Hoon Jai Chun
Suk-Kyun Yang
Myung-Gyu Choi
Editors

Therapeutic Gastrointestinal Endoscopy

A Comprehensive Atlas

Second Edition

Springer

EXTRAS ONLINE

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Preface

Current advances in technology including information technology, biotechnology, and nanotechnology have led to great progress of the medical society. Keeping pace with this progress, gastrointestinal endoscopy has also experienced remarkable changes in recent years. Image-enhanced endoscopy, ultra-magnification such as confocal endomicroscopy and endocytoscopy, and artificial intelligence for assessment of endoscopy findings are representative examples. Besides these brilliant changes in diagnostic endoscopies, therapeutic endoscopy has also showed enormous developments, which include various therapeutic third-space endoscopy procedures, novel therapeutic instruments, and endoscopic interventions to metabolic diseases such as obesity. Influenced by these distinct evolutions, we were encouraged to publish a revised edition of *Therapeutic Gastrointestinal Endoscopy: A Comprehensive Atlas*.

In the second edition, we once again aimed to provide the latest information on therapeutic gastrointestinal endoscopies. For this purpose, first of all, up-to-date details of sophisticated procedures such as peroral endoscopic myotomy and endoscopic submucosal dissection were described comprehensively. Elaborate explanations on basic, but highly effective, procedures like cold snare polypectomy and variceal ligation were also included. New instruments such as over-the-scope clip and various stents were introduced in relevant chapters. Secondly, several new chapters have been added to cover the cutting-edge technologies for endoscopic treatment of complex conditions including refractory gastroesophageal reflux disease and duodenal neoplasia. In these chapters, anti-reflux endoscopic intervention using radiofrequency ablation and high-tech endoscopic resection methods were depicted with detailed explanation and endoscopic pictures. Thirdly, we invited several new authors to add novel insights on various issues in therapeutic endoscopies. Some chapters were written by more than one author to maximize the latest contents in relevant topics.

In an endoscopy atlas, not only explanations by the text but also clear pictures are of crucial importance for the reader to easily understand the procedures. In the second edition of our *Therapeutic Gastrointestinal Endoscopy: A Comprehensive Atlas*, we changed roughly half of the pictures for new ones. Most of the new pictures were high-definition endoscopy photos, which should help readers effectively appreciate the details of therapeutic procedures. Schematic illustrations were also used for clear understanding of each step of complex therapeutic endoscopy procedures. Finally, interesting cases were added at the end of chapters for readers' concrete comprehension of endoscopic interventions. These case studies should help endoscopists adequately apply the therapeutic procedures for the appropriate indications in daily practices.

Thanks to these features, this second edition of ***Therapeutic Gastrointestinal Endoscopy: A Comprehensive Atlas*** will be essential for both inexperienced and experienced therapeutic endoscopists. We sincerely appreciate all the authors for their kind contribution to this second edition. We hope this atlas will be loved by endoscopy practitioners in the whole world.

Seoul, South Korea — Hoon Jai Chun
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Endoscopic Treatment of Esophageal Varices

1

Hyun Woong Lee and Young Hoon Youn

Abstract

Acute variceal hemorrhage is one of the most fatal complications of cirrhosis. About 30–50% of the patients with cirrhosis have esophageal varices at diagnosis, and about 10% of the patients with cirrhosis develop varices every year. Therefore, the most important examination in reducing the incidence and mortality of variceal hemorrhage is screening endoscopy for presence of varices, urgent endoscopic therapy for emergent active variceal bleeding, and prophylactic endoscopic treatment for prevention of variceal bleeding. Many guidelines and reviews suggest that endoscopy should be carried out within 12 h in the management of active variceal hemorrhage. The most effective endoscopic treatment for esophageal variceal hemorrhage is band ligation, so-called endoscopic variceal ligation (EVL). Endoscopic injectional sclerotherapy (EIS) has been replaced by EVL and should no longer be offered as standard of care in acute esophageal variceal hemorrhage. In this chapter, we discuss current endoscopic treatment of acute variceal hemorrhage and endoscopic prevention of variceal hemorrhage.

Key Summary

- The most effective endoscopic treatment for esophageal variceal bleeding is band ligation, so-called endoscopic variceal ligation (EVL).
- The endoscopic injectional sclerotherapy (EIS) by injection of sclerosant is still an option of treatment, but not recommended as a modality of primary and secondary prophylaxis for bleeding due to relatively high complication rate.
- In patients with current or prior bleeding from esophageal varices, EVL is the preferred endoscopic treatment and is superior to EIS.
- EVL is also effective for primary prophylaxis, but in most cases it should be reserved for patients who cannot tolerate or who have contraindications to beta-blocker and carvedilol therapy.
- Following an episode of bleeding from esophageal varices, EVL should be performed every 2–4 weeks until the varices are eradicated.
- The combination of nonselective beta-blockers and EVL reduces the risk of recurrent variceal bleeding and improves survival.

1.1 Definition

It is important to define the terms that should be used in the context of a variceal bleeding.

1.1.1 Esophageal Variceal Hemorrhage

Esophageal variceal hemorrhage is defined as bleeding from an esophageal varix at the time of endoscopy or the presence of large varices with blood in the stomach and no other recognizable cause of bleeding.

1.1.2 Variceal Rebleeding

Variceal rebleeding is defined as the occurrence of a single episode of clinically significant rebleeding from portal hypertensive sources from day 5. Clinically significant rebleeding is defined as recurrent melena or hematemesis.

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1.2 General Information

Esophageal varices are portosystemic collaterals, which are formed as a consequence of the portal hypertension. The portosystemic collaterals are preferentially formed in submucosa of the lower esophagus, and the rupture and bleeding from esophageal varices are the most severe complications of liver cirrhosis and are the second most common cause of mortality among the patients.

When patients are diagnosed with liver cirrhosis, approximately 30–50% of cirrhotic patients have esophageal varices, reaching 90% after approximately 10 years, and 30% of these will bleed. However, there are no reliable methods of predicting which cirrhotic patients will have esophageal varices, other than endoscopy [1]. So, the patients with Child's stage A liver cirrhosis with signs of portal hypertension, or those classified as Child's B or C at diagnosis, should have screening endoscopy.

Esophageal variceal bleeding is the most dangerous complication in patients with liver cirrhosis. Although when using the best treatment, mortality from variceal bleeding reaches about 10% because it is mainly due to blood loss in the first week and the result of the development of multi-organ failure in the next 6 weeks. However, mortality from variceal bleeding has greatly decreased in the last two decades from about 40% in the 1980s to 6–12% in the 2000s. This decrease results from the implementation of effective treatment options, such as endoscopic and pharmacological therapies and transjugular intrahepatic portosystemic shunt (TIPS), as well as improved general medical care.

1.3 Surveillance of Esophageal Varices

- The endoscopy is the gold standard for diagnosis of esophageal varices.
- In patients with compensated chronic liver disease without varices, endoscopic surveillance should be repeated at 2–3-year intervals.
- In patients with compensated chronic liver disease with small varices, endoscopic surveillance should be repeated at 1-year interval.
- The main limitations of endoscopy are intraobserver variability in the diagnosis of small or grade 1 esophageal varices.

1.4 Indication

- Urgent endoscopy is indicated for most patients with gastrointestinal hemorrhage, and immediate endoscopic hemostatic treatment should be performed if the endoscopy shows evident acute variceal bleeding.
- It should be performed as early (within 12 h) as possible as there is a direct correlation between a delay of more than 15 h and in-hospital mortality [2].
- After acute endoscopic hemostasis of bleeding from esophageal varices, the elective endoscopic treatment should be repeated until the eradication of esophageal varices, to prevent rebleeding (secondary prophylaxis).
- Prophylactic endoscopic treatment for varices which never have bled before, so-called primary prophylaxis, can be also effective. But in most cases it should be reserved for patients who cannot tolerate or who have contraindications to prophylactic treatment with beta-blocker or carvedilol. However, primary prophylactic endoscopic treatment can be considered when the risk of bleeding seems to be very high (large, tense varices with red spots).

1.5 Prerequisite

1.5.1 Endoscopic Features and Grading of Esophageal Varices

Esophageal varices are long columns of dilated veins, usually occurring within the lower third of the esophagus, immediately above the gastroesophageal junction (GEJ). Esophageal varices can be graded endoscopically according to size (Table 1.1, Fig. 1.1) [3].

Table 1.1 Grading of esophageal varices size

Size of varix	Two-size classification (AASLD)	Three-size classification (Italian liver cirrhosis project)
Small (grade 1)	<5 mm	Minimally elevated, small straight varices
Medium (grade 2)	–	Enlarged tortuous varices occupying less than one-third of the esophageal lumen
Large (grade 3)	>5 mm	Large coil-shaped varices occupying more than one-third of the esophageal lumen

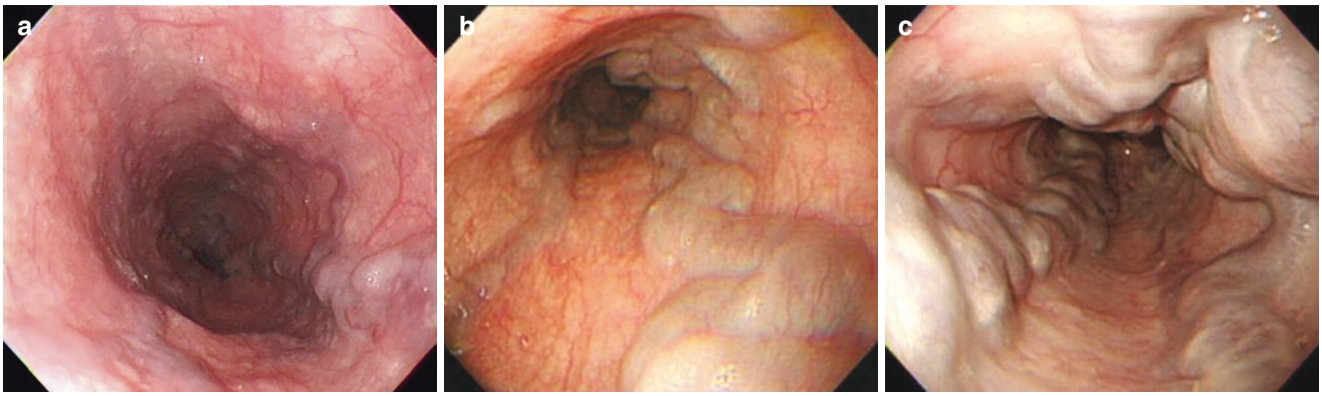

Fig. 1.1 Endoscopic grading of esophageal varices according to size. (**a**) Esophageal varices grade 1 (small), (**b**) esophageal varices grade 2 (medium), and (**c**) esophageal varices grade 3 (large) (Fig. 1.2)

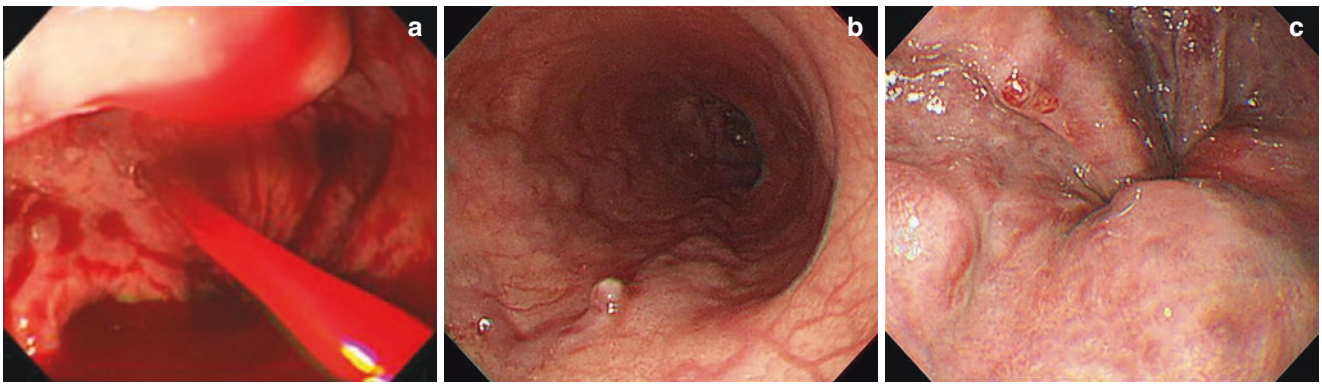

Fig. 1.2 Endoscopic features of esophageal variceal bleeding. (**a**) Active spurting bleeding from varices. (**b**) White plug on esophageal varix, which is a fibrin clot and the stigmata of recent bleeding point. (**c**) Red plug on esophageal varix, which is a blood clot and also the stigmata of recent bleeding

In patients with no varices or small varices, there is no indication to use beta-blockers to prevent the formation of varices. However, patients with small varices with red wale marks have an increased risk of bleeding and should be treated with nonselective beta-blockers (NSBB). Especially, either NSBB or endoscopic band ligation is recommended for the prevention of the first variceal bleeding of medium or large varices [4, 5].

1.5.2 Risk Factors of Variceal Bleeding

The most important predictive factor for bleeding is variceal size, as predicted by LaPlace's law, whereby wall tension increases with variceal radius and transmural variceal pressure. The mean risk of bleeding from larger varices (>5 mm) is 30% at 2 years, compared to 10% from small varices at 2 years. The other predictive factors are severity of liver dysfunction defined by the Child-Pugh classification and red color signs. The red color signs include cherry red spot, red wale mark, and hematocystic spots (Fig. 1.3).

1.6 Instruments

The adequate basic instruments for hemostatic procedure include a large-channel endoscope with the waterjet function, an additional suction unit, and a water irrigation pump.

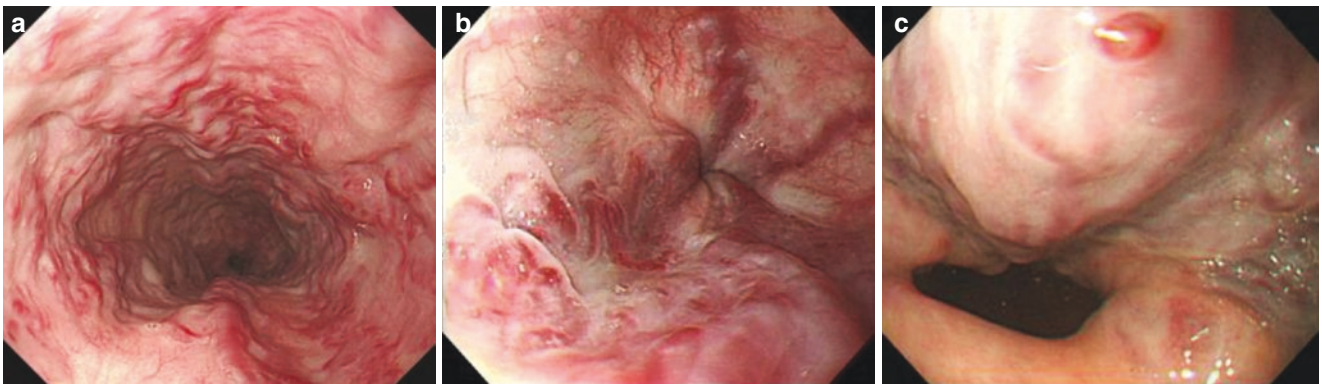

Fig. 1.3 Red color signs in esophageal varices. (**a**) Cherry red spots, which means another small, about 2-mm-sized veins on varix. (**b**) Red wale mark, which means another longitudinal veins on varix. (**c**) Hematocystic spot, which means reddish elevated bloody cyst on varix

Variceal band ligation devices consist of a transparent, hollow-chamber, friction-fit adapter affixed to the tip of the endoscope, preloaded elastic band(s), and a release mechanism. The target tissue is suctioned into the hollow chamber of the friction-fit adapter. A trigger mechanism deploys an elastic band, ligating the target tissue.

1.6.1 The Original Single-Shot Ligator

The original (and still available) banding device (Stiegmann-Goff ligator) usually requires the use of an overtube because the endoscope should be removed, reloaded, and repassed after each band is applied (Fig. 1.4a).

1.6.2 Multiple Ligating Devices

Multiple ligating devices have largely replaced the original single-shot ligators, since the procedure is much simpler and faster. The multiple band ligating systems have made use of the overtube less necessary since four to ten bands can be deployed without having to remove the endoscope. Since longer length of the multiple ligating devices increases the non-flexible tip length, the passage into the esophagus is more difficult in some patients. Overtube can be helpful in such a situation. The overtube also still offers advantages for acutely bleeding patients, even with the multiple ligating device, to protect against aspiration pneumonia. Currently, several companies are producing multiple ligating devices for treating esophageal varices (Fig. 1.4b–f).

1.6.3 The Sclerotherapy Needle

The regular sclerotherapy injection needle should have the smallest possible diameter to minimize the risk of back-bleeding from the injection site. An outer diameter of 0.5 mm is sufficient for liquid sclerosants. The length of needle should not exceed 5 mm, and the bevel should be short.

1.7 Technique

The two principal endoscopic treatment modalities available for esophageal varices are endoscopic sclerotherapy (EST) and endoscopic variceal ligation (EVL).

1.7.1 Endoscopic Injectional Sclerotherapy

Endoscopic injectional sclerotherapy (EIS) has been developing since the mid-1970s. A sclerosant is injected directly into the varicose veins of gastroesophageal junction region with 5% solution of ethanolamine oleate and 1% solution of aethoxysklerol. EIS has been used to treat variceal hemorrhage for about 50 years and is successful in controlling active bleeding in at least 62% of patients [6]. It significantly reduces the frequency of early recurrence and has a positive impact on early mortality.

EIS is achieved by injection of a sclerosing agent into the variceal lumen or adjacent to the varix. The sclerosant can be injected via the flexible needle-tip catheter through the working channel of endoscope (Fig. 1.5). Intravariceal injection of sclerosant induces immediate thrombosis of the vessel, and paravariceal injection induces compression by tissue edema and inflammation of the surrounding tissues. During active bleeding, sclerotherapy may achieve hemostasis, inducing variceal thrombosis and external compression by tissue edema. With repeated sessions, the inflammation of the vascular wall and surrounding tissues leads to fibrosis, resulting in variceal obliteration.

Recently, several agents (sodium tetradecyl sulfate, sodium morrhuate, ethanolamine oleate, polidocanol, and ethanol) have been used at varying concentrations, volumes, and treatment intervals. The volume of injection in EIS is

Fig. 1.4 Various variceal ligation kits. The device has a soft sheath potion that fits over the tip of the endoscope and a transparent hard plastic portion which the rubber bands are stretched over. (**a**) The original single-shot ligator (Stiegmann-Goff ligator), (**b**–**d**) 4, 6, and 10 Shooter Saeed Multi-Band Ligators (Wilson-Cook), and (**e**, **f**) SpeedBand SuperView Super 7 (Boston-Scientific)

usually 1–3 mL per each varix and can be administrated up to 10–15 mL per session. However, the volume of sclerosant in each injection and the interval of treatment vary greatly among operators.

When acute esophageal variceal bleeding was developed, emergency EIS has been compared with vasopressin, terlipressin, octreotide, and somatostatin. The advantages of EIS are that it is cheap and easy to use, the injection catheter fits through the working channel of a diagnostic gastroscope, and it can be quickly assembled, does not require a second oral intubation, and induces a rapid thrombosis.

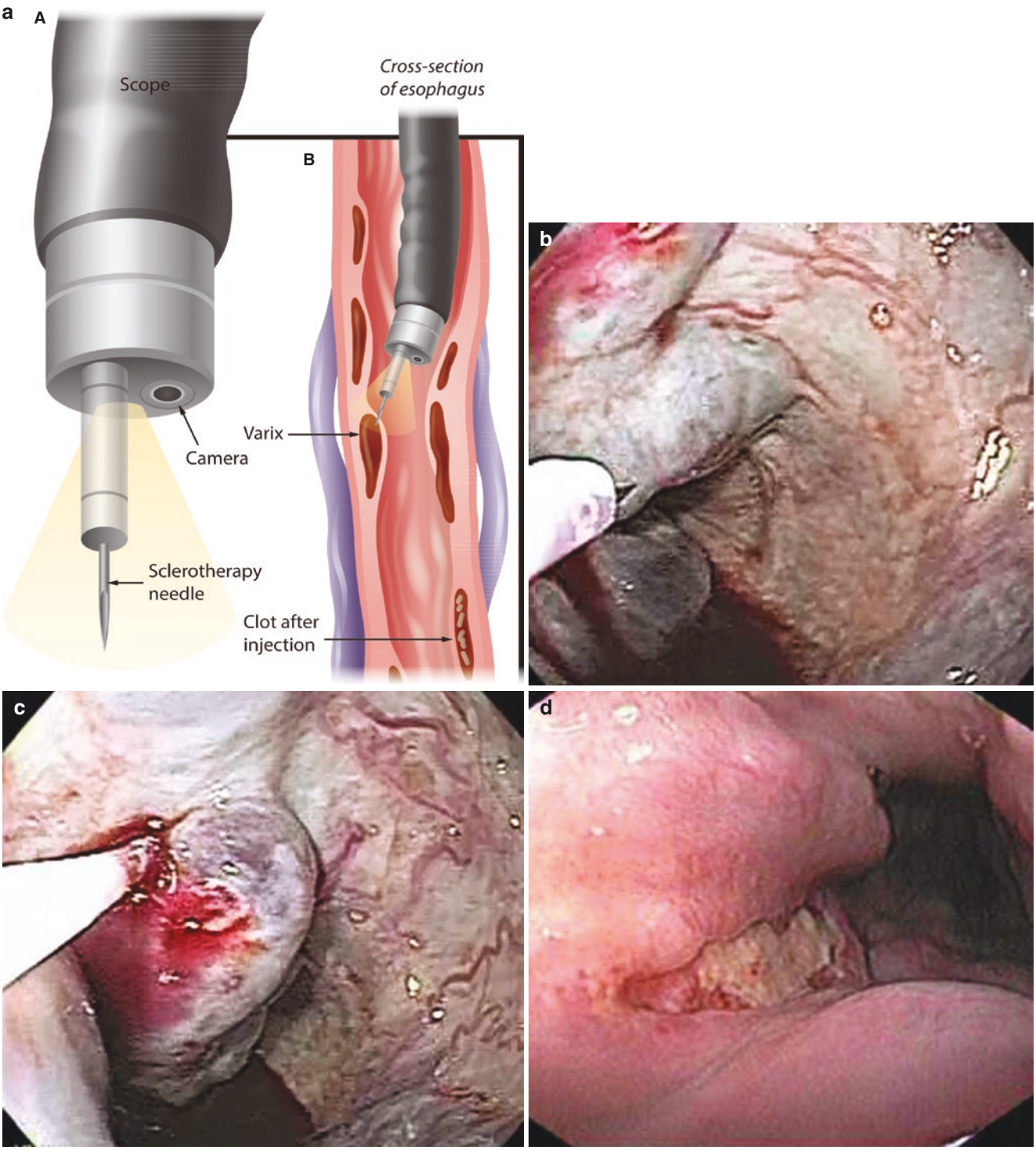

Fig. 1.5 Sclerotherapy for esophageal varices (**a**) Schematic illustration of endoscopic sclerotherapy of esophageal varices. (**b**) The sclerotherapy needle interfaces with the target varix. (**c**) The sclerosant is being injected into the variceal lumen through the needle catheter. (**d**) The typical longitudinal esophageal ulcer after sclerotherapy

The efficacy of EIS in control of acute variceal bleeding is comparable to that of band ligation, and EST still can be a treatment option for acute esophageal variceal bleeding. However, EIS have substantially higher complication rate than EVL, and ES is largely replaced by band ligation method which shows better clinical efficacy in bleeding control with lesser complication. So, EIS is currently not recommended as a method for primary and secondary prophylaxis of variceal bleeding.

1.7.2 Endoscopic Variceal Ligation

Endoscopic variceal ligation (EVL) was developed as an alternative for endoscopic treatment of esophageal varices with fewer complications than endoscopic injectional sclerotherapy (EIS), and the concept of EVL was based upon treatment of hemorrhoids with rubber band ligation. EVL controls bleeding in approximately 80–100% of patients and has equal or slightly better efficacy than EIS in achieving hemostasis.

EVL reduced the rebleeding rate and mortality rate with fewer incidences of esophageal strictures. Therefore, EVL is currently considered the endoscopic treatment of choice for patients to prevent esophageal variceal rebleeding.

Unlike the induction of chemical inflammation and thrombosis after the introduction of sclerosing agents, EVL obliterates varices by capturing all or part of a varix with rubber bands resulting in mechanical strangulation and occlusion from thrombosis (Fig. 1.6). The tissue then necrotizes and

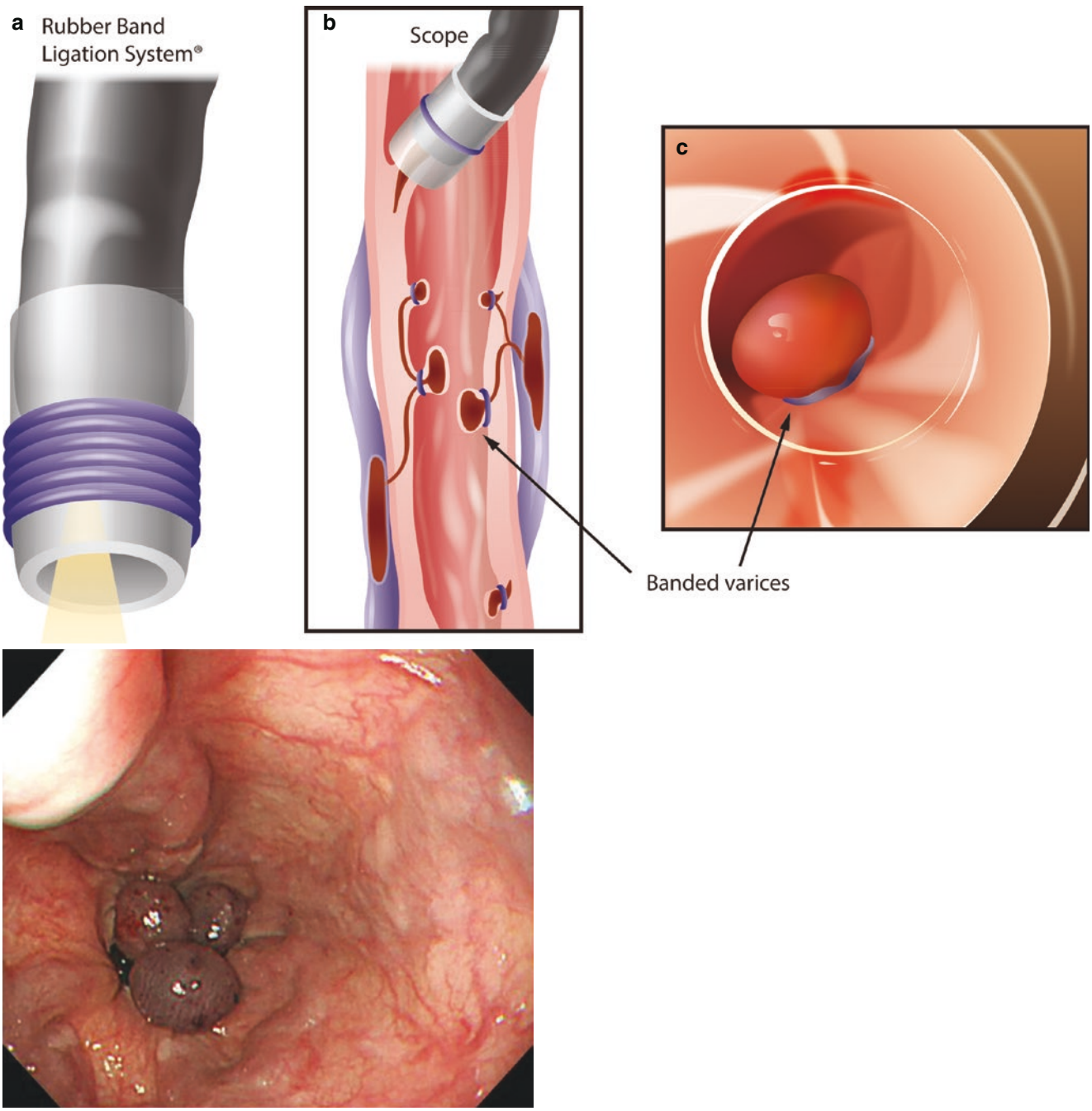

Fig. 1.6 Endoscopic variceal ligation

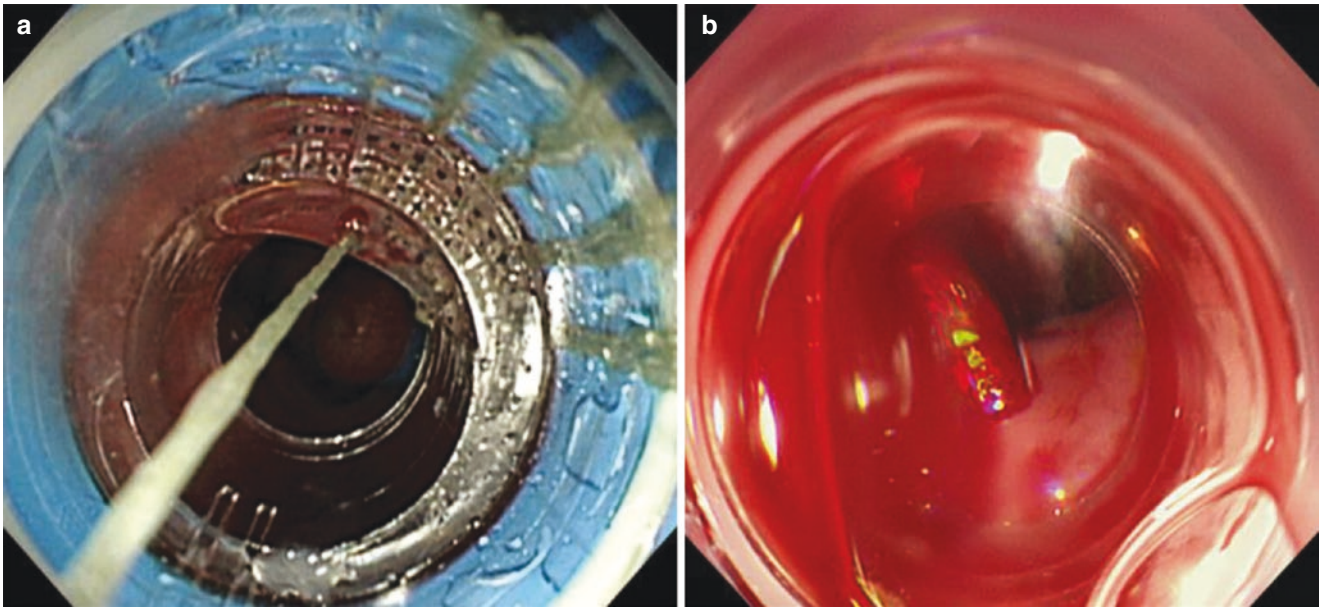

Fig. 1.7 Endoscopic views with attachment of banding device. (**a**) The vision of endoscope is often largely restricted and narrowed by the attachment of banding device. (**b**) In the setting of active bleeding, accumulation of blood in the tip of the device makes the visibility more difficult

sloughs off in a few days to weeks, leaving a superficial mucosal ulceration, which rapidly heals. EVL avoids the use of sclerosant and thus eliminates the deep damage to the esophageal wall that occurs after EIS. EVL has become the treatment of choice both for controlling variceal hemorrhage and for variceal obliteration in secondary prophylaxis, since it has better efficacy and lesser complications than EIS. In addition, the combined use of endoscopic EVL with terlipressin or octreotide was more effective than therapy with vasoactive drug alone [7].

EVL consists of the placement of rubber bands on variceal columns which are sucked into a plastic hollow cylinder attached to the tip of the endoscope. The EVL procedure should be started after a thorough endoscopic evaluation to identify the esophageal varices that are to be treated. It is helpful to measure the distance of the gastroesophageal junction and the target varices from the incisors before beginning EVL, since visibility may be reduced once the banding device is placed over the tip of the endoscope. The cylinder attachment restricts the field of vision, and blood accumulating in the tip of the device also hinder the clear vision (Fig. 1.7). Some experts claim that the cylinder attached to the endoscopy may obscure detection of the bleeding point when using EVL during active bleeding. These problems can be overcome by active flushing with water and suction. Use of an overtube may facilitate endoscope entry into the esophagus and protect airways during massive bleeding or massive vomitus at endoscopy. However, it may induce esophageal laceration or perforation.

Once the target varix is identified, the tip is pointed toward it and continuous suction applied so it can fill the cap. Once inside the cap, a "red out" sign should appear and at this point the band can be fired (Fig. 1.8).

Ideally, the rubber band should be delivered on the varix at the point of bleeding site, but if missed, banding of mucosa without a varix in it will not be harmful in contrast to injecting a sclerosant, which may cause considerable tissue damage as side effects. However, if the point of bleeding cannot be identified, it is possible to semi-blindly place bands at the gastroesophageal junction, which reduces torrential bleeding, and further bands can be fired afterward. Varices with stigmata indicating recent bleeding (such as a white fibrin plug or a red plug sign) should be also primary targets for ligation even if they are not located at the gastroesophageal junction.

It is important to try to get a "red out" (caused by close approximation of the mucosa overlying the varix to the lens within the ligating chamber cap), indicating that a sufficient amount of variceal tissue has been captured into the cap. However, the complete red out may not always be possible with multiple ligator devices since it has a longer chamber. The application of a band on a small, insufficiently sucked tissue often results in the immediate slide-off of the band, and it may also cause some mucosal damage with subsequent bleeding. Usually the application of the band is started at the gastroesophageal junction and ascended proximally in a helical fashion to avoid circumferential placement of bands at the same level (Fig. 1.9).

There is no standardized optimal number of bands to apply to esophageal varices per one session, and there is theoretically no limit to the number of bands that can be applied in one session. Six to ten bands are commonly used

Fig. 1.8 Band ligation of esophageal varices with active bleeding. (**a**) Spurting bleeding from esophageal varix. (**b**) "Red out" by suction of the target varix into the chamber cap and close approximation of the mucosa and the lens of endoscope. (**c**) Hemostasis could be achieved by a ball-like ligation of the varix. The ligation must be done after sufficient suction to make largely ligated balls of varices and to obliterate the blood flow

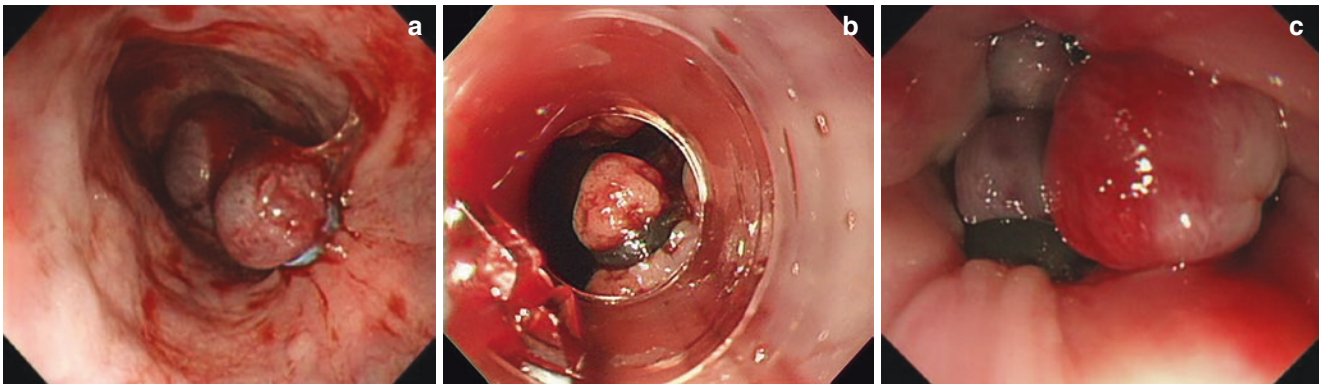

Fig. 1.9 The band-ligated esophageal varices immediate after EVL. (**a**) Sufficiently large balls of ligated varices. (**b**) Too small, inadequately ligated varices by insufficient suction, which often result in the immediate slide-off of the band, and subsequent bleeding. (**c**) Helical application of the band from the gastroesophageal junction to proximal esophagus

during the initial session, and fewer bands are usually required during subsequent sessions. However, placement of more than six bands per session did not improve patient outcomes but prolonged procedure time and increased the number of misfired bands [8].

After the application of rubber bands over esophageal varices, the patients can start with liquids for the first 12 h and then take soft foods gradually. The ligated tissues with rubber bands may fall off within a few days (range, 1–10 days). Following the sloughing of varices, shallow esophageal ulcers are ubiquitous at ligated sites, and esophageal varices become smaller in diameter (Fig. 1.10). The ligation-induced ulcers are shallower, have a greater surface area, and heal more rapidly than those caused by EIS. Posttreatment ulcer bleeding may occur in about 20% of patients receiving EIS and 2% of patients receiving EVL. Most of these patients may be treated conservatively, using vasoconstrictors, proton pump inhibitors, and sucralfate powder. