Endoscopic Treatment of Gastric Variceal Bleeding

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Abstract

Bleeding from esophageal and gastric varices is the most life-threatening complication of liver cirrhosis and portal hypertension. In gastric variceal bleeding, endoscopic management by injection of cyanoacrylate may be more effective than endoscopic ligation. Endoscopic injection of cyanoacrylate is a safe and effective hemostatic method for patients with gastric variceal bleeding. Repeat endoscopic treatment is less effective than the initial injection. Advanced-stage cirrhosis and hepatocellular carcinoma are major risk factors for failed hemostasis after cyanoacrylate injection of gastric varices.

2.1 General Information

Bleeding from esophageal (EVs) and gastric varices (GVs) is the most life-threatening complication of liver cirrhosis and portal hypertension. GVs are less common than EVs, occurring in 20% of patients with portal hypertension. GVs bleed less frequently but more severely than EVs. Unlike EVs, GV bleeding is complicated to control by routine band ligation, because it is difficult to have retroflex position of the scope to reach GVs. Furthermore, GVs are often associated with large draining splenorenal shunts that complicate the condition and contribute to hepatic encephalopathy. Once gastric fundal varices bleed, the mortality rate ranges from 25% to 55%. Patients with GV bleeding also have a higher risk of re-bleeding and a decreased rate of survival [1].

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2.2 Classification

2.2.1 Classification of Gastric Varices Proposed by Sarin et al. [2]

Sarin's classification is useful for considering the management of gastric varices. According to anatomical continuation with esophageal varices and their location, diagnosis is made. When the gastroesophageal varices (GOV) are an extension of esophageal varices, they are categorized into two types. The most common are Type 1 gastroesophageal varices (GOV1), which extend along the lesser curvature (Fig. 2.1). They are considered extensions of esophageal varices, and the recommended management is the same as that of esophageal varices. Type 2 gastroesophageal varices (GOV2) extend along the fundus. They tend to be longer and more tortuous than Type 1 gastric varices (Fig. 2.2).

Isolated gastric varices (IGV) occur in the absence of esophageal varices and are also classified into two types. Type 1 (IGV1) are located in the fundus and tend to be tortuous and complex (Fig. 2.3), and Type 2 (IGV2) are located in the body and antrum or around the pylorus (Fig. 2.4).

What You Should Know Here: Classification proposed by Sarin et al. [2]
Gastroesophageal varices (GOV)—gastric varices in continuity with esophageal varices
• GOV1—along the lesser curvature (usually 2–5 cm in length).
• GOV2—along the greater curvature extending towards the gastric fundus.
Isolated gasric varices (IGV)
• IGV1—isolated cluster of gastric varices in the gastric fundus.
• IGV2—isolated gastric varices in other parts of the stomach (body/antrum).

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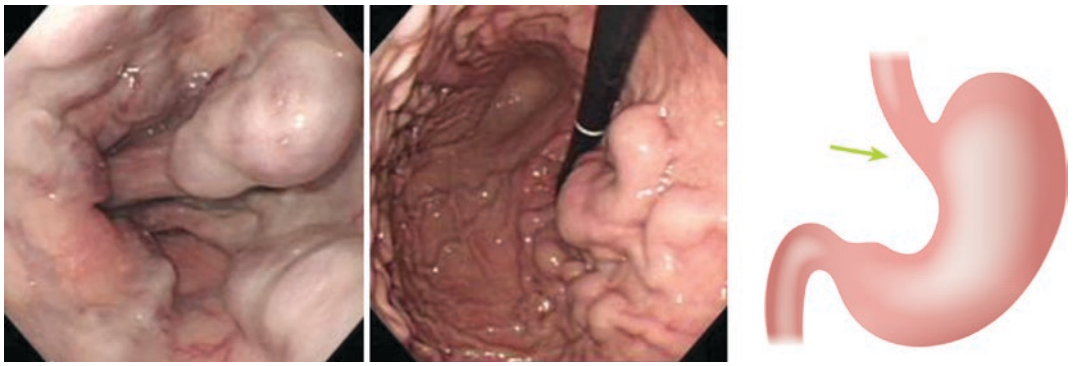

Fig. 2.1 Type 1 gastroesophageal varices (GOV1). They extend along the lesser curvature and are extensions of esophageal varices

