Treatment Modalities for Bleeding Esophagogastric Varices

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Abstract

Bleeding from esophageal varices (EVs) or gastric varices (GVs) is a catastrophic complication of chronic liver disease. In this paper, we review the management of bleeding EVs and GV.

Diagnosis of EVs and GV: The grading system for esophagogastric varices proposed by the Japan Society for Portal Hypertension classifies GV into those involving the cardia (Lg-c), the fundus (Lg-f), and both the cardia and the fundus (Lg-cf). In this review, we divide GV into 2 categories: Lg-c (cardiac varices: CVs) and Lg-cf or Lg-f (fundal varices: FVs).

Treatment Modalities for EVs and GV: Treatment modalities for EVs and GV include placement of a Sengstaken-Blakemore tube, pharmacologic therapy, surgery, interventional radiology, and endoscopic treatment.

Management of Bleeding EVs and GV: In Japan, endoscopic treatment has recently become the therapy of choice for bleeding EVs or GV. In other countries, especially the United States, vasoactive drugs and endoscopic treatment are routinely used to manage variceal hemorrhage.

Bleeding EVs: Endoscopic variceal ligation is useful for controlling bleeding from EVs. However, confirmation of ligation precisely at the site of bleeding is usually difficult in patients with massive variceal bleeding. The site of acute bleeding can generally be identified by means of water instillation and suction. Ligation is then performed at the bleeding point. If endoscopic hemostasis is unsuccessful, a Sengstaken-Blakemore tube is used as a temporary bridge to other treatments. Transportal obliteration is useful for blocking variceal blood flow.

Bleeding GV: Endoscopic injection sclerotherapy with a tissue adhesive, such as N-butyl-cyanoacrylate or isobutyl-2-cyanoacrylate, is effective for acute bleeding from GV. However, bleeding from the GV injection site and rebleeding from the rupture point have been reported in patients receiving endoscopic injection sclerotherapy. If endoscopic hemostasis is unsuccessful, a Sengstaken-Blakemore tube is used as a temporary bridge to other treatments. Balloon-occluded retrograde transvenous obliteration and portal obliteration are useful for the treatment of uncontrolled bleeding from GV.

Prevention of Recurrent Variceal Hemorrhage: Given the high recurrence rate, survivors of an acute variceal hemorrhage should receive treatment to prevent recurrence. Complete eradication of EVs or GV and maintenance of low portal venous pressure are essential for preventing recurrence of variceal hemorrhage.

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Key words: esophageal varices, gastric varices, bleeding, surgery, interventional radiology, embolization, endoscopic treatment

Abbreviations: esophageal varices (EVs), gastric varices (GVs), cardiac varices (CVs), fundal varices (FVs), endoscopic injection sclerotherapy (EIS), endoscopic variceal ligation (EVL), interventional radiology (IVR), partial splenic embolization (PSE), distal splenorenal shunt (DSRS), ethanolamine oleate with iopamidol (EOI)

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Introduction

Bleeding from esophageal varices (EVs) or gastric varices (GVs) is a catastrophic complication of chronic liver disease. Bleeding from GV is generally more severe than that from EVs¹ but is less frequent²⁻⁴. Many years ago, operation was the only treatment available. In the 1970s, techniques for interventional radiology (IVR) were developed and improved the survival rates of patients with bleeding EVs and GV. In the 1980s, endoscopic treatment further improved survival rates. In this paper, we review the management of bleeding EVs and GV.

Diagnosis of EVs and GV

The grading system for esophagogastric varices proposed by the Japan Society for Portal Hypertension⁵ classifies EVs and GV on the basis of color (white [Cw] and blue [Cb]), form (small and straight [F1], nodular [F2], and large or coiled [F3]), and red color signs (RC0-3). GV are divided into those involving the cardia (Lg-c), the fundus (Lg-f), and both the cardia and the fundus (Lg-cf). In this review, we divide GV into 2 categories: Lg-c (cardiac varices: CVs) and Lg-cf or Lg-f (fundal varices: FVs).

Bleeding signs are classified into those found during bleeding and those found after hemostasis. Bleeding is classified as gushing, spurting, or oozing. Findings after hemostasis are classified as red plug or white plug⁵.

