# EUS in portal hypertension

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## SUMMARY

**The mechanisms involved in the development and natural history of Portal Hypertension are far away to be clearly known. Endoscpic Ultrasonography is a branch of gastrointestinal endoscopy, that has achieved a world wide acceptance in the evaluation of many clinical settings during last years. Some of these indications are now clearly stated, while others are under evaluation. The possibility to apply EUS in portal hypertension has been studied by several Authors during last years, both in the diagnosis and in the management of this complication of liver cirrhosis. In fact EUS studies have been performed on the hemodynamic assessment of portal vein system, azygos vein, varices and portosystemic collaterals. In the management of portal hypertension EUS has been studied both for the assessment of the efficacy of drug therapy and for endocopic treatment. Data obtained are preliminary but very interesting and promising, and have given a great impulse to this field of clinical research.**


**Key Words:** Endoscopie ultrasonography, portal hypertension, bleeding, doppler

Portal hypertension is a continually evolving field of gastroenterology. Much progress has been achieved through hard work during recent years in the diagnosis and management of this complication of chronic liver disease. However, we are still far away from the definition of its patophisiology, natural history, and mechanisms of onset, and we have not given up looking for new methods to deal with it. In this setting, endoscopic ultrasonography has been proposed for the assessment of portal hypertension, promising that its applications in the future will be much wider than today, depending on the ongoing research and education of gastoenterologists in this method. Endoscopic ultrasonography (EUS) is a branch of gastrointestinal endoscopy that couples the endoscopic capabilities of a fiber optic endoscope to the echo graphic scanning provided by a high frequency ultrasound probe. This technique was reported for the first time during the early 80's, as a new method to study pancreatic parenchyma, and it was first reported as a possible new method in the investigation of portal hypertension in the late 1980s.[1] Since then, with the insistence of pioneers of EUS and the development of new instruments, which added Doppler and the operative ability (through an endosonographically guided needle) to our quiver, the application of this method has been much expanded. Today, it can already be appreciated as a progress in the diagnosis and management of portal hypertension. It seems possible that in a few years this method will be widely applied in this field, helping in the diagnosis and follow-up of portal hypertensive patients, the assessment of varices and their likelihood to bleed, and, finally, providing new options in their management with better outcomes.

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## INSTRUMENTS

Nowadays two main echoendoscopic systems are on the market. These are almost identical with respect to the fiberoptic-endoscope, but totally different in the echographic system.

The Olympus system has a dedicated echographic console, and a mechanical rotating echographic probe with a 360° scanning area, perpendicular to the longitudinal axis of the endoscope. The probe has only real time

capability and, due to probe orientation, it cannot be used to perform guided biopsies and operative procedures.

The Pentax–Hitachi system uses a multipurpose echographic console (Hitachi) that can be used for either conventional ultrasonography and echoendocopic exams and miniprobes devices (Fujinon). The probe is electronic, convex, with a scanning field of 105˚ and a longitudinal scanning plane. The system provides both real time and Doppler applications (Pulsed, Color and Power Doppler), and the probe orientation allows the possibility of any kind of operative procedures.

Recently a new kind of echoendoscopic procedure has been introduced: the *High-resolution endoluminal sonography (HRES)*. This is performed using very small catheter probes (frequencies ranging from 20 to 30 MHz), which are passed through the operative channel of the standard endoscopes used for visualization of the GI tract. The experience with these probes is limited and their fields of application are selected. They are of both radial and linear type and the usual operating frequency is 20 MHz.[2]

## DIAGNOSIS OF PORTAL HYPERTENSION

### *Haemodynamic assessment of Portal vein system*

Endoscopic ultrasonography can easily identify and examine the portal vein (PV the superior mesenteric vein (SMV) and the splenic vein (SV). These vessels are visualized from both the posterior wall of the stomach and the second part of the duodenum. The azygos vein is easily identified and examined scanning from the esophagus. Portosystemic collateral vessels can also be identified. With the use of a linear instrument we can perform Duplex and Color Doppler studies of these vessels. Measurements of the diameter and blood flow can be performed and luminal abnormalities can be recognized.[3]

As in transabdominal ultrasonograhy, the diameter of portal vein and its contributors is increased in most instances of portal hypertension. Blood flow can be assessed as to whether it is hepatopetal or hepatofugal and measured.