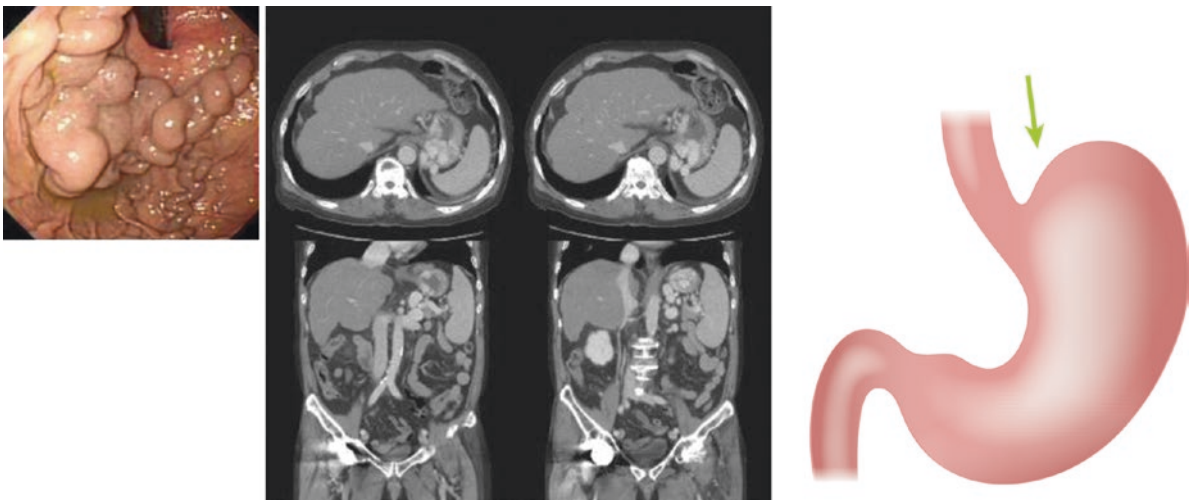

Fig. 2.2 Type 2 gastroesophageal varices (GOV2). They extend along the fundus and tend to be longer and more tortuous than GOV1

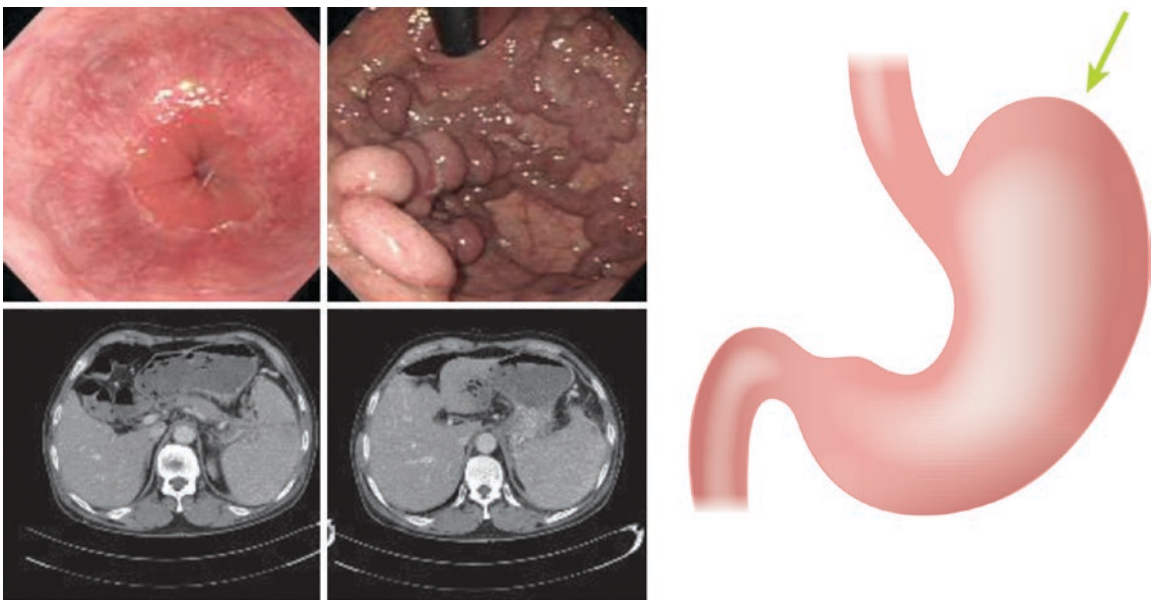

Fig. 2.3 Type 1 isolated gastric varices (IGV 1). They occur in the absence of esophageal varices. They are located in the fundus and tend to be tortuous and complex

