diagnosis and treatment.

In patients, this technique was first described in 2014, in a clinical case report [63], in which HVPG measurement was considered inaccurate considering the patient's symptoms (recurrent gastrointestinal bleeding), therefore, EUS measurement was conducted. Existing data proves that the technique is feasible in 91.61% of patients (95% CI 86.25–95.74) according to a meta-analysis [64]. Huang *et al.* [58] enrolled 28 patients and performed EUS-PPG measurement with a 100% success rate. They correlated EUS-PPG obtained with indirect signs of PH, including varices, low platelet count, and gastropathy. The study's limitation was the absence of validation with a standard PH assessment.

In addressing this concern, another study [60] enrolling patients with acute or subacute PH confirmed the consistency between EUS-PPG measurement and standard HVPG. The same study emphasized the availability of EUS-PPG where HVPG measurement was not feasible, such as Budd-Chiari syndrome, where the occlusion of the hepatic vein impeded catheterization or shunts involving hepatic vein resulted in underestimated HVPG values. Demonstrating the comprehensive 'all-in-one' concept, the clinically significant PPG greater than 10 mmHg found in 30.51% of cases, was correlated with the presence of varices [61],

suggesting that assessment for gastroesophageal varices and pressure measurement is feasible during the same procedure.

EUS in assessing vessel-related complications

Predicting the risk for the first variceal bleeding

Unlike endoscopy, EUS provides comprehensive data about gastroesophageal varices including diameters, velocities, feeding vessels and possible shunts. Para-esophageal or perigastric veins over 5 mm have been shown to be at risk for the first bleeding [65]. Experimentally, attempts were made to evaluate the intravariceal pressure [66], but these were abandoned due to possible complications. Detection of hematocystic spots on the surface of esophageal varice has been strongly correlated with the occurrence of variceal bleeding [67, 68]. By calculating the combined cross-sectional surface area of all esophageal varices in the distal esophagus, Miller *et al.* [69] demonstrated that EUS can predict the likelihood of variceal bleeding. For each 1 cm^2 increase, the annual risk of variceal bleeding increases 76-fold and a variceal cross-sectional surface area of 0.45 cm^2 had an 83% sensitivity for predicting future variceal bleeding.

In a study involving 114 participants, the Doppler-EUS mean velocities in gastric varices were higher (28.0 ± 6.1 cm/s) in patients experiencing bleeding than in the cases without bleeding (17.6 ± 5.5 cm/s) ($P < 0.001$). Additionally, the gastric varices wall was thinner in bleeding cases, measuring 1.2 ± 0.2 mm as opposed to 1.6 ± 0.3 mm in nonbleeding cases [70].

Predicting the variceal bleeding recurrence

The rebleeding rate from esophageal varices after initial hemostasis varies from 6% to 40%, depending on the complexity of the treatment used for variceal eradication [71, 72].

The rebleeding rate after treatment for gastric varices, as reported by Chandan *et al.*, was 4.9% in primary prophylaxis and 18.1% in secondary prophylaxis [73]. A meta-analysis, including gastric varices, reported a late rebleeding rate of 11.6% and an early rebleeding rate of 7.7% [74]. They found the rebleeding rate to be 16.3% in eight studies of gastric varices treated with cyanoacrylate alone, 16.3% in three studies using coils and 9.2% in 23 studies that combined cyanoacrylate and coils. Higher rebleeding rates were observed when HVPG was over 18 mmHg [75]. For treating recurrent bleeding, the endovascular balloon-occluded retrograde transvenous obliteration, recommended by Baveno VII consensus in gastroesophageal varices type 2 or isolated gastric varices type 1, provided better results compared to endoscopic cyanoacrylate injection [76]. However, a comparison with EUS-guided combined injections of cyanoacrylate and coils does not exist.

Following treatment for variceal bleeding, EUS has been effective in assessing the size and presence of feeding vessels, as well as the dimensions of the varices. These factors are crucial to be determined, as they have been identified as predictors of rebleeding [77]. A maximum gastric varices size greater than 17.5 mm had a 69% predictive accuracy for the need for re-intervention [78]. Additionally, the presence of red spots, the size of varix and the existence of a para-gastric vein have been identified as independent risk factors for the recurrence of variceal bleeding [79].

Predicting the variceal recurrence

Obliteration of varices, coupled with non-selective beta blockers, is the current gold standard for secondary prophylaxis of variceal bleeding. Identifying patients at risk of developing varices after the initial treatment is crucial, as it can prevent the burden of unnecessary procedures and reduce overall costs. The esophageal varices might recur in 29–58% in the first year after endoscopic eradication [45, 80].

A randomized controlled study proved that the presence of collaterals identified by EUS was associated with variceal recurrence [81]. In a retrospective study comprising 144 patients who underwent variceal ligation, the recurrence of varices was associated with para-esophageal vessel diameter exceeding 9 mm and perforating veins diameter exceeding 3.6 mm (OR = 1.51 and OR = 3.2, respectively) [45], being consistent with others published in the literature [80]. Furthermore, the presence of para-esophageal veins larger than 5 mm and multiple veins (more than 5 mm) were identified as independent factors for variceal recurrence [46]. Another study concluded that peri-esophageal collaterals and larger perforating veins predicted variceal recurrence ($P < 0.001$) [82]. Para-gastric veins were also associated with poor response to endoscopic therapy for treating gastroesophageal varices [83].

Findings in a study suggest that the diameter of esophageal varice did not correlate with recurrence of varices but was a predictor for the success rate of the therapy [84], corresponding with previous results of Jeong *et al.* [45] which showed that number and size of varices did not influence the recurrence.

Despite initial enthusiasm on the value of azygos vein hemodynamics in PH [85], the diameter of azygos vein had no correlation with variceal recurrence [86].

Therapeutic efficiency in gastroesophageal varices

For esophageal varices, the gold standard treatment is endoscopic band ligation but EUS-guided sclerotherapy has been used in a pilot study by Lahoti *et al.* [87] with successful eradication and no adverse effects.

