

Role Of Endoscopic Ultrasound In Diagnosis Of Esophageal Varices

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Abstract

Background: Bleeding esophageal varices constitute a digestive emergency with poor treatment response, numerous complications, and a high death rate. Moreover, bleeding for the first time is one of the most serious complications in cirrhotic patients. To decrease the death rate, predicting the occurrence of bleeding esophageal and gastric varices have been extensively explored. Previous research has shown that PHT can cause the occurrence of collateral and perforator veins, as well as varicose veins in the esophagus. After endoscopic treatment, patients with collateral and perforator veins are more likely to experience the recurrence of varicose veins. Transabdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are established diagnostic tools for abdominal diseases. Despite their widespread use, these techniques have limitations. In contrast, EUS complements these modalities, and has been proven useful for evaluating the mediastinum, pancreas, biliary tract, gastrointestinal tract, liver, and adrenal glands. EUS enables observation near esophageal varices and helps to understand the localized detailed hemodynamics of esophageal varices, this suggests that useful information can be obtained for the selection of treatment suited to the hemodynamics of each individual varix and for the prediction of recurrence. Furthermore, EUS is considered highly useful for determining the treatment response and can easily evaluate the presence or absence of residual blood flow that is difficult to determine by normal endoscopic observation. Over the past two decades, (EUS) has undergone a transition from being a novel imaging technique to a clinical diagnostic test that is necessary for the optimal management of gastrointestinal diseases. Along with established clinical indications, such as gastrointestinal and pancreatic tumor staging, differential diagnosis of submucosal lesions, evaluation of solid and cystic pancreatic masses, detection of lymph nodes and fine needle aspiration (FNA), new applications have been suggested such as a clinical role for EUS in PHT

Keywords: Endoscopic Ultrasound, Esophageal Varices

INTRODUCTION

Introduction

Bleeding esophageal varices constitute a digestive emergency with poor treatment response, numerous complications, and a high death rate. Moreover, bleeding for the first time is one of the most serious complications in cirrhotic patients. To decrease the death rate, predicting the occurrence of bleeding esophageal and gastric varices have been extensively explored. Previous research has shown that PHT can cause the occurrence of collateral and perforator veins, as well as varicose veins in the esophagus. After endoscopic treatment, patients with collateral and perforator veins are more likely to experience the recurrence of varicose veins (1).

Since Dimagno, an American physician, first reported on the application of EUS for examination of the digestive tract in 1980, the technology has greatly improved. EUS has mainly been used to determine the origin and nature of submucosal tumors in the digestive tract, determine tumor depth, diagnose pancreatic tumors accurately, and clearly observe the presence of mediastinal lesions. While EUS has been greatly developed in the above areas, the application of EUS in the evaluation of PHT has gradually progressed. Given that EUS can clearly reveal the esophageal branches and perforating veins, it has been employed by some researchers to predict bleeding and recurrence of varicose veins (2).

Transabdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are established diagnostic tools for abdominal diseases. Despite their widespread use, these techniques have limitations. In contrast, EUS complements these modalities, and has been proven useful for evaluating the mediastinum, pancreas, biliary tract, gastrointestinal tract, liver, and adrenal glands (3)