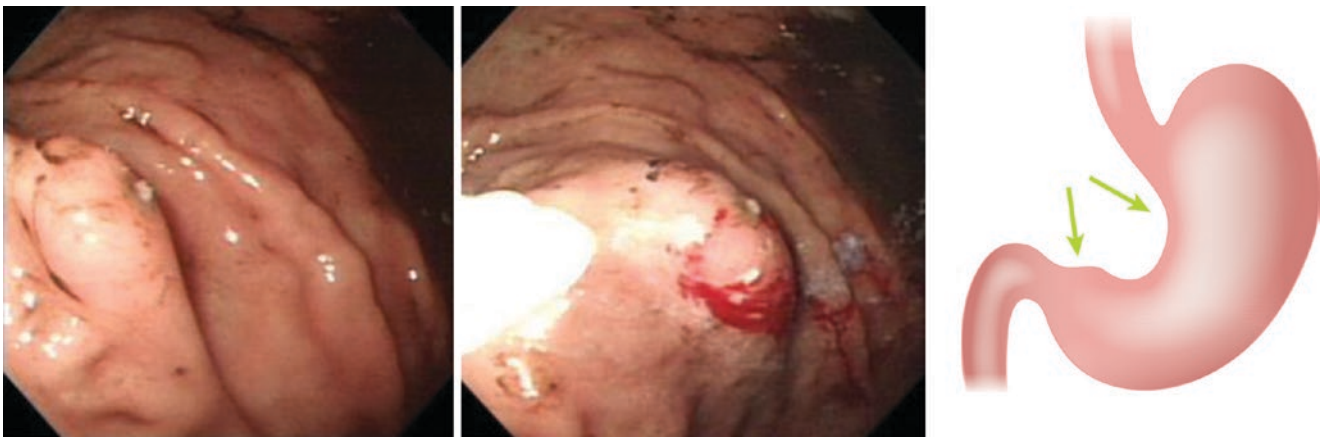

Fig. 2.4 Type 2 isolated gastric varices (IGV 2). They are located in the body and antrum or around the pylorus

2.2.2 Classification of Gastric Varices Proposed by Hashizume et al. [3]

The diagnosis of gastric varices based on the clinically significant endoscopic findings is established. Endoscopic findings of gastric varices were classified according to their form, location, and color. The form was classified into three types: tortuous (F1), nodular (F2), and tumorous (F3). The location was classified into five types: anterior (La), posterior (Lp), lesser (Ll) and greater curvature (Lg) of the cardia, and fundic area (Lf). The location of the gastric varices depends on hemodynamic factors. The color can be white (Cw) or red (Cr). The glossy, thin-walled focal redness on the varix was defined as red color spot (RC spot). The RC spot and large size were related to a significantly higher risk of gastric variceal bleeding.

2.3 Hemodynamic Changes

GOV1 form when a branch of the left gastric vein penetrates the gastric wall (cardiac vein) and joins the deep submucosal veins into the gastric zone directly connected to submucosal veins in the palisade zone. GOV1 are usually associated with large esophageal varices, while GOV2 are associated with large esophageal varices only in 50%.

A major portosystemic shunt, such as a gastrorenal shunt, is present in up to 85% of patients with gastric varices [4]. The volume of blood flowing through the shunt and the velocity of the portosystemic shunt are extraordinarily large. This is one reason why conventional endoscopic injection sclerotherapy is usually not sufficient. It could also be relative to possible serious complications, such as pulmonary embolism or massive ulcer bleeding.

IGV1 are associated with segmental portal hypertension (such as that due to splenic vein thrombosis) or the presence of spontaneous collaterals from the splenic vein to the renal vein to supply these varices. IGV1 drain into the inferior phrenic vein by gastrorenal shunts, gastrophrenic shunts, or gastropericardiac shunts, a part of which projects into the intragastric space. About 50% of cases of ectopic varices, including IGV2, are associated with portal vein thrombosis [5].

2.4 Endoscopic Management

Various techniques like endoscopic, surgical, and interventional radiology are available for the treatment of GV bleeding. Until now, no definite guidelines regarding bleeding control and prophylactic management for GVs are yet to be established. Although the effects of endoscopic treatment are not always sufficient as a curative method, endoscopy is an effective tool for attaining hemostasis in the majority of emergency cases of GVs. Several researchers showed that endoscopic management by injection of cyanoacrylate was more effective than endoscopic ligation [4]. In general, endoscopic ligation is not recommended for large gastric varices. We will give emphasis on the treatment of GV bleeding with cyanoacrylation.

Indications of endoscopic treatment are active bleeding from GVs, stigmata of recent bleeding, and history of bleeding and presence of gastric varices as the only possible source of bleeding. Among them, stigmata of recent bleeding are erosion/ulcer, clots, and red elevations on the surface of the varices (Fig 2.5a) [6]. Sometimes, they are flat and make a confusion to diagnose gastric varix bleeding (Fig 2.5b).

2.4.1 Risk Factors for GV Bleeding

Large size of the varices, presence of ascites, advanced chronic liver disease (Child-Pugh class C cirrhosis), high portal pressure (hepatic venous pressure gradient >12 mmHg), and red marks indicate high risk of variceal