Gastric varices, though less frequently observed than esophageal varices, pose a higher risk of mortality due to the increased severity of hemorrhage. Endoscopic therapy for gastric varices is often suboptimal, resulting in elevated rebleeding rates [88]. In addressing this challenge, EUS plays a crucial role, offering the possibility for substance injection, such as cyanoacrylate, gelfoam or thrombin [89] and embolization using coils.

In one study, EUS-guided coil embolization with cyanoacrylate of gastric varices proved to be superior to conventional endoscopic cyanoacrylate injection and required lower volume of cyanoacrylate injection [90]. Data from a randomized controlled study on EUS-guided cyanoacrylate injection versus direct endoscopic injection suggest similar immediate hemostasis, but with a lower bleeding rate in the EUS group (8.8% vs. 23.7%) [91] which are consistent with other published studies (Table 6). More recent data showed that the injection of thrombin was associated with fewer side effects compared to cyanoacrylate-based therapy, although the early and late rebleeding rate were similar [92].

A meta-analysis including eight studies with primary prophylaxis of gastric varices proved complete variceal obliteration in 95.4% of cases when both EUS-glue and coils therapy were used. Furthermore, the obliteration rate was 83% in secondary prophylaxis in 13 studies (84.6% under EUS glue, 91.6% under EUS-coil and 84.5% under EUS-glue-coil) having hemostasis efficiency of 91.9%. These results cannot answer if combined therapy was better than monotherapy for gastric varices, and the global rebleeding rate and variceal recurrence remained quite high (18.1% and 20.6%) [73]. Also, it remains debatable the number and type of coils needed for obtaining obliteration [79]. Combining the thrombin injection with coil embolization during EUS-guided

Table 6. EUS guided interventions for gastric varices

Author, year	No. of patients, type of study	Type of intervention	Indication	Obliteration rate (%)	Side effects (%)	Rebleeding (%)	Follow-up (months)	Survival (%)
Bazarbashi *et al.*, 2024 [120]	106, R	Coils	Active bleeding, primary and secondary prophylaxis	88.7	6.5	14.1	9	76.6
Sabry *et al.*, 2023 [94]	43, P	CYA	Primary prophylaxis	95.5	4.5	0	6	NA
Samanta *et al.*, 2023 [78]	58, R	Coil + CYA	Active bleeding, primary and secondary prophylaxis	93.1	0	13.8	3	NA
Wang *et al.*, 2023 [121]	89, P	EUS-CYA vs. DEI-CYA	Active bleeding	80 vs. 72.7	NA	8.9 vs. 22.7	9	100
Robles Meranda *et al.*, 2020 [122]	60, P	Coils + CYA vs. coils alone	Primary prophylaxis and secondary	86.7 vs. 13.3	6.7 vs. 3.3	3.3 vs. 20	12	70 vs. 73.3
Seven *et al.*, 2022 [123]	28, P	Coils + CYA vs. coils alone	Primary prophylaxis	NA	3.5 vs. 3.5	3.5 vs. 7	13	76.9 vs. 77.8
Bazarbashi *et al.*, 2020 [124]	40, P	Coil vs. CYA	NA	100 vs. 87	10 vs. 20	0 vs. 38	9	90 vs. 83.4
Bick *et al.*, 2019 [91]	64, P	CYA	Primary prophylaxis	75	20.3	8.8	6	NA
Franco *et al.*, 2014 [125]	20, P	CYA	Primary prophylaxis	100	15	5	31	100
Tang *et al.*, 2020 [126]	27, P	CYA	Secondary prophylaxis	66.7	3.7	14.8	6	51.8
Koziel *et al.*,2019 [127]	16, R	Coils with CYA	Primary and secondary prophylaxis	75	37.5	0	11	100
Lôbo *et al.*, 2019 [128]	32, P	Coils + CYA vs. CYA alone	Secondary prophylaxis	73.3 vs. 75	50 vs. 62.5	0	10	100 vs. 87.5
Frost *et al.*, 2018 [129]	8, P	Thrombin injection	Active bleeding	67	0	33	3	87.5
Mukkada *et al.*, 2018 [130]	30, R	Coils/CYA	Secondary prophylaxis	93	0	20	12	90
Khoury *et al.*, 2019 [131]	10, P	Coils	Primary and secondary prophylaxis	20	10	0	10	100
Zeng *et al.*, 2017 [132]	96, P	CYA + lauromacrogol vs. CYA + lipiodol	Prophylaxis	NA	33.3 vs. 37.5	10.4 vs. 12.5	6	93.7 vs. 95.8
Bhat *et al.*, 2016 [133]	152, R	Coil + CYA glue injection	Active bleeding, primary and secondary prophylaxis	93	7	11.2	14.5	97.6
Bang *et al.*, 2015 [134]	31, R	CYA	Active bleeding, primary and secondary prophylaxis	NA	47.4	7.7	8	NA
Fujii-Lau *et al.*, 2015 [95]	5, R	Coil vs. coil + CYA	Secondary prophylaxis	100 vs. 100	7	0 vs. 0	8 vs. 4	80
Romero-Castro *et al.*, 2013 [135]	30, R	CYA vs. coils	Secondary prophylaxis	94.7 vs. 90.9	57.9 vs. 9.1	0 vs. 9	21 vs. 11	80
Gonzalez *et al.*, 2012 [136]	3, R	CYA	Secondary prophylaxis	80	0	0	9	100
Binmoeller *et al.*, 2011 [137]	30, R	Coil and CYA glue injection	Active or recent bleeding	95.8	0	3.3	6.4	97.7
Romero-Castro *et al.*, 2007 [138]	5, P	CYA	Prophylaxis	100	0	0	10	80

DEI = direct endoscopic injection, CYA = cyanoacrylate, P = prospective, R = retrospective, NA = not applicable.

therapy proved recently to be very efficient, but more data are needed [93].