*Wiersema et al*[3] used a linear EUS instrument to examine 11 patients with non-diagnostic transabdominal ultrasound and suspected thrombosis of the splenic and/or portal veins or a portosystemic shunt and compared their results with CT, angiography and/or surgery or autopsy findings. They also compared the results with a control group. They found an 89% accuracy of EUS in cases where US failed to provide a diagnosis. In this study EUS seemed to be superior to CT in the assessment of portal vein system and its results were comparable with angiography (which is considered to be the "gold standard" in the assessment of the portal vein system status).

Patency of the examined vessel was defined by a continuous, low velocity pulsed (using an incident angle between 0 and 60 degrees) and color Doppler signal within it. Venous thrombosis was demonstrated by the absence of flow within the vessel, documented by pulsed and color Doppler with or without the finding of stationary echoes (solid thrombosis) within the lumen. Evaluation for stenosis was performed by measuring the peak systolic velocity at different points along the course of the shunt. Any evidence of an increase in peak velocity along the shunt associated with a greater than 70% lumen narrowing and presence of adjacent collaterals was considered significant. The diameter of the portal vein was found significantly greater in patients (18,5 ± 3,6 mm) in comparison with controls (10,7 mm).[3]

In the above study the authors illustrated the advantages of this method:

1. The close vicinity of the ultrasound probe to the target vessels. There is no interference of the transmitted and received echoes with air in the bowel, bone tissue, adipose tissue or the presence of ascites. The latter is a frequent finding in portal hypertensive patients, making the examination of the portal system very challenging and, not rarely, impossible by Transabdominal ultrasonography.
2. The higher frequency probes used with EUS for both B-mode and Doppler in comparison with transabdominal ultrasonography allows us to obtain images with better resolution (such high frequency cannot be used by US because it reduces the depth of imaging so much that interrogation of the portal system would be impossible).

   In some patients, portal vein flow is very slow and cannot be identified by the use of US (and, perhaps, a false diagnosis of occlusion is given). In such cases the higher frequencies provided by EUS Doppler can identify the flow.

   The evaluation of portosystemic shunts is also superior with EUS than US. The format has a higher sensitivity compared to US, not only to identify the presence of flow through the shunt, but also the stenosis that may exist in a shunt anastomosis.
3. In comparison with CT, EUS seems to have a higher

diagnostic yield and, furthermore, there is no need for use of contrast agents or radiation.

4. In comparison with angiography, EUS seems to have similar results and is a less invasive technique without needing a contrast agent or use of radiation.

In conclusion, the authors suggest that EUS can be considered as an alternative imaging study when US and/or CT are unsuccessful or equivocal.

### *Haemodynamic assessment of the azygos vein*

Many authors have studied the azygos vein flow using linear instruments. It is known that in most instances of portal hypertension, gastroesophageal collateral blood vessels drain into the superior vena cava through the azygos vein system. Previous investigations were performed using much more invasive techniques.[4,5] Among atients with portal hypertension, azygos vein blood flow has been found to be four to six times higher than normal and directly related to pressure in the portal system.[5] Lee et al[6] studied the azygos vein flow from the mid-esophageal level just before the vein enters the superior vena cava. They found significantly increased blood flow that correlated with the severity of liver disease according to Childe-Pugh score. The results confirmed the findings of Bosch et al[4,5] who measured blood flow in the azygos vein using the invasive thermo dilution technique. The authors suggested the use of EUS with Doppler capabilities for the assessment of the azygos vein flow as a less invasive technique.

Salama et al[7] reported that azygos vein diameter and blood flow were increased in patients with gastroesophageal varices compared with controls, but they did not correlate these findings with the severity of liver disease.

### *Varices and portosystemic collaterals*

The venous anatomy of the esophagus in normal and portal hypertensive subjects has been described.[8,9,10] The drainage system consists of four layers: a) the *intraepithelial channels* which run radially within the epithelium, draining the capillary network, b) the *superficial venous plexus* that lies immediately below the epithelium and receives blood from the intraepithelial channels, communicating also with the corresponding venous plexus in the stomach, c) the *deep intrinsic venous plexus* which lies in the submucosa and communicates with the superficial venous plexus and with corresponding submucosal veins in the stomach and, d) the *adventitial veins* which connect with the deep intrinsic veins via the *perforating veins*. All these channels become dilated in portal hypertensive patients. Varices seen endoscopically are thought to correspond to dilated deep intrinsic veins in the submucosa, while "red color signs" probably correspond to the dilated intraepithelial or subepithelial channels.