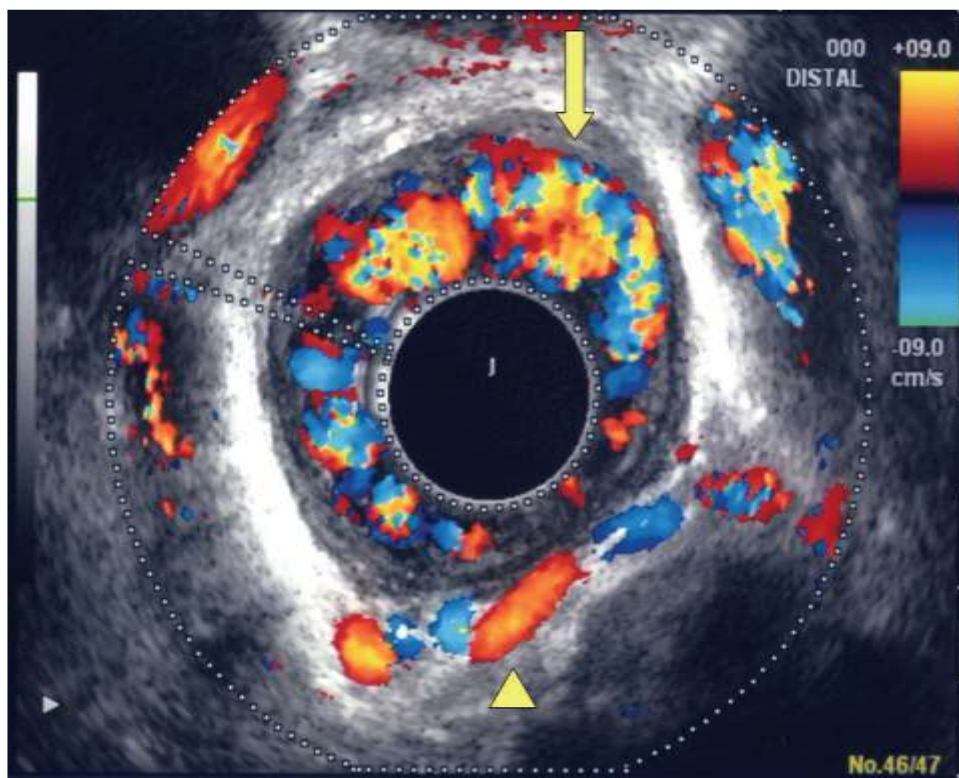
Esophageal varices are caused by the development of collateral circulation in the esophagus as a result of PHT. It is important to administer appropriate preventive treatment because bleeding varices can be fatal. To prevent the occurrence of varices, it is important to evaluate and understand the underlying hemodynamics associated with portal hypertension. In the actual preventive

treatment of varices, effective treatment methods and factors associated with recurrence after treatment differ according to hemodynamics (4). As in the case of other organs, contrast-enhanced CT (3D construction) and contrast-enhanced MRI are useful for determining portal vein hemodynamics in cases of portal hypertension. However, while these modalities are useful for understanding the state of the portal vein overall, they are insufficient for determining localized detailed hemodynamics of esophageal varices (4).

EUS enables observation near esophageal varices and helps to understand the localized detailed hemodynamics of esophageal varices, this suggests that useful information can be obtained for the selection of treatment suited to the hemodynamics of each individual varix and for the prediction of recurrence. Furthermore, EUS is considered highly useful for determining the treatment response and can easily evaluate the presence or absence of residual blood flow that is difficult to determine by normal endoscopic observation (5).

Over the past two decades, (EUS) has undergone a transition from being a novel imaging technique to a clinical diagnostic test that is necessary for the optimal management of gastrointestinal diseases. Along with established clinical indications, such as gastrointestinal and pancreatic tumor staging, differential diagnosis of submucosal lesions, evaluation of solid and cystic pancreatic masses, detection of lymph nodes and fine needle aspiration (FNA), new applications have been suggested such as a clinical role for EUS in PHT (6).

Since its first use in the assessment of patients with PHT in the mid-1980s, many conflicting studies have been published. EUS was used for the diagnosis of gastroesophageal varices and PHT, for the non-invasive assessment of portal hemodynamics and for the evaluation of efficacy of pharmaceutical and endoscopic therapy. However, an exact role of EUS in the diagnosis and management of PHT in routine clinical practice has not been established, yet (7).



Fig(1) Vessel images of esophageal varices (arrow) and paraesophageal veins (arrowhead) were delineated clearly with new electronic radial endoscopic color Doppler ultrasonography. (8)

EUS procedure for diagnosis of esophageal varices

Endoscopic ultrasonography (EUS) has become a very useful modality for the diagnosis of esophageal varices. EUS not only visualizes the surface of the varices but also provides detailed information about their internal structure. ECDUS is better able to observe the (9).

The venous anatomy of the lower oesophagus is composed of four layers: intraepithelial channels, superficial venous plexus, deep submucosal veins and adventitial veins radiating from the inner oesophageal mucosa to the outer layer. The innermost venous plexus communicates with the extrinsic plexus via perforating veins, which commonly are present 1–5 cm above the gastroesophageal junction. These, in turn, drain into the tributaries of either the portal or azygos veins. Development of PHT causes diversion of blood from the drainage bed of the portal vein to that of the azygos system causing engorgement of all the previous channels. Thus, the dilated deep submucosal veins are seen as variceal columns and the dilated adventitial veins form para-oesophageal varices (10).

Currently, the most widely accepted modality for screening gastroesophageal varices is oesophagogastroduodenoscopy (OGD), although it may be subjected to high interobserver variation in the assessment of variceal size, it lacks sensitivity in the diagnosis of gastric varices and it cannot assess the variceal wall thickness (11).

PHT causes engorgement and increased blood flow in the collateral vessels surrounding the lower oesophagus and proximal stomach outside the oesophageal wall. The collateral veins are divided into peri-oesophageal collateral vein (peri-OCV), which are located adjacent to the muscularis externa of the oesophagus, and para-oesophageal collateral veins (para-OCVs), which are external to the oesophageal wall, without any contact with the muscularis externa. Similarly, collateral veins surrounding the stomach are called para-gastric collateral veins (para-GCVs). Veins connecting peri-OCVs with para-OCVs are called the perforating veins. Although these vessels have been examined by percutaneous transhepatic portography, this is an invasive procedure which is also unable to differentiate the submucosal varices from peri-OCVs. Similarly, routine CT is highly costly and not very sensitive in detecting para-OCVs (12).

The significance of observing esophageal varices by EUS lies in determining the risk of bleeding, preoperative evaluation for safe and effective treatment, predicting recurrence, and determining the therapeutic response. ECDUS shows graphically esophageal varices, paraesophageal veins, and passage ways. **Sato et al.** have reported previously on the usefulness of convex type ECDUS for evaluating the hemodynamics of esophageal varices, **Hino et al.** analyzed the morphology and hemodynamics of the left gastric vein using ECDUS to evaluate the development of esophageal varices. They reported that hepatofugal blood flow velocity in the left gastric vein trunk increased with the size of the varices (13).

To administer safe preventive treatment of varices, it is indispensable to evaluate the underlying hemodynamics, and, in particular, preoperative evaluation by EUS is considered important. In conventional endoscopic observation, only esophageal varices within the esophageal lumen can be observed, and the extramural collateral pathways involved in the development of the varices cannot be observed. Endoscopic treatment of esophageal varices involves localized inhibition of blood flow. However, to execute such treatment safely and effectively, it is important to not only be able to see the esophageal varices by endoscopy, but also to understand the underlying structure, i.e., the hemodynamics, including the feeding vessels (14).

The use of EUS is needed to evaluate hemodynamics of localized esophageal varices include the peri-ECVs, para-ECVs and perforating vein (PV). The peri-ECVs are a group of blood vessels with a small diameter observed adjacent to the esophageal adventitia, and in developing cases, the margin of the esophageal muscularis propria (musculus longitudinalis externus) appears shaggy. Para-ECVs, however, are a group of blood vessels with a relatively large diameter found clearly apart from the esophageal wall. Para-ECVs have also been studied, and a histopathological causal relationship has been demonstrated by the existence of both peri-, and para-ECVs (15). Furthermore, these ECVs often communicate with esophageal varices via perforating vein (PVs), and such relationships can be observed in detail on EUS according to studies of the blood flow direction of the PVs using color Doppler EUS, it was found that most PVs in the lower esophagus served as inflow pathways. Thus, peri-ECVs and para-ECVs with PVs serve as feeding pathways from the lateral esophagus (16).