Direct injection of perforating veins compared to direct endoscopic injection was associated with a better obliteration rate after the first session of tissue adhesive injection (77.2% vs. 38.1%), fewer sessions until complete obliteration, and had a similar adverse effect rate [94], but the comparison between treatment of perforating veins and gastric varices under EUS guidance is not available.

Therapeutic efficiency in ectopic varices

Ectopic duodenal varices have a mortality rate of up to 40% and given their location, endoscopic treatment may be challenging. Successful coil and cyanoacrylate injection guided by EUS of duodenal varices have been reported, but the studies included few patients [95–97].

Para-stomal varices, although less frequently encountered, pose a significant challenge in the management of bleeding from ectopic varices. In cirrhotic patients, bleeding from the stoma

can occur in up to 27% of cases, with an associated mortality rate of up to 4%. Treatment options for para-stomal variceal bleeding range from local interventions, such as compression, epinephrine-soaked gauze and ligation, to more invasive approaches including surgically shunt formation or TIPS placement [98]. EUS plays a crucial role in managing para-stomal varices, offering embolization techniques similar to those used for gastric varices, such as cyanoacrylate injection [99]. However, in a more recent study, successful treatment of para-stomal variceal bleeding was achieved using human thrombin injection ± embolization coil(s) under EUS guidance [100].

The role of EUS in targeting rectal varices is yet to be established. Further cohort studies are awaited, as only case reports of injection therapy exist [101, 102].

Future of EUS in PH

EUS portal vein sampling

The transhepatic portal vein sampling for patients with metastatic pancreatic adenocarcinoma proved the presence of circulating tumor cells in portal vein blood [103]. Consequently, one study assessing the portal blood sampled during duodenopancreatectomy for periampullary tumors revealed that circulating tumor cells were significant predictors for liver metastases within 6 months after surgery [104]. However, in the context of PH, a recent small cohort study was conducted, enrolling 12 patients, and it was successful in 100% of the cases with no adverse effects. The study aimed to collect blood samples from the portal vein for metabolomic analysis [105].

Selective embolization of the portal vein

Prior 2–6 weeks before liver resection, embolization of the portal vein is used for obtaining compensatory hypertrophy of non-embolized remnant liver [106]. Embolization using cyanoacrylate and coils was performed by EUS guidance in animals and appears to be feasible [66, 107]. Despite good portal vein occlusion, coil dislodgements into the hepatic parenchyma were noted [66].

EUS-guided portosystemic shunts

The technique was performed in two studies in pigs, with placement of a metal stent or a lumen-apposing metal stent with distal and proximal ends positioned inside the portal vein and hepatic vein, respectively [108, 109], but no studies on humans exist. On the other hand, direct injecting of glue and coils into spontaneous portosystemic shunt may decrease the risk of encephalopathy [110].

Conclusions

EUS assessment could provide information on semiology and hemodynamic parameters of the portal vein system which correlate with the risk of variceal recurrence after treatment and the risk of rebleeding. EUS-PPG can be an alternative to traditional HVPG measurement but further studies comparing the new method to the standard of care are needed. The routine use of hemodynamic assessment in non-cirrhotic PH is eagerly anticipated. Additionally, EUS can provide tissue acquisition from portal vein and splenic vein thrombosis in selected cases. Regarding therapeutic efficiency, EUS has proven to be more reliable than conventional endoscopy for treating gastric varices. However, with the variety of available treatment options, further studies are needed to establish a standard of care. The future of EUS stands in its ability to guide interventional endohepatology, such as stent deployment for portosystemic shunts and venous embolization.

Authors' Contributions

I.D. collected the data, made original draft writing. C.P. and C.H. made critical revisions and revised the manuscript. B.P. made critical revisions and editing; R.S. made critical revisions, A.S. collected the data, edited, and supervised. All authors read and approved the final version of the manuscript.

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Conflicts of Interest

None declared.

References

1. Turco L, Villanueva C, La Mura V *et al.* Lowering portal pressure improves outcomes of patients with cirrhosis, with or without ascites: a meta-analysis. *Clin Gastroenterol Hepatol* 2020;**18**:313–27.e6.
2. Anastasiou J, Berzin T. Endoscopic ultrasound-guided vascular interventions: from diagnosis to treatment. *Saudi J Med Med Sci* 2018;**6**:61–7.
3. Kane L, Kahaleh M, Shami VM *et al.* Comparison of the grading of esophageal varices by transnasal endoluminal ultrasound and esophagogastroduodenoscopy. *Clin Gastroenterol Hepatol* 2005;**3**:806–10.
4. Min Lee C, Burgio A, Young Geong G *et al.* S. An updated review on the epidemiology, pathophysiology, etiology, and diagnosis of liver cirrhosis. *J Gastroenterol* 2021;**56**:593–619.
5. Naveau S, Perlemuter G, Balian A. Épidémiologie et histoire naturelle de la cirrhose. *Rev Prat* 2005;**55**:1527–32.
6. Kaplan DE, Ripoll C, Thiele M *et al.* AASLD practice guidance on risk stratification and management of portal hypertension and varices in cirrhosis. *Hepatology* 2023;**79**:1180–211.
7. Tetangco EP, Silva RG, Lerma EV. Portal hypertension: etiology, evaluation, and management. *Dis Mon* 2016;**62**:411–26.
8. Simonetto DA, Liu M, Kamath PS. Portal hypertension and related complications: diagnosis and management. *Mayo Clin Proc* 2019;**94**:714–26.
9. Engelmann C, Clària J, Szabo G *et al.* Pathophysiology of decompensated cirrhosis: portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction. *J Hepatol* 2021;**75**:S49–66.
10. Gracia-Sancho J, Marrone G, Fernández-Iglesias A. Hepatic microcirculation and mechanisms of portal hypertension. *Nat Rev Gastroenterol Hepatol* 2019;**16**:221–34.
11. Bosch J, Groszmann RJ, Shah VH. Evolution in the understanding of the pathophysiological basis of portal hypertension: how changes in paradigm are leading to successful new treatments. *J Hepatol* 2015;**62**:S121–30.
12. Fernandez M, Vizzutti F, Garcia-Pagan JC *et al.* Anti-VEGF receptor-2 monoclonal antibody prevents portal-systemic collateral vessel formation in portal hypertensive mice. *Gastroenterology* 2004;**126**:886–94.
13. Trebicka J, Reiberger T, Laleman W. Gut-liver axis links portal hypertension to acute-on-chronic liver failure. *Visc Med* 2018;**34**:270–5.