Why varices bleed is not yet completely understood. It seems that *variceal size* and *wall tension* are the most important factors.[11] Some investigators have assumed that varices themselves are not always the main pathway for portosystemic shunting, and that most shunting occurs at a deeper level from the adventitial veins, through the *paramural esophageal vessels*. In this case, varices are considered as a backwater that has developed as a result of high pressure in the periesophageal *veins*.[12,13] Paramural vessels communicate with the intramural veins (varices) via the perforating veins that pierce the muscular coat. The paramural vessels have been studied by several methods (angiography, CT, postmortem studies) and they recognized as feeders of the intramural veins (varices).[14] It is assumed that they are a major cause of variceal recurrence after eradication. For this reason, a closer follow up is suggested for patients with large Para esophageal collaterals. Many authors believe that the perforating veins may account for difficulties with variceal eradication and, therefore for variceal recurrence.[15] It is useful to mention that some investigators discrete paramural vessels in Para esophageal veins (mediastinal veins running longitudinally at some distance to the esophagus) and periesophageal veins (situated in the connective tissue surrounding the esophagus).[14] However, there is no clear distinction between the two compartments, so they are often collectively referred to as paramural vessels.[14]

Because of all the above-mentioned parameters (and difficulties) which influence the outcome of patients with varices, it was thought in the lates 1980s by some investigators that EUS could have an impact in their management.[1]

Caletti et al[16] performed EUS (using a radial instrument) in patients with portal hypertension and compared their results (regarding the finding of varices) with standard endoscopy. In EUS, varices are displayed as rounded echo-free structures just beneath the mucosal and submucosal layers. This study showed that EUS could identify only 14% of varices grade 1, 78% of varices grade 2 and 50% of varices grade 3 (grading was based on endoscopic findings) as compared with the "gold standard" of endoscopy. This relatively low achievement of EUS was attributed to problems in focusing the ultrasound display and to compression of varices by the water-filled balloon of the instrument. To avoid this problem and improve the visualization of esophageal varices, Urabe

et al[17] proposed not to use the water-filled balloon technique, but to fill the esophageal lumen with water and to use a balloon placed 7 cm proximal to the tip of the echoendoscope, to prevent reflux of the injected water. They reported a success rate of 100% in the visualization of untreated esophageal varices by EUS.

Another study by Sato et al[18] suggested that EUS using linear instruments with color Doppler may be superior to radial scanning EUS when used for detection of esophageal varices and perforating veins. They reported the detection of varices in 95,8% of patients and of perforating veins in 36,4% of them.

Generally, endoscopy is still considered superior to the EUS method in identifying esophageal varices (especially of lower grade), but results can be improved using minimal balloon inflation or the lumen water-filling technique.

Another "weak" point of EUS in comparison with standard endoscopy is that "red color signs" (for which the dilated intraepithelial and subepithelial channels are responsible) cannot be identified.

Some investigators consider that high-resolution endoluminal sonography (HRES) could be a more accurate method in the assessment of esophageal varices. Schiano et al[19] used a 20 MHz 6,2Fr ultrasound transducer (passed through the channel of a standard endoscope) to measure the radius and wall thickness of esophageal varices. They also studied the interobserver and intraobserver variation and found them extremely low, so the method is considered very reproducible. The use of these results combined with a measurement of intravariceal pressure, either obtained through direct variceal puncture or using non-invasive pressure measurements, means that now is possible to measure all the variables in the Laplace equation in vivo and thus calculate variceal wall tension.

In another study, again by Schiano et al,[20] the hematocystic spots on esophageal varices were evaluated using HRES with a 20 MHz catheter probe. Initially, they performed EGDS and found 10 patients with these spots. They, then performed HRES and in 6 of the above patients, the hematocystic spots appeared as saccular aneurysms on the variceal surface. 4 of 6 patients developed recurrent bleeding. The aneurysm-like projections were considered to represent focal weaknesses of the variceal wall that play a key role in the pathophysiology of variceal rupture.

EUS can visualize the esophageal paramural collaterals. Caletti et al[16] reported a prevalence of 80% in patients with esophageal varices (57% of patients with endoscopically grade 1 varices, 89% of patients with grade 2 and all patients with grade 3 varices). Increasing with the size of varices, an increased number of paramural collaterals can be detected. This could play an important role in the management of varices, as we shall see in the following.

