Chapter 9
The Role of Endoscopic Ultrasonography for Esophagogastric Varices

Atsushi Irisawa, Goro Shibukawa, Ai Sato, and Akane Yamabe

Abstract In patients with esophageal varices accompanied by complicating portal hypertension, a large network of portal-systemic collateral veins develops. Endoscopic ultrasonography (EUS), especially ultrasound mini-probe, allows for noninvasive imaging of collateral circulation in the esophagus as well as the inside and outside of the gastric wall and allows treatment selection tailored to the hemodynamics of each individual varix. The characteristics to be evaluated in a patient with esophagogastric varices with EUS include the following: (1) diameter of the varix, (2) perforating veins, (3) periesophageal veins/perigastric veins, and (4) paraesophageal veins/paragastric veins. The observation of these structures provides important information for safer and more effective treatments; in addition, EUS also provides information that is useful for the prediction of recurrence.

Keywords EUS · Esophageal varices · Gastric varices

9.1 Introduction

In patients with esophageal varices accompanied by complicating portal hypertension, a large network of portal-systemic collateral veins develops. Frequent and significant pathways of collaterals consist of gastroesophageal varices and veins outside the esophageal/gastric wall extending from the left and short gastric veins [1–4]. Therefore, in the treatment of esophagogastric varices, understanding the morphology of esophagogastric varices, the local hemodynamics of varices, and portal hemodynamics is extremely important for the safety and efficacy of treatment.

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Endoscopic ultrasonography (EUS) allows for noninvasive imaging of collateral circulation in the esophagus as well as the inside and outside of the gastric wall and allows treatment selection tailored to the hemodynamics of each individual varix [5–8]. In addition to this, in the posttreatment determination of treatment efficacy, EUS also provides information for determination of whether a complete recovery will be achieved by the treatment or whether additional treatment is necessary [9]. In this chapter, we explain the use of EUS for diagnosing esophagogastric varices and demonstrate the effective application of EUS before and after treatment.

9.2 EUS Divides and Methods

9.2.1 EUS Devices

The types of EUS that are used in the diagnosis of esophagogastric varices can be roughly classified into two major categories. The first one includes devices for exclusive use in endoscopic ultrasonography such as radial scanning EUS and linear scanning EUS. The second category includes the ultrasound mini-probe (UMP). UMP (20 MHz) is suitable for use in the determination of the local hemodynamics of esophagogastric varices; in particular, detailed observation using a UMP is required when to monitor esophageal varices [2]. On the other hand, devices for exclusive use with EUS are used in the assessment of blood vessels outside the gastric wall as well as the inflow circuit, features that cannot be evaluated with UMP because of an attenuation of the ultrasonic beam. Furthermore, the latest devices for exclusive use in electronic scan-type EUS have a color Doppler function, allowing assessment of the blood flow direction and blood flow rate in the perforating veins (Pv) of the esophagus and gastric wall [10]. For pre- and posttreatment evaluations, observations using UMP are sufficient. In this chapter, the images of UMP are mainly described.

9.2.2 Observation of Esophageal Varices

When a UMP is used, a cap with water supply function is attached to the accessory channel of the endoscope, and observations are carried out while the esophageal lumen is filled with degassed water using the water supply function. Specifically, the stomach is filled by injection with approximately 400 mL of degassed water; the air in the gastric fundus is suctioned, while degassed water is being sent into the esophagus, and then the UMP is inserted and observation is carried out (Fig. 9.1). The basic scanning method is as follows: the UMP is pulled out directly from under the cardia (the UMP is pulled out to approximately 20 mm from the tip of the scope, and then each scope is pulled out) as simultaneous observations are carried out. During endoscopic examination using a water supply function, users must keep in mind that the strong water flow may cause the formation of air bubbles, which may

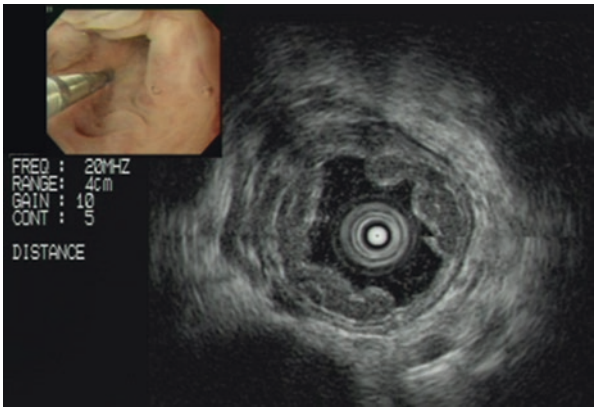

Fig. 9.1 The observation of esophageal varices using UMP. During UMP manipulation, degassed water is continuously supplied to fill in the esophageal lumen to obtain the clear image of UMP

interfere with the observation. The same procedure is utilized when we work with devices for exclusive use with EUS, but caution is required not to crush varices by insufflation of the tip-mounted balloon.