14. Wiest R, Lawson M, Geuking M. Pathological bacterial translocation in liver cirrhosis. *J Hepatol* 2014;**60**:197–209.
15. Gómez-Hurtado I, Such J, Francés R. Microbiome and bacterial translocation in cirrhosis. *Gastroenterol Hepatol (English Ed.)* 2016:687–96. doi: 10.1016/j.gastre.2015.10.002.
16. Iwakiri Y, Trebicka J. Portal hypertension in cirrhosis: pathophysiological mechanisms and therapy. *JHEP Rep* 2021; **3**:100316.
17. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006;**44**:217–31.
18. Angeli P, Bernardi M, Villanueva C *et al.*; European Association for the Study of the Liver. EASL clinical practice guidelines for the management of patients with decompensated cirrhosis. *J Hepatol* 2018;**69**:406–60.
19. Roberts D, Best LM, Freeman SC *et al.* Treatment for bleeding oesophageal varices in people with decompensated liver cirrhosis: a network meta-analysis. *Cochrane Database Syst Rev* 2021;**4**:CD013155.
20. Ibrahim M, Mostafa I, Devière J. New developments in managing variceal bleeding. *Gastroenterology* 2018;**154**:1964–9.
21. Gunarathne LS, Rajapaksha H, Shackel N *et al.* Cirrhotic portal hypertension: from pathophysiology to novel therapeutics. *World J Gastroenterol* 2020;**26**:6111–40.
22. Kiyosue H, Ibukuro K, Maruno M *et al.* Multidetector CT anatomy of drainage routes of gastric varices: a pictorial review. *Radiographics* 2013;**33**:87–100.
23. Sharma M, Rameshbabu CS. Collateral pathways in portal hypertension. *J Clin Exp Hepatol* 2012;**2**:338–52.
24. Wiechowska-Kozłowska A, Zasada K, Milkiewicz M *et al.* Correlation between endosonographic and Doppler ultrasound features of portal hypertension in patients with cirrhosis. *Gastroenterol Res Pract* 2012;**2012**:395345.
25. Alper E, Buyraç Z, Baydar B *et al.* Evaluation of flow and structure abnormalities of splanchnic system veins in cirrhotic patients without portal hypertension. *Minerva Gastroenterol Dietol* 2011;**57**:123–7.
26. Delconte G, Bhoori S, Milione M *et al.* Endoscopic ultrasound-guided fine needle aspiration of splenic vein thrombosis: a novel approach to the portal venous system. *Endoscopy* 2016; **48**:E40–1.
27. Komori K, Akahoshi K, Motomura Y *et al.* Endoscopic ultrasound diagnosis of a small splenic vein aneurysm. *Endoscopy* 2014;**46**:E5–6.
28. Chen K, Yang X J A splenic vein aneurysm diagnosed by EUS: the new application of contrast-enhanced and 3-dimensional imaging (with video). *Gastrointest Endosc* 2020;**91**:196–7.
29. Bodea R, Seicean A, Vasile T *et al.* Role of computer tomography and endoscopic ultrasonography in assessing portal and superior mesenteric vessels invasion in cephalo-pancreatic adenocarcinoma. *Ann Ital Chir* 2017;**88**:336–41.
30. Nitesh P, Biju P, Kalayarasan R. Superior mesenteric vein aneurysm with arteriovenous communication and portal vein thrombosis: a rare presentation in non-cirrhotic portal hypertension. *Cureus* 2023;**15**:e42595.
31. Li FH, Hao J, Xia JG *et al.* Hemodynamic analysis of esophageal varices in patients with liver cirrhosis using color Doppler ultrasound. *World J Gastroenterol* 2005;**11**:4560–5.
32. Willmann JK, Weishaupt D, Böhm T *et al.* Detection of submucosal gastric fundal varices with multi-detector row CT angiography. *Gut* 2003;**52**:886–92.
33. Xu XD, Dai JJ, Qian JQ *et al.* New index to predict esophageal variceal bleeding in cirrhotic patients. *World J Gastroenterol* 2014;**20**:6989–94.
34. Lei Z, Luo R, Lu H *et al.* Endoscopic ultrasound-guided portal pressure gradient measurement in patients with cirrhotic portal hypertension: a report of 52 cases. *China J Gen Surg* 2023; **32**:101–9.
35. Hino S, Kakutani H, Ikeda K *et al.* Hemodynamic assessment of the left gastric vein in patients with esophageal varices with color Doppler EUS: factors affecting development of esophageal varices. *Gastrointest Endosc* 2002;**55**:512–7.
36. Robles-Medranda C, Valero M, Nebel JA *et al.* Endoscopic-ultrasound-guided coil and cyanoacrylate embolization for gastric varices and the roles of endoscopic Doppler and endosonographic varicealography in vascular targeting. *Dig Endosc* 2019; **31**:283–90.
37. Zhang Z-G, Li Z, Yang Y *et al.* Hemodynamic effect through a novel endoscopic intervention in management of varices and hypersplenism (with video). *Gastrointest Endosc* 2022;**95**: 172–83.e2.
38. Sato T, Yamazaki K, Toyota J *et al.* Endoscopic ultrasonographic evaluation of hemodynamics related to variceal relapse in esophageal variceal patients. *Hepatol Res* 2009; **39**:126–33.
39. Hino S, Kakutani H, Ikeda K *et al.* Hemodynamic analysis of esophageal varices using color Doppler endoscopic ultrasonography to predict recurrence after endoscopic treatment. *Endoscopy* 2001;**33**:869–72.
40. Kuramochi A, Imazu H, Kakutani H *et al.* Color Doppler endoscopic ultrasonography in identifying groups at a high-risk of recurrence of esophageal varices after endoscopic treatment. *J Gastroenterol* 2007;**42**:219–24.
41. Kakutani H, Hino S, Koyama S *et al.* How do we select an endoscopic treatment for esophageal varices on the basis of hemodynamic analysis using color Doppler endoscopic ultrasonography. *Surg Laparosc Endosc Percutan Tech* 2012; **22**:410–4.
42. Lee YT, Sung JJ, Yung MY *et al.* Use of color Doppler EUS in assessing azygos blood flow for patients with portal hypertension. *Gastrointest Endosc* 1999;**50**:47–52.
43. Nishida H, Giostra E, Spahr L *et al.* Validation of color Doppler EUS for azygos blood flow measurement in patients with cirrhosis: application to the acute hemodynamic effects of somatostatin, octreotide, or placebo. *Gastrointest Endosc* 2001; **54**:24–30.
44. Pollo-Flores P, Soldan M, Santos UC *et al.* Three months of simvastatin therapy vs. placebo for severe portal hypertension in cirrhosis: a randomized controlled trial. *Dig Liver Dis* 2015; **47**:957–63.
45. Jeong SW, Kim HS, Kim SG *et al.* Useful endoscopic ultrasonography parameters and a predictive model for the recurrence of esophageal varices and bleeding after variceal ligation. *Gut Liver* 2017;**11**:843–51.
46. Masalaite L, Valantinas J, Stanaitis J. Endoscopic ultrasound findings predict the recurrence of esophageal varices after endoscopic band ligation: a prospective cohort study. *Scand J Gastroenterol* 2015;**50**:1322–30.
47. Konishi Y, Nakamura T, Kida H *et al.* Catheter US probe EUS evaluation of gastric cardia and perigastric vascular structures to predict esophageal variceal recurrence. *Gastrointest Endosc* 2002;**55**:197–203.
48. Seicean A. Endoscopic ultrasound in the diagnosis and treatment of upper digestive bleeding: a useful tool. *J Gastrointest Liver Dis* 2013;**22**:465–9.
49. DeLeve LD, Valla DC, Garcia-Tsao G; American Association for the Study Liver Diseases. Vascular disorders of the liver. *Hepatology* 2009;**49**:1729–64.