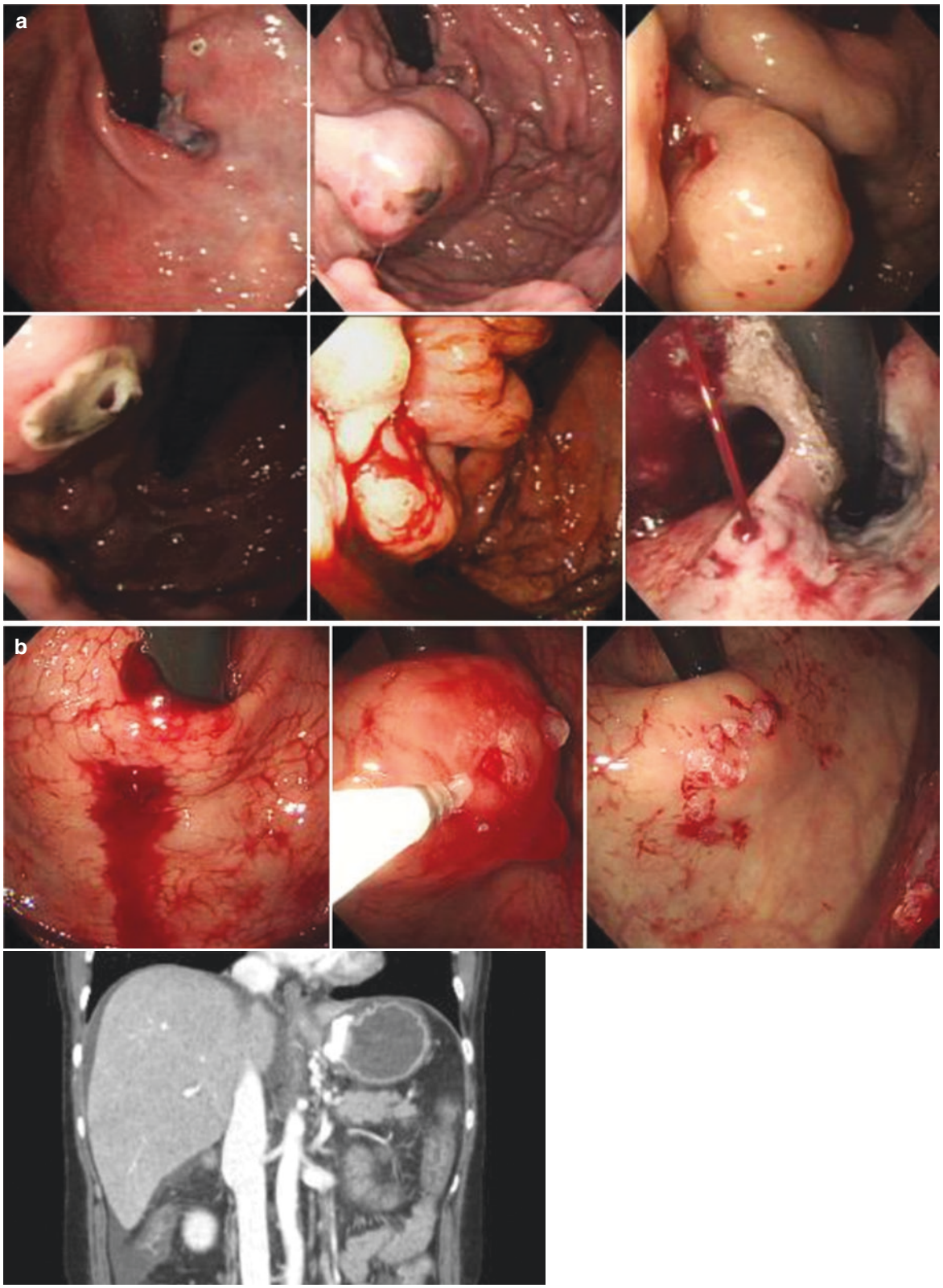

Fig. 2.5 Various types of stigmata of recent bleeding. (**a**) There are erosion/ulcer, clots, and red elevations on the surface of the varices. Active bleeding from gastric varices is also observed. (**b**) Various types of stigmata of recent bleeding. There is pumping vessel at gastric cardia. Bleeding varix is sometimes flat rather than tortuous vascular structure. Hemostasis is attained after endoscopic sclerotherapy of cyanoacrylate. Radiologic finding reveals complete obliteration of varix

bleeding. Isolated gastric varices (IGV1) are by themselves a risk factor of variceal bleeding.

What You Should Know Here: Risk factors for bleeding
• Large size of the varices (>10 mm).
• Variceal red spots (localized reddish mucosal area or spots on the mucosal surface of a varix).
• Presence of ascites.
• Advanced chronic liver disease (Child-Pugh class C cirrhosis).
• High portal pressure (hepatic venous pressure gradient >12 mmHg).

Modified from Hegab AM and Luketic VA. Postgraduate Medicine 2001; 109:75–89 [6]

2.4.2 Cyanoacrylate Injection Therapy

Endoscopic sclerotherapy using *n*-butyl-2-cyanoacrylate is a safe and effective hemostatic method for patients with GV bleeding. The discovery of tissue adhesive chemical has changed the management of GV bleeding. Cyanoacrylate (Histoacryl TM), a tissue adhesive, was first applied for endoscopic treatment of bleeding GVs in the 1980s. Thereafter, cyanoacrylate has become popular for this purpose in many countries. However, it is not available for use in the United States.