Choudhuri et al. reported that on observation of perforating veins connect the submucosal and para-ECVs channels in the lower esophagus by using EUS, these were 15% of patients with small varices and 85% with large varices. The perforating veins detected by ECDUS were classified into three types according to the flow direction. Type 1 showed inflow from the paraesophageal veins to the esophageal varices. Type 2 showed outflow from the esophageal varices to the paraesophageal veins. Type 3 was a mixed type that revealed both inflow and outflow. (17)

Color flow images of perforating veins were obtained by EUS revealed that the direction of blood flow in perforating veins is an important consideration in the therapeutic management of esophageal varices. Therefore, we should perform EIS on Type 1 for the purpose of obliterating esophageal varices and perforating veins. On the other hand, Type 2 is associated with diversion of esophageal variceal blood flow into the paraesophageal veins and is therefore equivalent to an extraesophageal shunt. One must use great caution in performing EIS for Type 2 and Type 3 variceal patients and EIS should be performed at the anal site of outflowing perforating veins. Endoscopic variceal ligation (EVL) may be the optimum treatment for this type of varices (18).

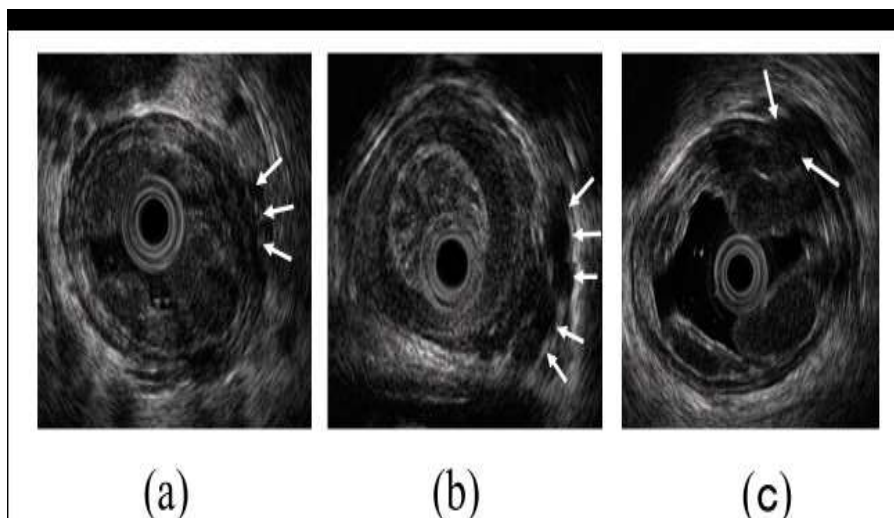


Fig (2) Intramural and extramural observation items of the esophagus. (a) Peri-ECVs. Many blood vessels of small diameter are observed adjacent to the esophageal adventitia (arrow). The existence of these vessels makes the margin of the musculus longitudinalis externus appear unclear. (b) Para-ECVs. Blood vessels with a relatively large diameter located distant to the esophageal adventitia (arrow). (c) Veins perforating esophageal wall. Perforating veins communicating between the esophageal varices and extramural ECVs (arrow). (18)