Perforating veins have also been evaluated by EUS, especially regarding their appearance or not after endoscopic therapy of varices (to be discussed later).[21,22]

Gastric varices were investigated using EUS and it was clear from the beginning that this new method is a better method for their demonstration than standard endoscopy. To distinguish between normal or enlarged gastric folds and varices is often difficult endoscopically and EUS can assist in this. Caletti et al[16] demonstrated gastric varices in all their patients with grade 3 esophageal varices. They also identified gastric varices in 29% of patients with grade 1 esophageal varices and in 56% of them with grade 2. To visualize these varices, the authors positioned the ultrasound probe just below the gastroesophageal junction and filled the stomach with water. EUS identified gastric varices as echo-free structures beneath the mucosa and submucosa of the fundus. Burtin et al[21] reported a diagnosis of gastric varices in 41% of their patients using EUS versus 17% using endoscopy. In addition, they were able to visualize perforating veins below the esophageal junction in 40% of patients with cirrhosis and never in controls. This information could be important in the management of varices.

Splenorenal collaterals can be visualized using EUS. Wiersema et al,[3] using a linear instrument with Doppler capabilities have shown that it is possible to identify and evaluate postsurgical splenorenal shunts.

Portal hypertensive gastropathy is another potential source of bleeding. The endosonographic pattern of this entity was described by Caletti et al.[16] It consists of multiple small, anechoic, rounded structures in the gastric submucosa. These authors found EUS to be equal to endoscopy in diagnosing portal hypertensive gastropathy, although others reported a slight superiority of EUS.[23]

It is sure that more studies are needed for the final evaluation of EUS in the diagnosis of portal hypertension. As more experience with this method is gained, the results are going to improve. An increasing number of gastroentorologists are becoming involved with it and with the addition of newer, more powerful instruments with advanced Doppler capabilities, it seems that EUS

will be an important tool in dealing with the portal hypertensive patient.

In conclusion, EUS seems to have already established its position in: a) the diagnosis of gastric varices, b) the evaluation of periesophageal (including the perforating veins) and perigastric veins and c) the hemodynamic assessment of the portal vein system and the azygos vein.

### *Other observations*

EUS (with a radial probe) was used by Parishes et al[24] to study the thoracic duct morphology in patients with portal hypertension. They found that it is dilated in the presence of ascites and esophageal varices. In patients without ascites or varices and in patients with exrahepatic portal hypertension the diameter of thoracic duct was not significantly different from that in controls. The study confirms the previous radiologic/surgical data indicating that the thoracic duct is dilated in hepatic cirrhosis, but it does not confirm that dilation is seen in all cases of hepatic cirrhosis and portal hypertension. The reason for this discrepancy is unknown. It can be hypothesized that lymphagiography may alter lymphatic dynamics by the injection of contrast under pressure. This may cause spurious duct dilation. They concluded that EUS is a unique method to study the thoracic duct (without manipulating it) and a dilated duct found endosonographically may be a sign of advanced cirrhosis with ascites and varices.

Dhiman et al[25] studied the rectal venous system in patients with portal hypertension using a radial probe. They found that EUS was superior to endoscopy in identifying rectal varices (75% versus 43,3%). The development of these varices is significantly influenced by previous endoscopic sclerotherapy, which was found to increase their prevalence. There was no correlation with the grade of esophageal varices, the etiology of portal hypertension, or the severity of liver disease. In patients with portal hypertension, submucosal veins in the rectum, exceeding 2 mm in diameter, may be defined as rectal varices.

During recent years, the use of contrast agents to improve color Doppler images has been proposed. Ernst et al[26] used Levovist to study esophageal varices. They performed endosonography (with color Doppler) before and after the injection of this agent and found a significantly improved image in the second examination. The authors suggest that use of contrast agents can help to visualize flow in esophageal perforating veins and periesophageal vessels more clearly, and may provide new insights into the hemodynamics of portal hypertension.

## MANAGEMENT OF PORTAL HYPERTENSION

EUS has been used to monitor patients before, during and after treatment. In some cases recently it was used to actually treat the patients.

### *Pharmacologic treatment*

As has previously been described, EUS is suitable for the hemodynamic assessment of the portal system and the azygos vein. The ability to measure blood flow using Doppler technique could be used to assess the effects of certain drugs (thought to affect the portosystemic circulation).[14]

Many investigators have studied azygos vein blood flow by using invasive techniques (e.g. the before mentioned thermodilution technique by Bosch et al). Studies have also been performed after the administration of certain drugs (propranolol, nitrates, terlipressin, somatostatin). They documented a reduction in azygos vein flow, but because of their invasive nature it is difficult to expand their application in clinical practice.[6,14]

Lee et al[6] monitored azygos vein blood flow before and after the i.v. administration of terlipressin and somatostatin in patients with portal hypertension, using a linear EUS instrument. They found a remarkable decrease of the flow after injecting these drugs. The authors suggest that this method is less invasive than the previous ones used and may prove useful in monitoring patients with portal hypertension receiving vasoactive agents or β-blockers. Further studies are needed in this field.