2.4.3 Technique of Injection of Cyanoacrylate (Fig. 2.6)

It is always better to do the procedure after initial resuscitation of the patient. If the patient is agitated, noncooperative, or unstable, endotracheal intubation should be considered. If it is known that a gastric variceal bleed is to be treated, the cyanoacrylate solution should be prepared. The endoscopist and endoscopic assistant should wear gloves and have eye protection during cyanoacrylate mixture preparation. Commercially available sclerotherapy injection catheters, with a 6 mm 21-gauge needle, are used. The injection catheters are flushed with Lipiodol. Lipiodol is a contrast agent that prevents cyanoacrylate to become solidified prematurely. The cyanoacrylate is then mixed with Lipiodol in a ratio of 1:1, and 10 cc syringes are prefilled with water for injection and some others with Lipiodol [4].

After complete endoscopic examination, a clear endoscopic view of the fundus/cardia is obtained by sucking remaining clots of blood and by flushing through the biopsy channel with normal saline. Then the injection catheter is inserted with the instrument in a straight view and is advanced at variceal bulge or near the sign of recent bleeding. The needle of injection catheter is advanced by the assistant. Cyanoacrylate mixture (the injection catheter in its full length of lumen contains about 1 cc of fluid) is injected into the varix. The injection catheter is slowly withdrawn from the varix, and its lumen is flushed with water for prevention of obstruction. The procedure is repeated as above, until GV bleeding is treated. If the injection catheter becomes obstructed after glue injection, it is carefully removed and replaced by a new one (Fig. 2.6). All patients who have endoscopic therapy are recommended to receive intravenous broad-spectrum antibiotics prophylactically. However, antibiotic prophylaxis is still controversial.

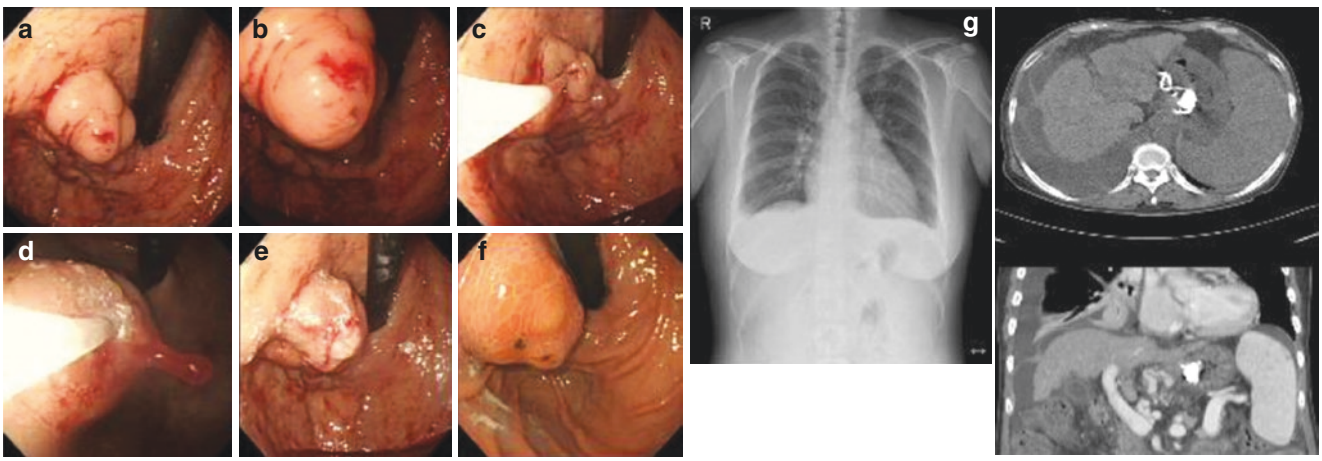

Fig. 2.6 Technique of injection of cyanoacrylate. (**a**) After complete endoscopic examination, a clear endoscopic view of the fundus/cardia is obtained. (**b**) There is erosion on the surface of varix and it is stigma for recent bleeding. (**c**) Cyanoacrylate mixture is injected into the varix. (**d**) After injection of cyanoacrylate, the varix has relatively hard consistency. (**e**) The injection catheter is slowly withdrawn from the varix. (**f**) The varix with edematous mucosa is observed on second-look endoscopy. (**g**) Radiologic findings reveal complete obliteration of varix

2.4.4 Complications from Cyanoacrylate Injection

Cyanoacrylate injection of gastric varices, although highly effective and with a good safety profile, has been criticized for its potential to cause rare but severe complications. The most severe complication is systemic embolization. Fortunately, most cases of embolization by cyanoacrylate have been presented as case reports, and the frequency of this complication is extremely low. Previously, case series of portal/splenic vein thrombosis and splenic infarction after cyanoacrylate injection were also reported [7, 8]. Slower injection of cyanoacrylate into gastric varix is recommended to avoid the complication. In some cases, damage to the endoscope due to extravasation of solution can occur.