Treatment Modalities for EVs and GV

Treatment modalities for EVs and GV include placement of a Sengstaken-Blakemore (SB) tube, pharmacologic therapy, surgery, IVR, and endoscopic treatment.

The SB Tube

The SB tube, first described in 1950s⁶, is a multiluminal plastic tube with 2 inflatable balloons. The proximal balloon is used to arrest bleeding by directly compressing EVs. The distal balloon compresses the feeding veins of the EV. The

effectiveness of balloon tamponade with the SB tube is reported to be 90%⁶. Aspiration of secretions is the most common complication of balloon tamponade, occurring in 10% to 20% of cases⁷. Esophageal rupture and acute upper airway obstruction are rare fatal complications of treating bleeding EVs or GV with an SB tube⁸⁻¹¹. Currently, balloon tamponade is only used as a temporary bridge to other strategies when other hemostatic treatments are unsuccessful. Balloon tamponade is more effective in patients with less severe hepatic dysfunction. Previous endoscopic therapy may increase the effectiveness of tamponade without increasing the risk of esophageal perforation¹².

Pharmacologic Therapy

Splanchnic vasoconstrictors, such as vasopressin and somatostatin (and their analogues octreotide and vapreotide), are administered parenterally and used only in an acute care setting. Pharmacologic therapy has 2 major advantages: it is generally applicable and can be started as soon as variceal hemorrhage is suspected. A recent meta-analysis of 15 trials comparing emergency sclerotherapy and pharmacologic treatment (vasopressin, nitroglycerin, terlipressin, somatostatin, or octreotide) showed similar efficacy, with fewer side effects for pharmacologic therapy. Pharmacologic therapy is considered the first-line treatment for variceal bleeding¹³.

Surgery

Many years ago, surgery was only treatment for bleeding EVs or GV. Several surgical procedures have been developed to manage EVs and GV. They can be broadly classified as shunting procedures and nonshunting procedures¹⁴.

Shunting procedures: The goal of shunting is to reduce the incidence of variceal bleeding by lowering the pressure in the portal system by means of a portosystemic shunt. A standard portocaval shunt effectively reduces the incidence of variceal bleeding; however, impaired metabolism of hepatic proteins after shunting frequently causes hepatic encephalopathy due to hyperammonemia¹⁵⁻¹⁷. In 1967 Warren et al. developed the distal

splenorenal shunt (DSRS) to preserve portal blood flow through the liver while lowering variceal pressure¹⁸. This approach was developed in the hope of preventing bleeding as well as hyperammonemia. Despite initial expectations, DSRS has been found to effectively prevent rebleeding but not to eliminate the risk of hyperammonemia. To solve this problem, our group designed a DSRS with splenopancreatic disconnection and gastric transection, modifications to prevent the loss of shunt selectivity. Our modified DSRS has been confirmed to reduce the incidence of postoperative hyperammonemia¹⁹.

Nonshunting procedures: As an alternative to shunting, Hassab²⁰ and Sugiura and Futagawa²¹ developed techniques for gastroesophageal decongestion and splenectomy to manage varices. The Hassab operation devascularizes the distal esophagus and proximal stomach. Splenectomy, selective vagotomy, and pyloroplasty can be performed concomitantly with the procedure. Sugiura and Futagawa²¹ developed a procedure for esophageal transection in patients with EVs and GVs. While the procedures of Hassab and of Sugiura and Futagawa solve the problem of hepatic encephalopathy, varices are likely to recur earlier after these procedures than after DSRS²².

IVR

In the 1970s, IVR techniques were developed for the treatment of EVs and GVs. Before IVR is performed, portal hemodynamics should be evaluated. Angiography can be used to assess the hemodynamics of varices during embolization.

Transportal obliteration: Two methods have been used to obliterate the feeding veins of EVs or GVs: percutaneous transhepatic obliteration and transileocolic vein obliteration. These procedures are performed in similar ways. A catheter is inserted directly into the portal vein, and the portal circulation is visualized with portography. A balloon catheter is inserted selectively into the inflow site of the feeding veins of the varices. The balloon is inflated, and a test dose of contrast medium is injected to determine the optimal volume of sclerosant. Five percent ethanolamine oleate iopamidol (EOI), 50% glucose, or both are injected to

obliterate the feeding vein(s). Steel coils are then used to complete obliteration²³.