50. Chen P-H, Chen W-C, Hou M-C *et al.* Delayed endoscopy increases re-bleeding and mortality in patients with hematemesis and active esophageal variceal bleeding: a cohort study. *J Hepatol* 2012;**57**:1207–13.
51. Sørensen M, Larsen LP, Villadsen GE *et al.* β-blockers improve presinusoidal portal hypertension. *Dig Dis Sci* 2018;**63**:3153–7.
52. Vu, Tuan, Eberly, Hanel, Zheng, Amy, *et al.* Clinical significance of measuring hepatic venous pressure gradient on transjugular liver biopsy for patients with pre-cirrhotic bridging fibrosis liver disease. *Clin Imaging*. 2023;**96**:44–8.
53. de Franchis R, Bosch J, Garcia-Tsao G *et al.*; Baveno VII Faculty. Baveno VII—renewing consensus in portal hypertension. *J Hepatol* 2022;**76**:959–74.
54. Da BL, Surana P, Kapuria D *et al.* Portal pressure in noncirrhotic portal hypertension: to measure or not to measure. *Hepatology* 2019;**70**:2228–30.
55. Liu B, Zhang D, Dong C *et al.* Correlation between hepatic venous pressure gradient and portal pressure gradient in patients with autoimmune cirrhotic portal hypertension and collateral branches of the hepatic vein. *Hepatol Res* 2023; **53**:1084–95.
56. Lai L, Poneros J, Santilli J *et al.* EUS-guided portal vein catheterization and pressure measurement in an animal model: a pilot study of feasibility. *Gastrointest Endosc* 2004;**59**:280–3.
57. Giday SA, Clarke JO, Buscaglia JM *et al.* EUS-guided portal vein catheterization: a promising novel approach for portal angiography and portal vein pressure measurements. *Gastrointest Endosc* 2008;**67**:338–42.
58. Huang JY, Samarasena JB, Tsujino T *et al.* EUS-guided portal pressure gradient measurement with a simple novel device: a human pilot study. *Gastrointest Endosc* 2017;**85**:996–1001.
59. Schulman AR, Thompson CC, Ryou M. Endoscopic ultrasound-guided direct portal pressure measurement using a digital pressure wire with real-time remote display: a survival study. *J Laparoendosc Adv Surg Tech A* 2017;**27**:1051–4.
60. Zhang W, Peng C, Zhang S *et al.* EUS-guided portal pressure gradient measurement in patients with acute or subacute portal hypertension. *Gastrointest Endosc* 2021;**93**:565–72.
61. Choi AY, Kolb J, Shah S *et al.* Endoscopic ultrasound-guided portal pressure gradient with liver biopsy: 6 years of endohepatology in practice. *J Gastroenterol Hepatol* 2022;**37**:1373–9.
62. Lesmana CRA. Technique innovation of endoscopic ultrasound portal pressure gradient measurement using standard manometer set for portal hypertension assessment. *Clin Case Rep* 2022;**10**:e6658.
63. Fujii-Lau LL, Leise MD, Kamath PS *et al.* Endoscopic ultrasound-guided portal-systemic pressure gradient measurement. *Endoscopy* 2014;**46**:E654–6.
64. Sreenivasa Reddy YP, Puli S. S59 EUS-guided portal pressure gradient measurements to diagnose cirrhosis: a systematic review and meta-analysis. *Am J Gastroenterol* 2022;**117**:e44.
65. Faigel DO, Rosen HR, Sasaki A *et al.* EUS in cirrhotic patients with and without prior variceal hemorrhage in comparison with noncirrhotic control subjects. *Gastrointest Endosc* 2000; **52**:455–62.
66. Miller LS, Dai Q, Thomas A *et al.* A new ultrasound-guided esophageal variceal pressure-measuring device. *Am J Gastroenterol* 2004;**99**:1267–73.
67. Miller LS. Endoscopic ultrasound in the evaluation of portal hypertension. *Tech Gastrointest Endosc* 2005;**7**:41–8.
68. Schiano TD, Adrain AL, Vega KJ *et al.* High-resolution endoluminal sonography assessment of the hematocystic spots of esophageal varices. *Gastrointest Endosc* 1999;**49**:424–7.
69. Miller L, Banson FL, Bazir K *et al.* Risk of esophageal variceal bleeding based on endoscopic ultrasound evaluation of the sum of esophageal variceal cross-sectional surface area. *Am J Gastroenterol* 2003;**98**:454–9.
70. Sato T, Yamazaki K, Toyota J *et al.* Observation of gastric variceal flow characteristics by endoscopic ultrasonography using color Doppler. *Am J Gastroenterol* 2008;**103**:575–80.
71. Hu Z, Zhang D, Swai J *et al.* Risk of rebleeding from gastroesophageal varices after initial treatment with cyanoacrylate: a systematic review and pooled analysis. *BMC Gastroenterol* 2020;**20**:181.
72. Albillos A, Zamora J, Martínez J, Baveno Cooperation *et al.* Stratifying risk in the prevention of recurrent variceal hemorrhage: results of an individual patient meta-analysis. *Hepatology* 2017;**66**:1219–31.
73. Chandan S, Nguyen A, Mohan BP *et al.* S1086 endoscopic ultrasound (EUS) guided therapies for primary and secondary prophylaxis in gastric varices—an updated systematic review and meta-analysis. *Am J Gastroenterol* 2022;**117**:e789–90.
74. Mohan BP, Chandan S, Khan SR *et al.* Efficacy and safety of endoscopic ultrasound-guided therapy versus direct endoscopic glue injection therapy for gastric varices: systematic review and meta-analysis. *Endoscopy* 2020;**52**:259–67.
75. Wu L, Fang Q-Q, Huang X-Q *et al.* Risk factors associated with failure of endoscopic combined treatment to prevent varices rebleeding in patients with liver cirrhosis. *Expert Rev Gastroenterol Hepatol* 2023;**17**:301–8.
76. Luo X, Xiang T, Wu J *et al.* Endoscopic cyanoacrylate injection versus balloon-occluded retrograde transvenous obliteration for prevention of gastric variceal bleeding: a randomized controlled trial. *Hepatology* 2021;**74**:2074–84.
77. Thiruvengadam SS, Sedarat A. The role of endoscopic ultrasound (EUS) in the management of gastric varices. *Curr Gastroenterol Rep* 2021;**23**:1.
78. Samanta J, Nabi Z, Facciorusso A *et al.* EUS-guided coil and glue injection versus endoscopic glue injection for gastric varices: international multicentre propensity-matched analysis. *Liver Int* 2023;**43**:1783–92.
79. Ma L, Tseng Y, Luo T *et al.* Risk stratification for secondary prophylaxis of gastric varices due to portal hypertension. *Dig Liver Dis* 2019;**51**:1678–84.
80. Zheng J, Zhang Y, Li P *et al.* The endoscopic ultrasound probe findings in prediction of esophageal variceal recurrence after endoscopic variceal eradication therapies in cirrhotic patients: a cohort prospective study. *BMC Gastroenterol* 2019;**19**:32.
81. Andrade De Paulo G, Ardengh JC, Nakao FS *et al.* Treatment of esophageal varices: a randomized controlled trial comparing endoscopic sclerotherapy and EUS-guided sclerotherapy of esophageal collateral veins. *Gastrointest Endosc* 2006;**63**: 396–402; quiz 463.
82. Irisawa A, Saito A, Obara K *et al.* Endoscopic recurrence of esophageal varices is associated with the specific EUS abnormalities: severe periesophageal collateral veins and large perforating veins. *Gastrointest Endosc* 2001;**53**:77–84.
83. Tseng Y, Ma L, Luo T *et al.* Patient response to endoscopic therapy for gastroesophageal varices based on endoscopic ultrasound findings. *Gut Liver* 2018;**12**:562–70.
84. Abe M, Furuichi Y, Takeuchi H *et al.* Prognostic and recurrence factors after endoscopic injection sclerotherapy for esophageal varices: multivariate analysis with propensity score matching. *Dig Endosc* 2022;**34**:367–78.
85. Kassem AM, Salama ZA, Zakaria MS *et al.* Endoscopic ultrasonographic study of the azygos vein before and after endoscopic