9.2.3 Observation of Gastric Varices

To observe gastric varices, first approximately 300–500 mL of degassed water is used to fill the stomach lumen, and ultrasonographic observation is carried out while the device is immersed in the water. This applies to devices both for exclusive use with EUS and UMP. When UMP is used, all of the gastric varices can be regularly observed without difficulty through inverted scanning under direct endoscopy, but fundamentally, with EUS devices, observations are carried out by looking down, and for that reason, it is difficult to determine whether all varices have been observed or not. On the other hand, when observing blood vessels outside the gastric wall, assessments using UMP can be difficult because of attenuation.

9.3 Diagnosis of Esophagogastric Varices by Endoscopic Ultrasonography

According to the Japanese clinical guidelines for the management of portal hypertension (third edition) [11], the characteristics to be evaluated in a patient with esophagogastric varices with EUS include the following: (1) diameter of the varix, (2) Pv, (3) periesophageal veins/perigastric veins, and (4) paraesophageal/gastric veins. The following section describes observation methods focused on the aforementioned items, as well as their clinical significance. Additionally, the methods indicated in the guidelines are shown in Table 9.1.

Table 9.1 General rules for recording EUS findings of esophagogastric varices (modified from "The general rules for study of portal hypertension, Third Edition" [11])

General rules for recording EUS findings of esophagogastric varices
1. Diameter [*D*]
Describe the maximum shoort-axis diameter (mm) of varix
D(0) is used for those that do not have a luminal image after treatment
2. Perforating veins [Pv]
Presence/absence is indicated by (+) (−), and if it is present, the maximum diameter (mm) is added
3. Periesophageal/gastric vein [Peri-v]
Presence/absence is indicated by (+) (−)
4. Paraesophageal/gastric vein [Para-v]
Presence/absence is indicated by (+) (−)

9.3.1 Esophageal Varices

9.3.1.1 Local Endoscopic Ultrasonographic Analysis of Esophageal Varices

There is a considerable variation in the development of collateral circulation resulting from portal hypertension, but from the perspective of the development of collateral circulation based on existing vascular networks, the basic hemodynamics are generally predetermined [2, 12]. Figure 9.2 shows collateral circulation found inside and outside the esophageal wall through observation using EUS (particularly UMP). In every case, the degree of development of each blood vessel should be evaluated on the basis of this figure. In addition, the resulting EUS images allow for estimation of the efficacy of endoscopic varicealography during injection sclerotherapy (EVIS) and are useful for the selection of the proper endoscopic treatment (endoscopic injection sclerotherapy [EIS] or endoscopic variceal ligation [EVL]) (the selection criteria will be described in detail later).

9.3.1.2 Morphology of Esophageal Varices

In the observation of the morphology of esophageal varices, the two important factors are diameter and internal morphology. Esophageal varices are present mainly in the submucosal layer and are observed as images of the hypoechoic lumen. Their morphology can be classified into two types: that with an oval or elliptic shape observed as a single isolated blood vessel (solitary type, Fig. 9.3a) and that made of thin varices stacked upon each other (reticular type, Fig. 9.3b). The reticular type usually requires a larger quantity of sclerosing agents and more frequent treatment sessions than the solitary type. In addition, appropriate selection of puncture needle (diameter and length) depending on the morphology and diameter is important for proper treatment.

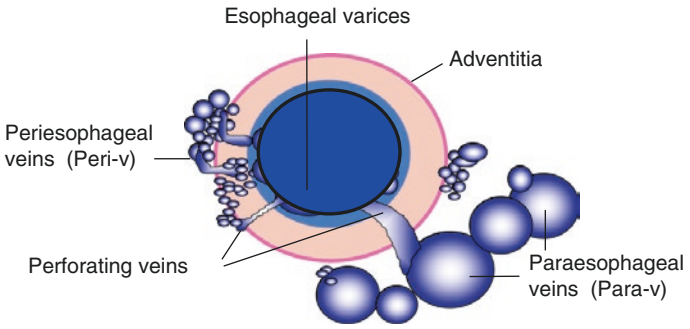

Fig. 9.2 The schema of the UMP image inside and outside esophageal wall (Modified from Irisawa et al. [6])

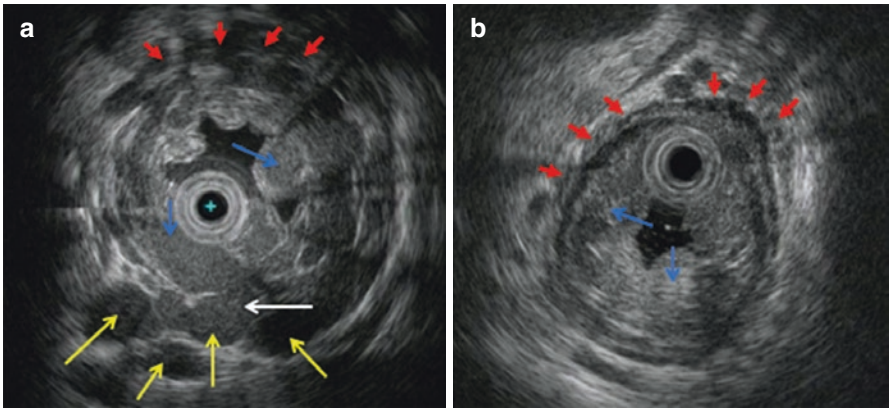

Fig. 9.3 (**a**) Solitary-type esophageal varices were seen (*blue arrows*). In addition, periesophageal veins (*red arrows*), paraesophageal veins (*yellow arrows*), and the perforating vein between esophageal varix and paraesophageal vein (*white arrow*) were identified. (**b**) Reticular-type esophageal varices were seen (*blue arrows*). In addition, periesophageal veins (*red arrows*) were identified. Due to the existence of periesophageal veins, the esophageal adventitia becomes "shaggy," and observation may show the outer longitudinal muscle layer as even more hypoechoic

After treatment, the presence or absence of residual lumen in the esophageal wall should be checked, or when consolidation therapy is performed, the thickening of the esophageal wall should be checked (Fig. 9.4). The risk of recurrence is extremely low if a uniform wall thickening without a luminal structure is observed.

9.3.1.3 Perforating Veins (Pv) of the Esophageal Wall

Pv of the esophageal wall are blood vessels that communicate with varices in the esophageal wall and blood vessels outside the esophageal wall. Such Pv can be observed relatively easily with UMP (Fig. 9.3a). Studies using color Doppler EUS have shown that most Pv serve as inflow paths (Fig. 9.5); therefore, in a sense, Pv also serve as variceal inflow vessels from the side of the esophagus [5, 13].

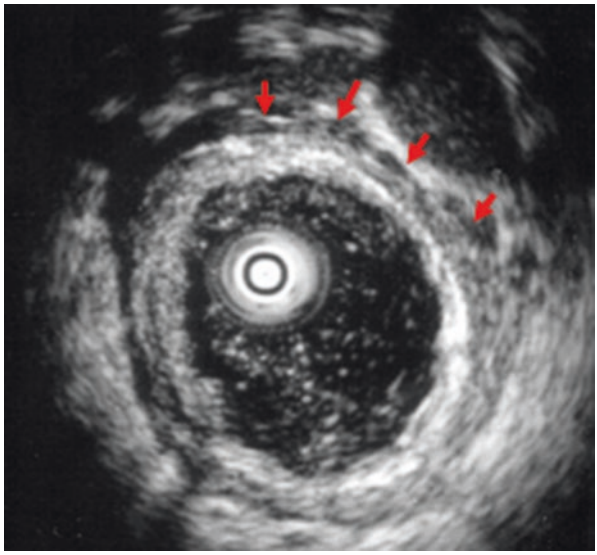

Fig. 9.4 UMP image after treatment (sclerotherapy). Wall thickness without esophageal varices was seen; however, remaining periesophageal veins (*red arrow*) were seen. This finding indicates the high risk of recurrence after treatment