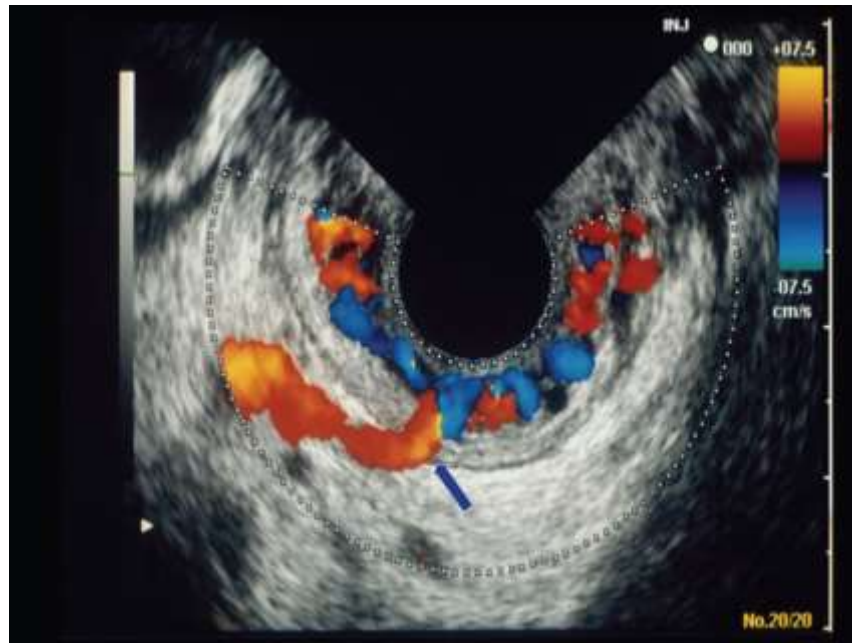


Fig (3) Inflow type perforating vein showed color flow image from the paraesophageal veins to the esophageal varices. (18)

EUS role in prediction of recurrence of esophageal varices

Ito k et al. reported that the incidence of variceal relapse was lower in patients with non variceal systemic portal shunts than in patients without these shunts. ECDUS can be used to evaluate the hemodynamic characteristics of esophageal varices before and after EIS and the data obtained can be used to predict the early recurrence of esophageal varices. In particular, detection of cardiac intramural vein and inflowing perforating vein by ECDUS after EIS showed a strong correlation with early variceal recurrence. (19)

EUS can identify hematocystic spots on the surface of EVs, whose presence is closely associated with a high risk of esophageal variceal rupture. These appear as saccular aneurysms, similar to projections on the variceal surface as observed using high resolution endoluminal sonography. Moreover, paraesophageal and paragastric varices detected by EUS have been shown to correlate with the presence and severity of portal hypertension and may be a risk factor for variceal bleeding (20).

Before endoscopic therapy, knowledge of the inflow pattern of the varices might be useful to make a treatment plan. Esophageal varices drain portal blood flow from the cardiac submucosal veins or perforating veins. If the varices receive blood from only the cardiac veins, endoscopic treatment should be focused in the cardia and esophagogastric junction. This cardiac inflow pattern of esophageal varices was seen in 60% of cirrhotic patients. Large collateral veins and perforating veins might be connected to the esophageal varices (21).

Previous studies showed large para-ECVs (>5 mm) were associated with high rates of variceal recurrence and rebleeding. The increased risk of bleeding seems to be associated with large perforating veins. Therefore, the high-risk patients need more intensive treatment and close follow-up. The anterior branch of left gastric vein was associated with poor response to endoscopic treatments. The morphology and blood flow of the vein can be evaluated with color Doppler EUS (21).

EUS can be used to assess the efficacy of EVL, Residual veins in the esophagus wall have been reported to be associated with a high risk of the reoccurrence of varices. Based on this, we recommend EUS after EVL; however, the patient may refuse that. In consideration of the high risk of recurrence, he underwent endoscopy 6 months later, and the recurrence of esophageal varices was observed. The 2 factors leading to the recurrence of esophageal varices are the regeneration of veins within the esophageal mucosa and the repatency of varicose veins. These recurrence factors are closely related to the existence of collateral and perforating veins (22).