obliteration of esophagogastric varices by injection sclerotherapy. *Endoscopy* 2000;**32**:630–4.
86. Carneiro FOAA, Retes FA, Matuguma SE *et al.* Role of EUS evaluation after endoscopic eradication of esophageal varices with band ligation. *Gastrointest Endosc* 2016;**84**:400–7.
87. Lahoti S, Catalano MF, Alcocer E *et al.* Obliteration of esophageal varices using EUS-guided sclerotherapy with color Doppler. *Gastrointest Endosc* 2000;**51**:331–3.
88. Levy MJ, Wong Kee Song LM. EUS-guided angiotherapy for gastric varices: coil, glue, and sticky issues. *Gastrointest Endosc* 2013;**78**:722–5.
89. Robles-Medranda C, Oleas R, Del Valle R *et al.* EUS-guided therapy of gastric varices (with video). *Endosc Ultrasound* 2020; **9**:280–3.
90. Chen D, Fu S, Shen R. Efficacy and safety of EUS-guided coil embolization in combination with cyanoacrylate injection versus conventional endoscopic cyanoacrylate injection in the treatment of gastric varices with spontaneous portosystemic shunts. *Gastroenterol Rep (Oxf)* 2024;**12**:goae026.
91. Bick BL, Al-Haddad M, Liangpunsakul S *et al.* EUS-guided fine needle injection is superior to direct endoscopic injection of 2-octyl cyanoacrylate for the treatment of gastric variceal bleeding. *Surg Endosc* 2019;**33**:1837–45.
92. Bhurwal A, Makar M, Patel A *et al.* Safety and efficacy of thrombin for bleeding gastric varices: a systematic review and meta-analysis. *Dig Dis Sci* 2022;**67**:953–63.
93. O'Rourke J, Todd A, Shekhar C *et al.* EUS-guided thrombin injection and coil implantation for gastric varices: feasibility, safety, and outcomes. *Gastrointest Endosc* 2024 Feb 3: S0016-5107(24)00088-9. DOI: 10.1016/j.gie.2024.01.044.
94. Sabry F, Seif S, Eldesoky A *et al.* EUS-guided cyanoacrylate injection into the perforating vein versus direct endoscopic injection in the treatment of gastric varices. *Endosc Int Open* 2023; **11**:E202–10.
95. Fujii-Lau LL, Law R, Wong Kee Song LM *et al.* Endoscopic ultrasound (EUS)-guided coil injection therapy of esophagogastric and ectopic varices. *Surg Endosc* 2016;**30**:1396–404.
96. Bahdi F, George R, Patel K. EUS-guided coiling and cyanoacrylate injection of ectopic duodenal varices. *VideoGIE* 2021; **6**:35–7.
97. Kimura G, Hashimoto Y, Ikeda M. Successful obliteration of bleeding duodenal varices by EUS-guided injection of N-butyl-2-cyanoacrylate. *VideoGIE* 2017;**2**:317–9.
98. Oey RC, de Wit K, Moelker A *et al.* Variable efficacy of TIPSS in the management of ectopic variceal bleeding: a multicentre retrospective study. *Aliment Pharmacol Ther* 2018;**48**:975–83.
99. Tsynman DN, Decross AJ, Maliakkal B *et al.* Novel use of EUS to successfully treat bleeding parastomal varices with N-butyl-2-cyanoacrylate. *Gastrointest Endosc* 2014;**79**:1007–8; discussion 1008.
100. Todd A, Shekhar C, O'Rourke J *et al.* Technical and clinical outcomes following EUS-guided thrombin injection and coil implantation for parastomal varices. *BMJ Open Gastroenterol* 2023 Aug;**10**:1–10. DOI: 10.1136/bmjgast-2021-000819.
101. Rana SS, Sharma R, Gupta R. Refractory rectal variceal bleeding treated with EUS-guided coil embolization. *Endosc Ultrasound* 2021;**10**:141–2.
102. Bazarbashi AN, Thompson CC, Ryou M. Targeting the perforator vein: EUS-guided coil embolization for the treatment of bleeding rectal varices. *VideoGIE* 2020;**5**:434–6.
103. Catenacci DVT, Chapman CG, Xu P *et al.* Acquisition of portal venous circulating tumor cells from patients with pancreaticobiliary cancers by endoscopic ultrasound. *Gastroenterology* 2015;**149**:1794–803.e4.