2.4.5 Limitation of Cyanoacrylate Injection

GOV1 is expected that conventional treatments for esophageal varices such as endoscopic ligation, sclerotherapy, and transjugular portosystemic shunt (TIPS) would be effective. On the other hand, the management of bleeding from the cardiac or fundic varices, which are classified into GOV2 or IGV1, is quite different from GOV1. It has been reported that traditional endoscopic injection therapy is ineffective for the treatment of the isolated gastric varices. The reason is that gastric varices exist associated with a gastrorenal shunt or a gastro-inferior vena caval shunt, resulting in outflow into the systemic circulation. Therefore, it will be needed further studies to isolated cardiac or fundic gastric varices classified into GOV2 and IGV1.

Endoscopic injection of cyanoacrylate affects only part of GVs, and necrosis caused by cyanoacrylate may induce massive bleeding from still open varices (Fig. 2.7). For this reason, complex techniques with two or more methods are required for the treatment of GV bleeding. Yoshida et al. used a detachable snare to strangulate the main gastric varix, sclerotherapy with ethanolamine oleate to inject the smaller GV, and then rubber bands to ligate these smaller varices [9]. Lee et al. used detachable snares for gastric varices larger than 2 cm in diameter and elastic bands for smaller gastric

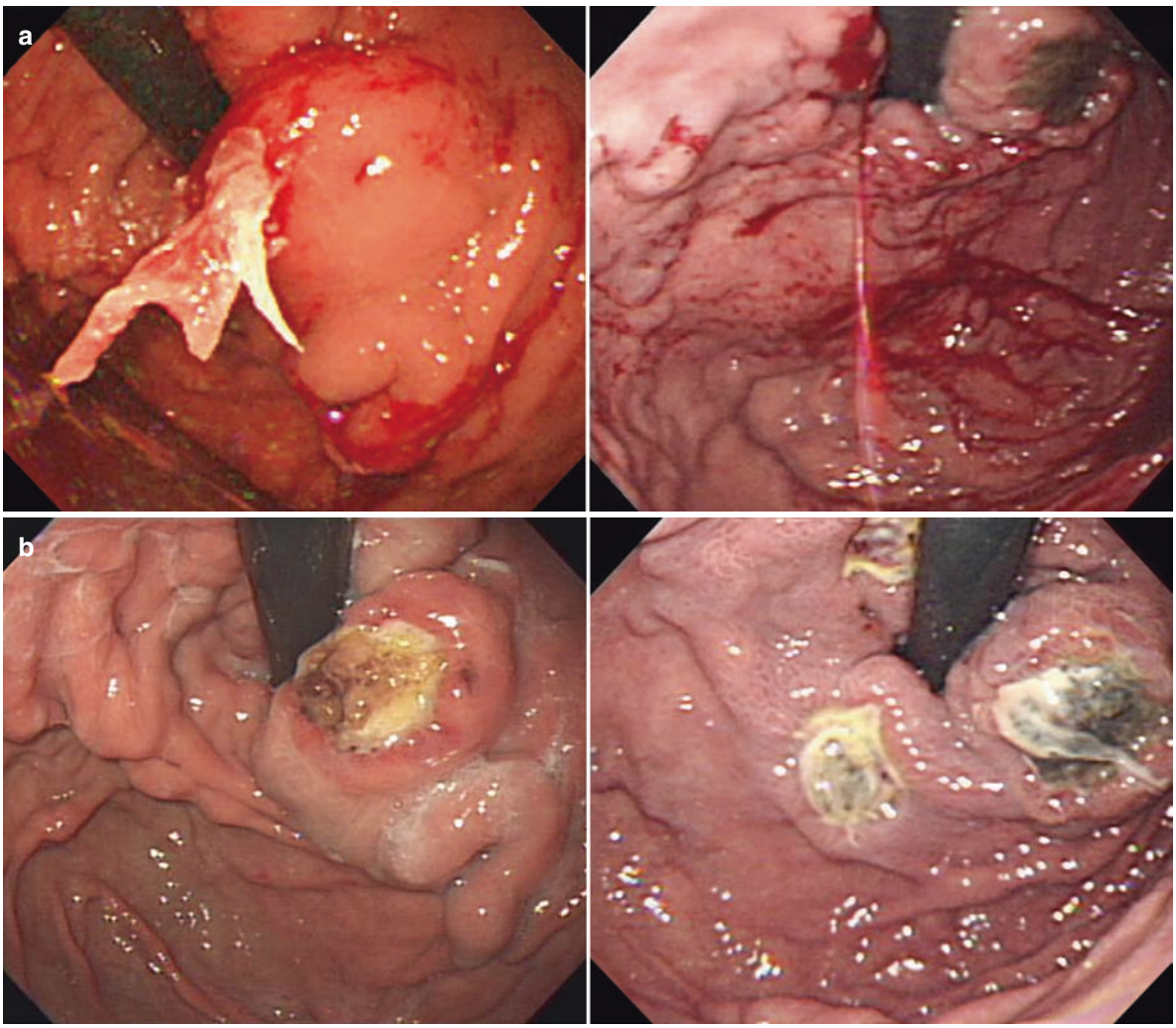

Fig. 2.7 Re-bleeding of gastric varix. (**a**) Endoscopic management for gastric varix bleeding is done by injection of cyanoacrylate. (**b**) After endoscopic sclerotherapy, necrosis caused by cyanoacrylate may induce massive bleeding from still open varices

varices and had an overall hemostatic result of 82.9% and variceal eradication rate after repeated treatments of 91.7%. Such combined techniques can be highly effective, although they are operator-dependent [10].

2.5 Other New Agents

The alternative agent for endoscopic treatment is thrombin. Previously, Ramesh et al. reported experience with the use of human thrombin in 13 patients. Interestingly, the rates of hemostasis and re-bleeding from gastric varices were 92% and 0%, respectively [11]. The limitation of both studies was small patient number and short duration. When thrombin may leak into systemic circulation in the case of gastric varices with gastrorenal shunt, intravascular injection of thrombin could induce disseminated intravascular coagulation (DIC) or pulmonary embolism.

2.6 Future Prospects

Liver transplant must be considered for uncontrollable variceal bleeding, and approximately 25% of patients receiving transplants have variceal bleeding as a component of their end-stage disease (Fig. 2.8). However, availability of donor organs is the major limiting factor. In previous report, urgent liver transplantation is effective and feasible for the small subset of patients with uncontrollable variceal bleeding and end-stage liver disease. Every patient with variceal bleeding does not have end-stage disease, and it requires full evaluation and docu-