Endosonographically detected para-oesophageal varices are excellent indicators of variceal recurrence after endoscopic sclerotherapy or ligation. Patients with large (>5 mm) para-OCVs have a greater risk of variceal recurrence and bleeding than those with small or without para-OCVs, These findings were confirmed subsequently. (22). Severe type peri-OCVs and large perforating veins were detected endosonographically, 3 months before endoscopic variceal recurrence indicating that these vessels may be used as well, for the early prediction of variceal recurrence after endoscopic treatment. Additionally, the presence of multiple intramural vessels in the cardia may predict recurrence (22).

The hepatofugal blood flow velocity in the left gastric vein trunk, and its branching pattern, were associated with variceal recurrence after endoscopic therapy. After endoscopic variceal ligation or sclerotherapy, the increased hepatofugal velocity and the anterior branching pattern, documented by CD-EUS, were found to be risk factors for recurrence. The detection rate and diameter of the perforating veins may also be a predictor of variceal recurrence (22).

Hepatofugal flow velocity was also shown to increase with varices of an increasing size. A study included 68 patients treated for moderate or large EVs who underwent CD-EUS after EVL and sclerotherapy. Patients with a high hepatofugal flow velocity in the LGV (>12 cm/s) were classified into a high-risk group. Half of the patients showed a recurrence of EVs within half a year, whereas it took nearly 2 years for half of the patients in the other group to exhibit a recurrence (23).

Evaluation of the pharmaceutical and surgical treatment response

Observation by EUS following completion of variceal treatment provides useful information about the need for additional treatment and follow-up observation. As a result of thrombus formation in varices after treatment, the hypoechoic signals disappear and change to hyperechoic signals on ultrasound images. However, when hypoechoic lumen is observed in hyperechoic images, it can be understood to mean that the thrombus formation is incomplete. **Pontes et al.** examined variceal changes after treatment and reported that EUS showed insufficient variceal thrombosis in (17%) patients who appeared to have variceal eradication at endoscopy after treatment (24).

With EUS, the azygos vein diameter as well as valuable quantitative and qualitative data, such as the blood flow volume index, can be obtained. Azygos blood flow (AzBF) and diameter can serve as an index of blood flow via gastroesophageal collateral vessels and varices in portal hypertension. **Lee YT et al** studied the feasibility of assessing AzBF using CD-EUS and of monitoring the effects of vasoactive agents on AzBF, and these authors found that there was a marked decrease in AzBF after 1, 5, and 10 min bolus injections of terlipressin and somatostatin. However, the control group showed no significant change in AzBF. (25)

Liao WC et al was used EUS to evaluate the volumetric change of paraesophageal and periesophageal varices in patients treated with propranolol who achieved EV eradication using primary EVL. (26)

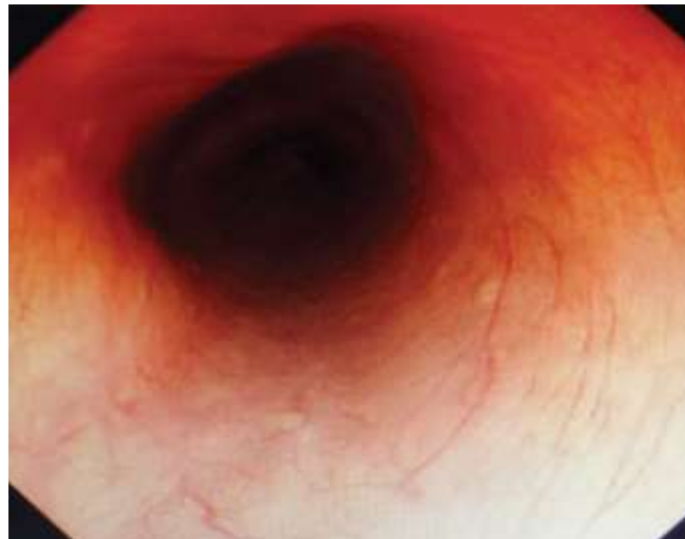


Fig (4) No esophageal varices were found under the ordinary endoscopy. (25)