104. Tien YW, Kuo H-C, Ho B-I *et al.* A high circulating tumor cell count in portal vein predicts liver metastasis from periampullary or pancreatic cancer a high portal venous CTC count predicts liver metastases. *Med (United States)* 2016;**95**:e3407.
105. Ryou M, Stylopoulos N. Endoscopic ultrasound-guided sampling and profiling of portal circulation in human patients for metabolic research studies and biomarker assessment. *Am J Physiol Gastrointest Liver Physiol* 2020;**319**:G584–8.
106. Mann R, Goyal H, Perisetti A *et al.* Endoscopic ultrasound-guided vascular interventions: current insights and emerging techniques. *World J Gastroenterol* 2021;**27**:6874–87.
107. Matthes K, Sahani D, Holalkere NS *et al.* Feasibility of endoscopic ultrasound-guided portal vein embolization with enteryx. *Acta Gastroenterol Belg* 2005;**68**:412–5.
108. Buscaglia JM, Dray X, Shin EJ *et al.* A new alternative for a transjugular intrahepatic portosystemic shunt: EUS-guided creation of an intrahepatic portosystemic shunt (with video). *Gastrointest Endosc* 2009;**69**:941–7.
109. Schulman AR, Ryou M, Aihara H *et al.* EUS-guided intrahepatic portosystemic shunt with direct portal pressure measurements: a novel alternative to transjugular intrahepatic portosystemic shunting. *Gastrointest Endosc* 2017;**85**:243–7.
110. Rathi S, Kalantri A, Shastri A *et al.* Endoscopic ultrasound-guided transgastric shunt obliteration for recurrent hepatic encephalopathy. *Am J Gastroenterol* 2023;**118**:1895–8.
111. Lai R, Stephens V, Bardales R. Diagnosis and staging of hepatocellular carcinoma by EUS-FNA of a portal vein thrombus. *Gastrointest Endosc* 2004;**59**:574–7.
112. Storch I, Gomez C, Contreras F *et al.* Hepatocellular carcinoma (HCC) with portal vein invasion, masquerading as pancreatic mass, diagnosed by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). *Dig Dis Sci* 2007;**52**:789–91.
113. Michael H, Lenza C, Gupta M *et al.* Endoscopic ultrasound-guided fine-needle aspiration of a portal vein thrombus to aid in the diagnosis and staging of hepatocellular carcinoma. *Gastroenterol Hepatol (NY)* 2011;**7**:124–9.
114. Moreno M, Gimeno-García AZ, Corriente MM *et al.* EUS-FNA of a portal vein thrombosis in a patient with a hidden hepatocellular carcinoma: confirmation technique after contrast-enhanced ultrasound. *Endoscopy* 2014;**46**:E590–1.
115. Kayar Y, Turkdogan KA, Baysal B *et al.* EUS-guided FNA of a portal vein thrombus in hepatocellular carcinoma. *Pan Afr Med J* 2015;**21**:86.
116. Rustagi T, Gleeson FC, Chari ST *et al.* Remote malignant intravascular thrombi: EUS-guided FNA diagnosis and impact on cancer staging. *Gastrointest Endosc* 2017;**86**:150–5.
117. Gimeno Garcia AZ, Aparicio JR, Barturen A *et al.* Short article: endoscopic ultrasound-guided fine-needle aspiration of portal vein thrombosis in patients with chronic liver disease and suspicion of hepatocellular carcinoma. *Eur J Gastroenterol Hepatol* 2018;**30**:418–23.
118. Eskandere D, Hakim H, Attwa M *et al.* Role of endoscopic ultrasound-guided fine-needle aspiration of portal vein thrombus in the diagnosis and staging of hepatocellular carcinoma. *Clin Endosc* 2021;**54**:745–53.
119. Romero-Castro R, Carmona-Soria I, Jiménez-García VA *et al.* Endoscopic ultrasound-guided portal pressure gradient measurement: improving safety and overcoming technical difficulties. *Endoscopy* 2023;**55**:E878–80.
120. Bazarbashi AN, Aby ES, Mallery JS *et al.* EUS-guided coil injection therapy in the management of gastric varices: the first U.S. multicenter experience (with video). *Gastrointest Endosc* 2024;**99**:31–7.