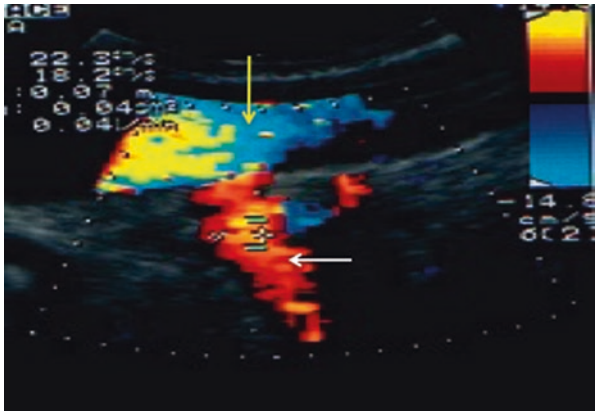

Fig. 9.5 Color Doppler EUS showed that the perforating veins (*white arrow*) served as inflow paths to the esophageal varix (*yellow arrow*)

In the actual delivery of treatment, the significance of the observation of Pv has two aspects. The first is that they serve as an outflow path for sclerosant during sclerotherapy, and the second is that if residual Pv remain present after treatment, they can serve as variceal inflow vessels for recurrent varices [14].

(a) Outflow pathway of the sclerosant
With EIS, variceal inflow vessels need to be embolized completely through intravascular injection of 5% ethanolamine oleate (EO), but in patients with large Pv, the injected EO can leak into the general circulation through the Pv (esophageal extramural shunt), and for this reason, the variceal inflow vessels should not be embolized in this situation (Fig. 9.6). In addition, the leaked EO is also likely to cause various complications, such as hemolysis, renal failure,

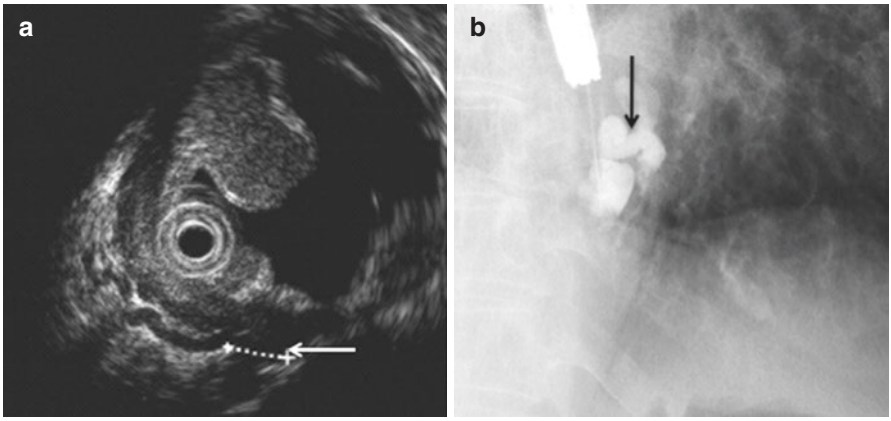

Fig. 9.6 (**a**) UMP showed a large perforating vein (*white arrow*) between esophageal varix and para-esphageal vein. (**b**) Endoscopic varicealography during injection sclerotherapy showed that sclerosant with contrast medium did not come into the feeding vein due to flow-out of injected sclerosant through the perforating vein (*black arrow*)

and heart failure. Conducting observations using EUS and determining the presence of Pv as well as their diameters before treatment are useful to ensure safe and effective treatment.

(b) Inflow circuit of recurrent varices
When sclerotherapy using the intravascular injection method is performed, endothelial cells in the Pv are also at risk of being damaged by the EO, and in most cases, those Pv are embolized as well. On the other hand, with the EVL method, the Pv are not necessarily ligated and often remain present. If EUS observations after treatment reveal the presence of residual Pv, the risk of recurrence is high and, therefore, additional treatments such as consolidation therapy should also be taken into consideration [10].

9.3.1.4 Extramural Vessels of the Esophagus

The venous systems that can be observed outside the esophageal wall include the paraesophageal venous system and the azygos vein system. The paraesophageal venous system can be observed as it is subdivided into two categories depending on their location around the esophageal wall: the periesophageal veins (Peri-v, Fig. 9.3) and the paraesophageal veins (Para-v, Fig. 9.3) [2, 7]. Peri-v are a group of blood vessels that are in contact with the esophageal adventitia or which partially penetrate the muscularis of the esophageal wall (in many cases, the esophageal adventitia becomes “shaggy” and observation may show the outer longitudinal muscle layer as even more hypoechoic). Para-v are a group of slightly larger blood vessels that are present separately from the esophageal adventitia.