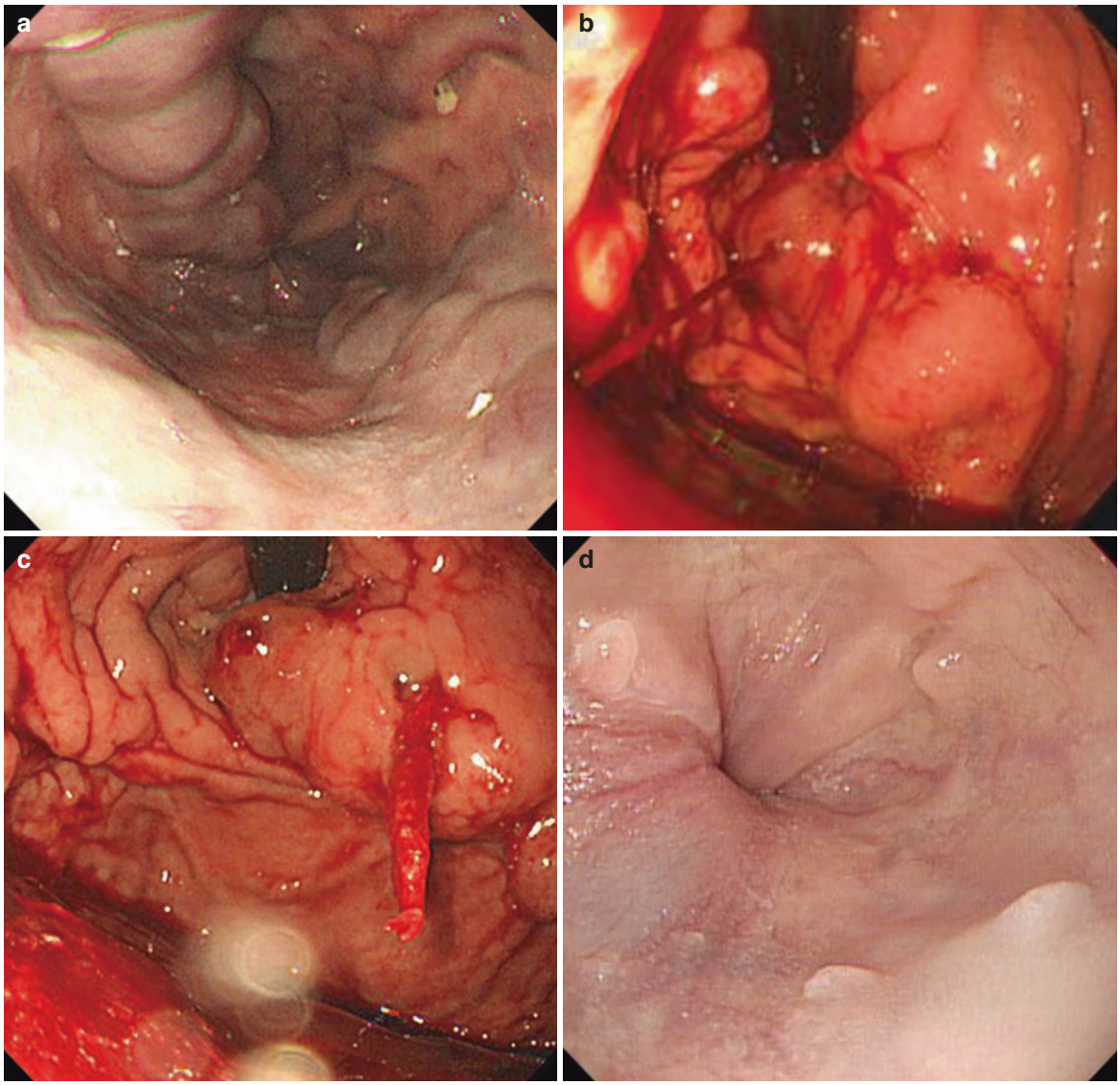

Fig. 2.8 Variceal change after liver transplantation. (**a**) Marked esophageal varices are observed. (**b**) There is pumping at gastric varix. (**c**) Hemostasis is attained after endoscopic sclerotherapy of cyanoacrylate. (**d**, **e**) After liver transplantation, pre-existing esophageal and gastric varices completely disappeared

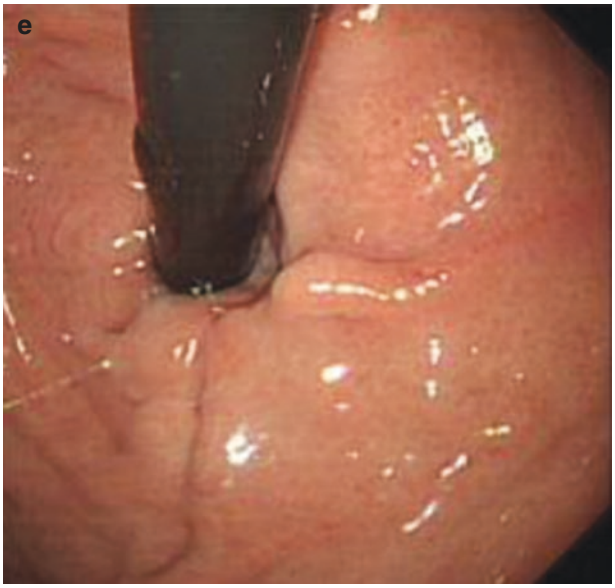

Fig. 2.8 (continued)

mentation of a patient's disease and its progression to reach a decision to transplant [12, 13].

References

1. Sarin SK, Lahoti D, Saxena SP, et al. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 1992;16:1343–9.
2. Sarin SK, Kumar A. Gastric varices: profile, classification, and management. Am J Gastroenterol. 1989;84:1244–9.
3. Hashizume M, Kitano S, Yamaga H, et al. Endoscopic classification of gastric varices. Gastrointest Endosc. 1990;36:276–80.
4. Hashizume M, Akahoshi T, Tomikawa M. Management of gastric varices. J Gastroenterol Hepatol. 2011;26(Suppl 1):102–8.
5. Ryan BM, Stockbrugger RW, Ryan JM. Review article: a pathophysiologic, gastroenterologic, and radiologic approach to the management of gastric varices. Gastroenterology. 2004;126:1175–89.