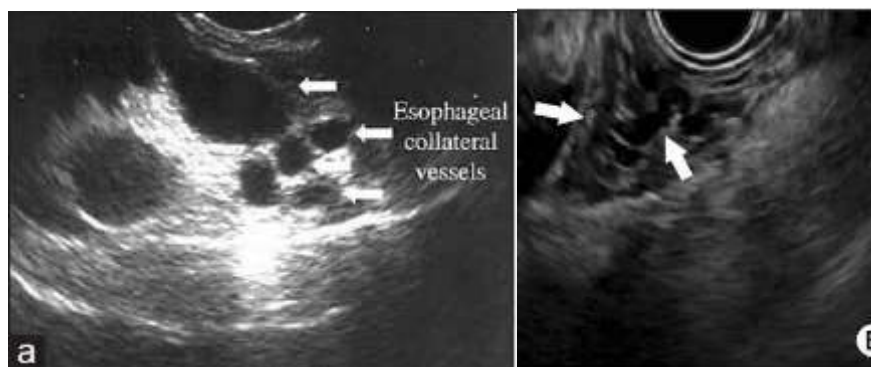


Fig (5): Esophageal mucosa, esophageal submucosal, paraesophageal varices were found under the EUS. (25)

Role of EUS in treatment of esophageal varices

It is well known that varices recurrence more commonly among patients who underwent endoscopic variceal ligation compared to those who had sclerotherapy, as ligation provokes mechanical strangulation of the varices in the mucosal and submucosal layers, leaving the perforating veins, which join the submucosal vascular channels to para-OCV, untouched. On the other hand, sclerotherapy may be able to obliterate the perforating veins and feeding veins, while chemical irritation caused by the sclerosants induce fibrosis and thickening of the inner oesophageal wall, preventing variceal recurrence (25).

By using miniprobes, perforating veins can be identified and bands can be applied on them, thus increasing the success of ligation and the variceal recurrence-free interval. Moreover, by using CD-EUS, the sclerosant can be injected until the varix is seen to be completely thrombosed, as indicated by the absence of flow on Doppler, or it can be directed to the level of the perforating veins. Thus, the number of sessions required for obliteration of oesophageal varices and the recurrence rate may be decreased (26)

The same stands for the gastric varices, which cannot be easily detected endoscopically, mostly after cyanoacrylate injection for controlling gastric variceal bleeding. EUS can easily identify residual gastric varices as submucosal anechoic vascular channels with a colour Doppler signal. Persistence of blood flow as detected by CD-EUS is associated with a higher failure rate of variceal obliteration by endoscopic treatment and with a higher risk of gastric variceal recurrent bleeding compared to those without detectable blood flow. It is also noteworthy that patients who underwent repeated EUS-guided cyanoacrylate injection had a significantly lower risk of rebleeding. Even though the overall mortality was not significantly changed, there was an improvement, in comparison to the patients who received on-demand injection only at the time of recurrent bleeding. (26)

Assistance in endoscopic intrahepatic portosystemic shunt:

The ability to access the portal vein via the stomach or duodenum may provide potential future therapeutic use, such as the direct placement of an EUS-guided intrahepatic portosystemic shunt (IPSS). **Buscaglia JM et al** studied the feasibility of EUS-guided IPSS creation in a live porcine model. Under linear-array EUS guidance, these authors punctured the hepatic vein and subsequently the portal vein using a 19-gauge FNA needle, and a metal stent was deployed under EUS and fluoroscopic guidance. The distal end of the stent was positioned inside the portal vein, and the proximal end was within the hepatic vein. There was no evidence of bleeding or damage to any intraperitoneal organs after the entire procedure. There were also no complications during the follow-up period over the next 2 weeks. Taken together, these data suggest that EUS-guided creation of an IPSS might become a useful alternative to conventional transjugular intrahepatic portosystemic stent-shunt. (27)

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