(a) Periesophageal veins (Peri-v)
Previous studies have shown Peri-v to be involved in the development of esophageal varices as well as in their recurrence after treatment [10]. At the time of the initial treatment, the complete disappearance of Peri-v is important for the treatment to be effective. If the development of Peri-v is confirmed before treatment, EO needs to be injected until EVIS findings show a group of thin blood vessels around the esophageal varices. In other words, in the treatment of varices with hemodynamics with developed Peri-v, the risk of recurrence is believed to be higher with EVL because it is less likely to affect extramural blood vessels; therefore, EIS using intravascular injection should be selected if possible. In addition, if EUS observation after treatment reveals the presence of Peri-v, the possibility of relapse may be high, and close follow-up needs to be carried out [10].

(b) Paraesophageal veins (Para-v)
While previous reports have shown that massive development of Para-v was associated with low risk of variceal recurrence, other reports have stated that Para-v were closely related to recurrence because they acted as variceal inflow vessels for Pv; therefore, no consensus has yet been reached whether or not to eradicate Para-v [10]. However, if Para-v develop in the absence of Pv, they may act as collateral circulation to reduce the portal blood pressure after treatment of esophageal varices [8]. From this perspective, cases with EUS showing no Pv and with noticeable Para-v are good indications for EVL [5].

9.3.2 Gastric Varices

9.3.2.1 Local EUS Analysis of Gastric Varices

Gastric varices are depicted as echo-free images of lumens inside the third layer (submucosal layer) of the gastric wall. With EUS especially, the outer layer of gastric varices can be depicted as thinner than the superficial layer of healthy gastric mucosa, indicating that erosive changes at the surface were a risk factor for a rupture of gastric varices. Figures 9.7 and 9.8 (schema and real images) show collateral circulation inside and outside the gastric wall as observed using EUS.

9.3.2.2 Morphology of Gastric Varices (Diameter of Varix)

Even if some varices seem extremely large under endoscopic observation, all varices do not necessarily consist entirely of thick varices. With UMP, the actual size of the gastric varices can be seen objectively. Previous report [15] has shown that the diameter of gastric varices is correlated with blood flow; thus, when performing EIS in gastric varices with a diameter of 5 mm or greater, cyanoacrylates are needed in order to control the voluminous blood flow. Also, after treatment, EUS is highly useful for confirming the complete disappearance of lumens representing the gastric varices. The rate of recurrence has been found to be high in cases showing residual

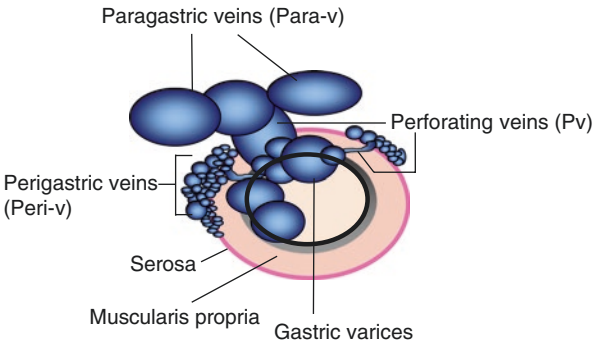

Fig. 9.7 The schema of the UMP image inside and outside gastric wall

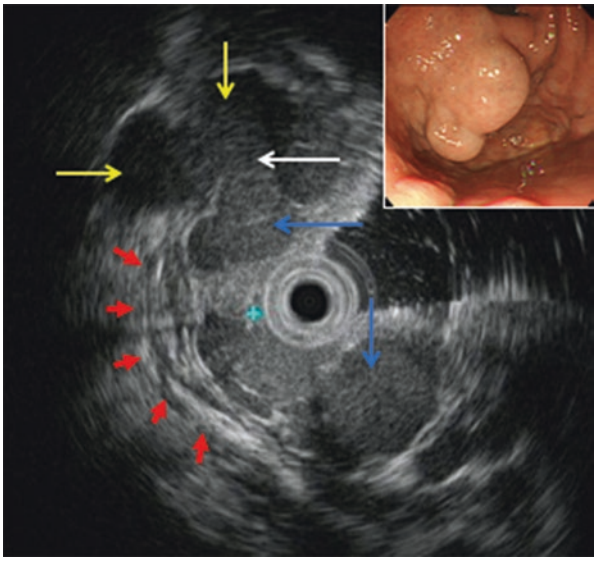

Fig. 9.8 Gastric varices were seen (*blue arrows*). In addition, periesophageal veins (*red arrows*), paraesophageal veins (*yellow arrows*), and the perforating vein between gastric varix and paraesophageal vein (*white arrow*) were identified

lumen; thus, EUS also provides information that is useful for the determination of the need for additional treatment. Wakatsuki et al. [16] reported recommended concentration of cyanoacrylate (alpha-cyanoacrylate monomer) to be injected according to the EUS findings; if the minor axis of gastric varices by EUS is identified as smaller than 10 mm, 62.5% cyanoacrylate is recommended; if it is identified as 10 mm or over, 75% cyanoacrylate is recommended to prevent leakage of cyanoacrylate from gastric varices to general circulation via gastrorenal shunt [17]. After cyanoacrylate injection, UMP can evaluate whether variceal lumens were completely eradicated or not (Fig. 9.9).

9.3.2.3 Perforating Veins [Pv] of the Gastric Wall

Through identification of gastric wall Pv communicating with gastric varices and gastric extramural blood vessels, observation of the deeper layers allows for the

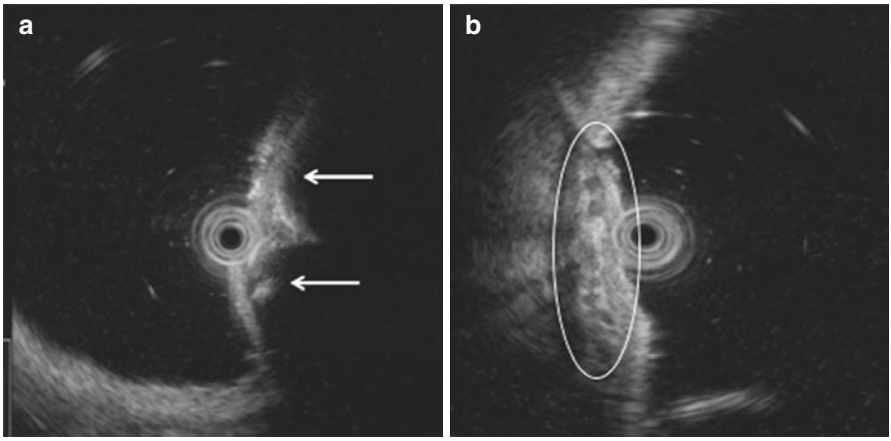

Fig. 9.9 (**a**) UMP image after cyanoacrylate injection. UMP showed hyperechoic layers with acoustic shadow (*white arrow*). Gastric varices were completely obliterated. (**b**) UMP revealed the remaining small varices in the gastric wall (*oval line*) after treatment

estimation of the presence or absence of variceal inflow vessels or the presence of a shunt between the portal vein and systemic circulation (gastrorenal shunt). However, such an assessment requires an observation using devices for exclusive use in EUS. In addition, the injected cyanoacrylate has been thought to be at risk of leaking into the systemic circulation when the diameters of the Pv are large; therefore, this observation is also important to avoid procedure-related adverse effect [18]. Of note is that the presence of residual Pv after treatment has been thought to be involved in recurrence.

9.3.2.4 Extramural Blood Vessels of the Gastric Wall

The blood vessels outside the gastric wall can be classified into two categories, namely, the Peri-v that are groups of small blood vessels in contact with the gastric serosa or that in some cases penetrate the muscularis of the gastric wall and the Para-v that are slightly larger in size and are located away from the gastric wall [7]. The clinical significance of evaluating Peri-v and Para-v before treatment remains undetermined. However, the presence of residual Pv and Peri-v communicating with Para-v has been shown to be involved in recurrence. In the same way as in the case of the esophagus, confirmation of the presence of those groups of blood vessels during EUS observation suggests that consolidation therapy should be performed in order to prevent recurrences.

9.3.2.5 Relationship with Esophageal Varices

The continuity between the lumen of gastric varices and esophageal varices can be confirmed using EUS. In other words, EUS allows for diagnosing whether gastric

varices are solitary or not. If the findings suggest a continuity, it can be predicted that the gastric varices can be properly treated by injection of a sclerosant from the esophageal side of the varices.

9.4 Conclusion

Esophagogastric varices can be treated even without performing EUS. However, performing EUS before and after treatment allows the treatment to be safer and more effective; in addition, EUS also provides information that is useful for the prediction of recurrence. EUS is an essential tool for optimal treatment and management of esophagogastric varices.

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