6. Hegab AM, L uketic VA. Bleeding esophageal varices. Postgrad Med. 2001;109:75–89.
7. Shim CS, Cho JD, Kim JO, et al. A case of portal and splenic vein thrombosis after Histoacryl injection therapy in gastric varices. Endoscopy. 1996;1996:461.
8. Cheng PN, Sheu BS, Chen CY, et al. Splenic infarction after histoacryl injection for bleeding gastric varices. Gastrointest Endosc. 1998;48:426–7.
9. Yoshida T, Harada T, Shigemitsu T, et al. Endoscopic management of gastric varices using a detachable snare and simultaneous endoscopic sclerotherapy and O-ring ligation. J Gastroenterol Hepatol. 1999;14:730–5.
10. Lee MS, Cho JY, Cheon YK, et al. Use of detachable snares and elastic bands for endoscopic control of bleeding from large gastric varices. Gastrointest Endosc. 2002;56:83–8.
11. Ramesh J, Limdi JK, Sharma V, Makin AJ. The use of thrombin injections in the management of bleeding gastric varices: a single-center experience. Gastrointest Endosc. 2008;68:877–82.
12. Wood RP, Shaw BW, Rikkers LF. Liver transplantation for variceal hemorrhage. Surg Clin North Am. 1990;70:449–61.
13. Murray KF, Carithers RL Jr, AASLD. AASLD practice guidelines: evaluation of the patient for liver transplantation. Hepatology. 2005;41:1407.