### *Endoscopic treatment*

Sclerotherapy has been the standard endoscopic treatment for varices for many years and band ligation has lately emerged as a possibly better choice. We have already seen that EUS can visualize the perforating and periesophageal veins which obviously cannot be visualized by standard endoscopy.

Some investigators thought they could combine the ultrasonographic and endoscopic abilities of EUS to improve results of sclerotherapy. In a recently published study Lahoti et al[27] reported EUS-guided sclerotherapy of esophageal varices using a linear instrument (with Doppler capabilities). The patients were admitted because of upper GI hemorrhage but were not bleeding at the time of endoscopy. They were stabilized and given octreotide i.v. The initial EGD was immediately followed by EUS. With the echoendoscope within the esophageal

lumen, esophageal varices were imaged as elongated, superficial, anechoic, structures parallel to the image axis. Perforating (feeding) veins were imaged as elongated, deep, anechoic structures perpendicular or oblique to the image axis. Continuous color flow Doppler was used to visualize flow within the vessels. Sclerosant was then injected using a catheter injector needle. The sclerosant was directed to the perforating veins and was delivered until flow was completely impeded as determined by color Doppler. Patients had follow-up EGD with EUS-guided sclerotherapy at 2-week intervals until EUS documented obliteration of esophageal varices. The number of sessions required for complete obliteration of the varices was 2:2 and there was only 1 complication, which was a stricture successfully, treated with balloon dilatation. Although the number of patients was too small (only 5) to judge the method, the results were satisfactory since there was no recurrent bleeding and no deaths during the study period at a mean follow up of 15 months. In conclusion, the authors suggest that EUS-guided sclerotherapy can be performed in a safe and effective manner in patients who are not actively bleeding. The sclerosant can be injected until the varix is seen to be completely thrombosed and the absence of flow documented by color Doppler. Furthermore, the sclerosant can be directed to the level of the perforating veins thereby interdicting the underlying pathophysiology more effectively. Neither of the above is possible now with standard sclerotherapy or band ligation. Possibly, with this method we could decrease the number of sessions required for variceal obliteration and also the recurrence rate of esophageal varices after obliteration. According to the authors, large prospective, multicenter, randomized trials are warranted to expand these encouraging preliminary results.

The idea of monitoring the results of sclerotherapy using EUS was not new. Ziegler et al[28] reported in 1991 that it was possible to assess the extent of thrombosis within the varices after sclerotherapy so that the need for additional therapy and the risk of recurrent bleeding could be evaluated.

In another study, by Lo et al,[29] EUS was used to visualize paraesophageal varices and gastric varices in a group of patients who underwent sclerotherapy and another group whose patients underwent band ligation. The prevalence of paraesophageal varices was higher in the ligation group compared with the sclerotherapy group (86% vs. 51%). Varices recurred in 70% of the ligation group, compared with 43% of the sclerotherapy group. There was a positive correlation between the severity of paraesophageal varices and variceal recurrence in both groups. Although the rates of recurrent bleeding were not significantly different between the two groups, all patients who had rebleeding had paraesophageal varices on EUS. This study strengthens the role of endoscopic ultrasound in evaluating the risk of recurrence and rebleeding after endoscopic treatment.

The direction of blood flow in perforating veins using color Doppler EUS was studied by Sato et al[30] in 30 patients with recurrent esophageal varices after endoscopic treatment. They obtained color flow images in 60 % of them. The direction of flow in perforating veins was divided into three categories: type 1, inflow from paraesophageal to esophageal varices; type 2, outflow from esophageal to paraesophageal varices; and type 3, a mixture of types 1 and 2. The authors found that most patients (83,3%) had type 1 blood flow. A potential correlation between blood flow direction and the risk of recurrent bleeding should be very interesting and further studies are needed.

As we have already seen, EUS is established as a suitable method to visualize gastric varices. Some authors thought that it might also be suitable for treating them. Lee et al[31] evaluated the EUS-guided injection of cyanoacrylate (CYA) in bleeding gastric varices. In their study, patients with cirrhosis presenting with bleeding gastric varices were enrolled. In the first group of patients, they performed "on demand" injection of CYA to control bleeding from gastric varices. Further injections were given only in cases of recurrent bleeding. In the second group, after initial hemostasis was achieved, patients were evaluated by EUS biweekly and repeated CYA injections were given to obliterate residual gastric varices. The first EUS examination was performed 7 days after the initial endoscopy. The anatomic position(s) of gastric varices was noted by recording location (lesser or greater curvature) and distance from the cardia. Then, the echo-endoscope was withdrawn and a forward viewing gastroscope was inserted for the injection. The treatment endpoint was the disappearance of hypoechoic vascular channels in all parts of the stomach. After obliteration of gastric varices, patients were followed-up halfyearly with EUS and injections were repeated if gastric varices recurred. Patients in the first ("on demand") group underwent an average of 1,3±0,5 sessions of endoscopic therapy using a median 2 doses of CYA injections. Of course, obliteration of varices was not determined in these patients. Patients in the second group needed an average of 2,2±1,7 sessions in 5,3±3,8 weeks using a median of 3 doses of CYA injections. Complication rate (usually ulcers) was higher in the second group

directly related to the higher amount of CYA used. Although early recurrence of bleeding (<48 hours) was the same in the two groups, there was a significant reduction of rebleeding in the second group after the first 48 hours, excluding patients with HCC. Despite this reduction of rebleeding in the latter group, there was no difference in long-term survival between the two groups. Excluding patients with HCC, there was a trend towards longer survival in the second group. Based on these results, the authors suggest aggressive treatment of gastric varices aiming at total eradication of residual varices in the fundus and cardia with the exclusion of patients with HCC and portal vein thrombosis. According to the authors, EUS contributed to the success of repeated injection in the second group in reducing the recurrent bleeding. Further studies are needed to evaluate this method. Other investigators (Iwase et al)[32] using a linear echoendoscope in an older study, found that persistent blood flow in gastric varices after CYA injection therapy was associated with a higher rate of recurrent bleeding.

In our opinion, the above study of Lee et al is very interesting and it may give new ideas on this very difficult aspect of bleeding gastric varices, but it was not exactly an EUS-guided injection, since the authors had to remove the echoendoscope and then use a standard endoscope. In this way, the injection was performed under endoscopic view. Of course, the authors used a radial EUS instrument and, as we have noted before, with this type of instruments it is not possible to guide a needle. It might be considered that the method (described earlier) by which Lahoti et al dealt with esophageal varices might have an application in gastric varices. With the use of a linear instrument we could avoid the second intubation of the patient and perform EUS-guided sclerotherapy in one step. We could also have a "real-time" visualization of the thrombotic process in the injected varix and, with the use of Doppler, an immediate assessment of blood flow. Further investigation is needed to evaluate the usefulness of EUS in the management of gastric varices.

As we have seen, there is much interest in the studying of the hemodynamics of the azygos vein in portal hypertensive patients using a linear echoendoscope. Kassem et al[33] studied the azygos vein before and after endoscopic obliteration of esophagogastric varices by injection sclerotherapy. The authors found a statistically significant increase in azygos vein blood flow (and also in vein diameter) after sclerotherapy. However, other authors reported a decreased flow in the azygos vein after injection sclerotherapy or band ligation. Kassem et al suggest that a possible explanation for these conflicting results might be the differences in the methods of variceal obliteration: the effect of band ligation is mainly localized at the site of the varix, while endoscopic injection sclerotherapy may be associated with an intravascular spread of sclerosant. Differences between studies using sclerotherapy may occur depending on whether injection is predominantly intravariceal or paravariceal.

At present, there is no clear clinical application of the above observations. First of all, larger studies are needed using standard methods in order to obtain reproducible results, as for as possible. It far be very interesting if we could identify a threshold for azygos vein blood flow beyond which there is significant possibility of recurrent bleeding after endoscopic therapy.

It is obvious that EUS techniques in the treatment of portal hypertension are only at the beginning, but there are many good reasons to continue investigation in this area, since preliminary reports seem very encouraging. EUS now can clearly be used to evaluate the presence of periesophageal (and perforating veins) before and after endoscopic treatment and assist in the prognosis of possible recurrent bleeding and the need for further therapy. It also seems possible that in the near future it will be used to: a) detect the blood flow in the azygos vein before and after pharmacologic treatment, replacing other more invasive techniques, and b) perform injection sclerotherapy in esophageal and gastric varices under direct ultrasonogrophacic guidance. Much work is still needed to establish these applications of EUS, but interest in the method is continually growing.

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