121. Wang Z, Zeng Z, Chen L *et al.* Endoscopic ultrasonography-guided injection of cyanoacrylate in the treatment of gastroesophageal varices type 1: a single-center randomized study. *Surg Endosc* 2023;**37**:8277–84.
122. Robles-Medranda C, Oleas R, Valero M *et al.* Endoscopic ultrasonography-guided deployment of embolization coils and cyanoacrylate injection in gastric varices versus coiling alone: a randomized trial. *Endoscopy* 2020;**52**:268–75.
123. Seven G, Musayeva G, Seven OO *et al.* Comparison of endoscopic ultrasound-guided coil deployment with and without cyanoacrylate injection for gastric varices. *Arab J Gastroenterol* 2022;**23**:115–9.
124. Bazarbashi AN, Wang TJ, Thompson CC *et al.* Endoscopic ultrasound-guided treatment of gastric varices with coil embolization and absorbable hemostatic gelatin sponge: a novel alternative to cyanoacrylate. *Endosc Int Open* 2020;**8**:E221–7.
125. Franco MC, Gomes GF, Nakao FS *et al.* Efficacy and safety of endoscopic prophylactic treatment with undiluted cyanoacrylate for gastric varices. *World J Gastrointest Endosc* 2014;**6**:254–9.
126. Tang RSY, Kyaw MH, Teoh AYB *et al.* Endoscopic ultrasound-guided cyanoacrylate injection to prevent rebleeding in hepatocellular carcinoma patients with variceal hemorrhage. *J Gastroenterol Hepatol* 2020;**35**:2192–201.
127. Kozieł S, Pawlak K, Błaszczyk Ł *et al.* Endoscopic ultrasound-guided treatment of gastric varices using coils and cyanoacrylate glue injections: results after 1 year of experience. *J Clin Med* 2019;**8**(11):1786. DOI: 10.3390/jcm8111786.
128. De Almeida Lôbo MR, Chaves DM, De Moura DTH *et al.* Safety and efficacy of EUS-guided coil plus cyanoacrylate versus conventional cyanoacrylate technique in the treatment of gastric varices: a randomized controlled trial. *Arq Gastroenterol* 2019;**56**:99–105.
129. Frost J, Hebbar S. EUS-guided thrombin injection for management of gastric fundal varices. *Endosc Int Open* 2018;**6**:E664–8.
130. Mukkada RJ, Antony R, Chooracken MJ *et al.* Endoscopic ultrasound-guided coil or glue injection in post-cyanoacrylate gastric variceal re-bleed. *Indian J Gastroenterol* 2018;**37**:153–9.
131. Khoury T, Massarwa M, Daher S *et al.* Endoscopic ultrasound-guided angiotherapy for gastric varices: a single center experience. *Hepatol Commun* 2019;**3**:207–12.
132. Zeng X-Q, Ma L-L, Tseng Y-J *et al.* Endoscopic cyanoacrylate injection with or without lauromacrogol for gastric varices: a randomized pilot study. *J Gastroenterol Hepatol* 2017;**32**:631–8.
133. Bhat YM, Weilert F, Fredrick RT *et al.* EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue: a large U.S. experience over 6 years (with video). *Gastrointest Endosc* 2016;**83**:1164–72.
134. Bang JY, Al-Haddad MA, Chiorean MV *et al.* Mo1485 comparison of direct endoscopic injection (DEI) and EUS-guided fine needle injection (EUS-FNI) of 2-octyl-cyanoacrylate for treatment of gastric varices. *Gastrointest Endosc* 2015;**81**:AB437.
135. Romero-Castro R, Ellrichmann M, Ortiz-Moyano C *et al.* EUS-guided coil versus cyanoacrylate therapy for the treatment of gastric varices: a multicenter study (with videos). *Gastrointest Endosc* 2013;**78**:711–21.
136. Gonzalez J-M, Giacino C, Pioche M *et al.* Endoscopic ultrasound-guided vascular therapy: is it safe and effective? *Endoscopy* 2012;**44**:539–42.
137. Binmoeller KF, Weilert F, Shah JN *et al.* EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). *Gastrointest Endosc* 2011;**74**:1019–25.
138. Romero-Castro R, Pellicer-Bautista FJ, Jimenez-Saenz M *et al.* EUS-guided injection of cyanoacrylate in perforating feeding veins in gastric varices: results in 5 cases. *Gastrointest Endosc* 2007;**66**:402–7.

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