Balloon-occluded retrograde transvenous obliteration: Balloon-occluded retrograde transvenous obliteration (B-RTO) is a notable IVR procedure developed especially for the treatment of FVs. This treatment is performed by inserting a balloon catheter into the outflow shunt (gastric-renal shunt or gastric-inferior phrenic vein shunt) via the femoral or internal jugular vein. Any existing collateral veins are treated with coils, absolute ethanol, or a small amount of 5% EOI. The balloon is inflated, and a test dose of contrast medium is injected to determine the optimal volume of the sclerosant. Five percent EOI is slowly injected through the catheter until the shunt is filled with the sclerosant. The catheter is removed after 24 hours of balloon occlusion²⁴⁻²⁶. A high rate of FV eradication or shrinkage can be expected if the B-RTO procedure is technically successful²⁷. Indeed, long-term eradication of treated FVs without recurrence is achieved in most patients^{24,28}. Kanagawa et al.²⁴ confirmed eradication of FVs in 31 of 32 patients treated with B-RTO, and no FVs recurred in any patient within a mean follow-up period of 14 months. In earlier studies, the eradication rate of FVs exceeded 89%, and the recurrence rate was less than 7%. Given the minimal invasiveness and high safety of the procedure, B-RTO can be performed on either an elective or emergency basis to treat FVs.

Partial splenic embolization: Partial splenic embolization (PSE) has been used to treat hypersplenism, EVs, GVs, portal hypertensive gastropathy, pancreatic carcinoma, splenic aneurysm, and portal-systemic encephalopathy^{23,29-41}.

The femoral artery approach is used for superselective catheterization of the splenic artery. The tip of a catheter is placed as distally as possible in either the hilus of the spleen or in an intrasplenic artery. Embolization is achieved by injecting 2-mm gelatin-sponge cubes suspended in a saline solution containing antibiotics^{33,34,42}. As with transportal obliteration, complete disappearance of EVs or GVs is difficult to achieve with PSE alone. PSE is thus a supplemental treatment for EVs or GVs.

Transjugular intrahepatic portosystemic shunt:

Placement of a transjugular intrahepatic portosystemic shunt (TIPS) is currently considered a salvage therapy for the 10% to 20% of patients in whom standard medical therapy fails. However, 2 randomized, controlled trials have shown that early placement of such a shunt (within 24 to 48 hours after admission) is associated with significantly improved survival among high-risk patients (i.e., patients with a hepatic venous pressure gradient of >20 mm Hg⁴³ or with Child class C disease with a score of 10 to 13 points⁴⁴). Therefore, early placement of a TIPS is a treatment option in such patients. Although the potential benefits and risks of TIPS placement require further investigation, the decision to use this approach as salvage therapy in this subgroup of high-risk patients should be made sooner rather than later.

Transportal obliteration and B-RTO are techniques for embolization of the collateral veins of the portal system due to portal hypertension. PSE reduces inflow of the portal system. TIPS increases outflow of the portal system. The IVR techniques of PSE and TIPS both reduce portal pressure.

Endoscopic Treatment

Two endoscopic techniques are used to treat EVs or GV: endoscopic injection sclerotherapy (EIS) and endoscopic variceal ligation (EVL)⁴⁵⁻⁵¹.

EIS: EIS can be accomplished with either intravariceal EIS or extravariceal EIS^{46-48,52}. First, the endoscope is introduced. Then, a flexible endoscopic sheath is positioned to permit reinsertion of the endoscope and prevent aspiration.

1) Intravariceal EIS: An anal-side balloon is inserted into the stomach, and a 22-gauge needle is inserted into the target EV 2 to 3 cm proximal to the gastroesophageal junction. The sclerosant (5% EOI) is infused into the EV, and flow is monitored with fluoroscopy to confirm filling of the feeder vessel or the pericardiac venous plexus. Suction is maintained at the puncture point while the needle remains in the EVs. The same procedure is then repeated for other variceal columns in the lower esophagus. After injection has been completed, the injection site is compressed by inflating the anal-side balloon with air.

In the treatment of EVs, intravariceal EIS obliterates both the interconnecting perforating veins and the feeding veins of EVs. Nearby, however, some dilated winding cardiac veins might transverse the submucosa and directly join the EVs. This relationship allows most CVs to be treated concomitantly with EVs when the latter are being corrected with intravariceal EIS. Intravariceal EIS is useful for obliterating feeding veins of recurrent EVs after operation⁴⁸. However, EIS has high incidences of local and systemic complications⁵³.

Traditional EIS with 1% polidocanol, 5% EOI, or thrombin has been less successful and is associated with a high mortality rate in patients with GV, especially FVs¹⁵⁴⁻⁵⁷. These outcomes are attributed to GV being associated with a gastroduodenal shunt or a gastric-inferior vena caval shunt, resulting in outflow into the systemic circulation²⁴. These anatomic characteristics of a major portosystemic shunt create a higher blood flow volume through the shunt, with resultant rapid escape of sclerosant into the systemic circulation during EIS. Consequently, conventional EIS does not allow the sclerosing agent to start thrombosis on the surface endothelium of the GV. Furthermore, there is a risk of serious complications. For example, the sclerosant can cause pulmonary embolism via the major shunt, and massive ulcer bleeding can be induced through the puncture of large GV⁵⁸.

2) Extravariceal EIS: Extravariceal EIS is performed with 1% polidocanol to treat remaining varices by paravariceal injection⁵⁹. The end point of primary treatment is the complete eradication of any residual varices between the ulcers created by extravariceal EIS during the first hospitalization. Extravariceal EIS achieves local eradication but does not completely disrupt the interconnecting perforating and feeder vessels⁶⁰.

Post-EIS management is as follows: (1) after 6 to 8 hours of fasting, liquid food is permitted; (2) administration of antibiotics to prevent infection; (3) use of medication to lower portal vein pressure as required; and (4) close monitoring the patient for signs of complications, such as bleeding, perforation, fever, sepsis, and embolization of distant vascular beds.

EVL

EVL is increasingly used because of its safety and simplicity and because no sclerosant is required⁴⁵. EVL achieves local eradication, but does not completely disrupt interconnecting perforating and feeder vessels⁶⁰. Nevertheless, early recurrence of EVs after EVL has been reported⁴⁶.

The endoscope is introduced with a flexible endoscopic sheath. The endoscope is then removed and attached to a pneumatically activated EVL device (Sumitomo Bakelite, Tokyo, Japan). The endoscope is reinserted, and suction on the varix is maintained. As the varix is pulled into the ligator cap, air is injected into the tube to accomplish the EVL. At the first treatment session, all varices are ligated from the gastroesophageal junction to the oral side. Each varix is ligated with 1 to 2 bands. During the second and third sessions, the remaining varices undergo EVL⁵⁰.

Post-EVL management: After the operation, the patient should fast for 24 hours and be closely observed for complications, such as hemorrhage (bleeding caused by the incision of bands), sloughing off of the bands (early recurrence of hemorrhage), fever, and a local choking sensation. Prophylactic antibiotics are given to all patients for 3 days. The antibiotic dosage is then adjusted on the basis of the results of sensitivity testing in patients confirmed to have an infection.

Combination of EIS and EVL: Several investigators have examined the efficacy of EVL combined with EIS for the treatment of EVs⁶¹⁻⁶³. Saeed et al.⁶¹ and Laine et al.⁶² have compared a single session of treatment with EVL plus low-volume EIS with a single session of EVL alone and concluded that EVL alone is superior to combination therapy. EVL was performed first, followed by intravariceal EIS immediately proximal to the ligature. The main limitation of this method is that only half of the feeding vessels are treated because the sclerosant is injected into the EV proximal to the ligature; distal vessels, therefore, do not undergo sclerosis.

EVL followed by EIS differs fundamentally from

EIS followed by EVL. Moreover, the combination of intravariceal EIS and EVL differs from that of extravariceal EIS and EVL. EVL and extravariceal EIS both eradicate varices locally, with no effect on interconnecting perforating or feeding vessels⁶⁰. Takase et al.⁶⁴ have concluded that feeder vessels must be obliterated to prevent recurrence.

We have developed a new technique combining EVL with EIS called endoscopic scleroligation (ESL). In this technique, intravariceal EIS is performed before ligation. The puncture needle is removed after sclerosant infusion, and EVL, including the placement of bands at the injection site, is performed simultaneously. The same procedure is repeated for other EVs around the lower esophagus. Additional sclerosant is not injected. Intensive EVL is performed for EVs in the lower to middle esophagus⁴⁶.

New methods for the management of EVs-Bimonthly EVL: EVL and extravariceal EIS are not always effective, and early recurrences have been reported⁴⁶. Furthermore, most patients with endoscopically treated EVs require follow-up therapy for recurrent varices. Proper management of recurrent EVs can significantly improve patients' quality of life.

We conventionally perform EVL treatment once every 2 weeks (biweekly). We compared the short- and long-term results of EVL performed in 3 sessions with a total of 16 O-rings at 2 different intervals, i.e., biweekly (conventional interval) and bimonthly. The overall rates of variceal recurrence and additional treatment were both higher after biweekly EVL than after bimonthly EVL ($P<0.001$). We concluded that EVL once every 2 months (bimonthly) produces better outcomes than EVL once every 2 weeks (biweekly) in patients with EVs. Treatment sessions separated by a longer interval had a higher rate of total eradication and lower rates of recurrence and additional treatment⁵⁰.

Combination of Endoscopic Treatment and IVR

Treatment of GV solely with endoscopic modalities or with IVR is occasionally inadequate. Our group has previously reported that treatment combining IVR and endoscopic modalities has

significant effects on long-term rebleeding and retreatment rates in patients with EVs or GVs^{23,35,37,38}. Cumulative retreatment rates in patients with Child's class C disease are lower after endoscopic treatment plus IVR than after endoscopic treatment alone ($P=0.025$). The combination of endoscopic therapy and IVR was shown to be effective for EVs, especially in patients with poor liver function²³. In patients who undergo elective therapy, complete GV treatment should be performed to minimize the risk of rebleeding. The combination of IVR and endoscopic therapy is highly effective and provides an alternative to surgery in patients with EVs or GVs^{30,65}.

Management of Bleeding EVs and GVs

Endoscopic treatment has recently become the treatment of choice for bleeding EVs or GVs in Japan^{65,66}. In other countries, especially the United States, vasoactive agents and endoscopic treatment are routinely used to manage variceal hemorrhage.

Management before Endoscopic Examination

The management of variceal hemorrhage relies on adequate fluid resuscitation, blood volume resuscitation, airway protection, prophylactic antibiotics, and antiulcer drugs. Treatment strategies for early-stage, moderate, and severe bleeding include correction of hypovolemic shock, stopping hemorrhage, prevention of complications due to gastrointestinal hemorrhage, and monitoring vital signs and urine volume.

Both H_2 -receptor antagonists and proton-pump inhibitors can increase the pH of the stomach, stimulate the aggregation of platelets and the formation of fibrin clots, and prevent or dissolve early blood clots. These agents are, therefore, beneficial for stopping bleeding and preventing rebleeding⁶⁷.

Inflammation and edema of gastric and esophageal mucous membranes commonly develop during active bleeding. Prophylactic use of antibiotics is helpful for controlling active hemorrhage and may decrease the incidence of early rebleeding and prevent infection. A meta-analysis has suggested

that the use of antibiotics increases survival rates by decreasing rebleeding and infection⁶⁸. Therefore, short-term treatment with prophylactic antibiotics should be considered in all patients with cirrhosis and acute variceal hemorrhage.

Endoscopic Examination

After premedication with an intramuscular injection of scopolamine butylbromide (20 mg) and an intravenous injections of atropine sulfate (0.25 mg), pentazocine (15 mg), hydroxyzine (25 mg), and diazepam (5 mg), a 1-channel endoscope is introduced. A flexible endoscopic sheath is then inserted. Endoscopic examination is performed to check for active bleeding sites or plugs. Bleeding signs are classified according to those found during bleeding and those found after hemostasis. Bleeding is classified as gushing, spurting, or oozing, and findings after hemostasis are classified as red plug or white plug⁵.

If massive coagula preclude examination of the bleeding site, the endoscope is removed, the flexible endoscopic sheath is left in place, and the patient's position is changed from the full left-lateral position to the right-lateral position. As a result, the massive coagula move from the fundus to the antrum. Furthermore, hemostasis of GVs is occasionally achieved because the bleeding site is elevated when the patient is placed in the right-lateral position.

Bleeding EVs (Fig. 1)

EVL is useful for controlling bleeding from EVs. However, confirming ligation precisely at the site of bleeding is usually difficult when treating massive variceal bleeding. For patients with acute bleeding, the bleeding point is identified by instilling water and applying suction. Ligation is then performed at the bleeding point. Subsequently, each varix is ligated with 1 or 2 bands.

Matsutani et al. have reported that after EVL of the bleeding site of an EV, an unusual white ball-like appearance (white ball appearance) is noted. This finding differs markedly from the purple ball-like appearance that is usually observed after EVL of an

Fig. 1 Treatment of bleeding esophageal varices

Fig. 2 Treatment of bleeding gastric varices

EV at a site without bleeding. This finding is useful for confirming the successful EVL of an EV at its bleeding site⁶⁹.

Intravariceal EIS is also useful for controlling bleeding from EVs. The sclerosant (5% EOI) is infused near the bleeding site of EV under fluoroscopic guidance to confirm filling of the feeder vessel or the pericardiac venous plexus.

As for the best endoscopic therapy, a meta-analysis of 10 randomized controlled trials including 404 patients showed a nearly significant benefit of EVL as compared with EIS for the initial control of bleeding (pooled relative risk, 0.53; 95% confidence interval, 0.28–1.01)⁷⁰.

If endoscopic hemostasis is unsuccessful, balloon tamponade with an SB tube is used as a temporary bridge to other treatments. Transportal obliteration is useful for blocking variceal blood flow.

Narahara et al.⁷¹ have compared the efficacy of TIPS with that of EIS in the long-term management of bleeding from EVs in patients with cirrhosis. They found no significant differences between the treatment groups in rebleeding from any source or in rebleeding from EVs. The mortality rates were similar in both treatment groups. Shunt dysfunction occurred in 71% of the patients in the TIPS group. During follow-up, rehospitalization was more frequent in the TIPS group (2.6 ± 0.4 cases) than in the EIS group (1.1 ± 0.2 cases; $P < 0.01$). TIPS and EIS were equally effective for preventing rebleeding from EVs. However, TIPS was associated with a high incidence of shunt dysfunction, leading to more rehospitalizations. Therefore, TIPS may not be

suitable as a first-line treatment for preventing rebleeding from EVs in patients with cirrhosis who are in stable condition.

Bleeding GV's (Fig. 2)

As compared with EIS or EVL, endoscopic variceal obturation with EIS and a tissue adhesive, such as N-butyl-cyanoacrylate (Histoacryl, TissueSeal LLC, Ann Arbor, MI, USA) or isobutyl-2-cyanoacrylate, is more effective for acute bleeding from FVs. The advantages of EIS include a better rate of controlling the initial hemorrhage^{72–78}. However, bleeding from the GV injection site and rebleeding from rupture points have been reported in patients EIS^{2,57}.

While Although EVL is generally safe and effective for the treatment of CVs and FVs⁷⁹, it sometimes causes deep or extensive ulcers and increases the risk of ensuing ulcer hemorrhage or secondary bleeding⁸⁰. FVs are usually 2 to 3 times as large as EVs and are directly connected to an extremely dilated left gastric or posterior gastric vein⁸¹. The volume of blood flow through an FV, therefore, usually exceeds that through an EV⁸². A mucosal injury remains on varices after endoscopic treatment. If blood flow in the varices cannot be stopped completely, bleeding may recur at the site of this mucosal injury. This possibility of rebleeding underlines the importance of ensuring the complete obliteration of blood flow when treating FVs endoscopically.

An international consensus meeting at the Baveno

IV workshop in 2005 recommended that a tissue adhesive, such as a cyanoacrylate, is the only agent that should be used to control bleeding from FVs⁸³. Prospective randomized controlled studies have recently examined the management of bleeding from GV⁸⁴⁻⁸⁷. However, comparing results among different studies remains difficult because various types of GV⁸⁴⁻⁸⁷ have been included, with no clear explanation or classification of the varices.

GVs have also been treated with an endoscopic technique combining the use of a detachable snare with simultaneous EIS and O-ring ligation⁸⁸. This technique is not yet in widespread use, however. Our group has reported on the treatment of ruptured GV⁸⁹ by means of EIS with N-butyl-cyanoacrylate followed by O-ring ligation (endoscopic scleroligation [EISL])⁴⁹. EISL was developed as a treatment for EVs to prevent bleeding from the injection site during needle removal^{46,89}. When treating GV⁸⁹ by means of EIS with N-butyl-cyanoacrylate, immediate freezing of the N-butyl-cyanoacrylate around the needle hinders its removal after injection. In some patients, bleeding from the GV injection site or rebleeding from the rupture point also occurs^{2,57}. Our group has used EISL to treat bleeding from GV⁸⁹ with punctures near the bleeding point by simultaneously ligating the injection site and the bleeding point. EISL effectively stops bleeding from GV⁸⁹, enables swift and easy needle removal, and successfully eliminates both bleeding from the injection site and rebleeding from the bleeding point. An O-ring is placed at the point of EISL injection with N-butyl-cyanoacrylate and is left in place for a prolonged time. As of this writing, EISL with N-butyl-cyanoacrylate is considered the most promising treatment for bleeding from GV⁸⁹.

If endoscopic hemostasis is unsuccessful, balloon tamponade with an SB tube is used as a temporary bridge to other treatments. B-RTO or transportal obliteration is useful for treating uncontrolled bleeding from GV⁸⁹.

Some studies have suggested that B-RTO is effective for the secondary prophylaxis of bleeding GV⁸⁹. The long-term rate of rebleeding from FV⁸⁹ was reported to be much lower after B-RTO than after previous endoscopic treatments with a

cyanoacrylate. Most studies have shown that prophylactic treatment with B-RTO effectively prevents bleeding of large GV⁸⁹ without a history of bleeding, and a 100% nonbleeding rate has been reported after long-term follow-up^{28,90-92}. The treatment of FV⁸⁹ with B-RTO has 2 important effects: eradication of the FV⁸⁹ themselves and obliteration of the unified portosystemic shunt. Most of the benefits and adverse effects of B-RTO are related to the latter effect. Such benefits as decreased blood ammonia levels and improvement in portosystemic encephalopathy are sometimes observed. Possible adverse effects include transient ascites, worsening ascites, pleural effusion, and the appearance of EV⁸⁹ manifesting red color signs. These adverse effects may be caused by elevated portal pressure due to occlusion of the portosystemic shunt.

Transportal obliteration is also effective for the treatment of GV⁸⁹, because the feeding veins of GV⁸⁹ are obliterated. The procedure is highly effective, although the rate of complete disappearance of GV⁸⁹ is not so high after transportal obliteration alone. B-RTO combined with transportal obliteration is more useful for the treatment of GV⁸⁹.

Collateral veins, including feeding veins of GV⁸⁹, decrease portal hypertension. Obliteration of collateral veins by such procedures as B-RTO and transportal obliteration thus increases portal congestion and portal pressure, especially in patients with cirrhosis. PSE has been performed incrementally to reduce portal venous pressure to the level it was before the obliteration of collateral veins^{23,30,33,36,37,42,47,93,94}.

Several studies have demonstrated the value of TIPS for uncontrolled bleeding from GV⁸⁹. Bleeding control rates exceeding 90% have been obtained. Although bleeding from GV⁸⁹ has been suggested to be more difficult to control with TIPS than is bleeding from EV⁸⁹, a prospective study comparing salvage TIPS for uncontrolled bleeding from FV⁸⁹ with that from EV⁸⁹ showed equal efficacy for both types of varix, with control of hemorrhage in all but 1 patient with each type of varix⁹⁵.

A comparison of DSRS and TIPS has found no significant difference in the rate of rebleeding or the

rate of the first encephalopathy event. Rates of thrombosis, stenosis, and reintervention were significantly higher with TIPS⁹⁶, although TIPS may be more cost effective⁹⁷.

The threshold for the placement of TIPS to control bleeding is lower for GV than for EVs. TIPS can be recommended if endoscopic therapy is not possible or after a single failure to respond to endoscopic treatment.

Prevention of Recurrent Variceal Hemorrhage

Given the high recurrence rate, patients who survive an acute variceal hemorrhage should undergo treatment to prevent recurrence. Complete eradication of EVs or GVs and maintenance of low portal venous pressure are essential for the prevention of recurrent variceal hemorrhage.

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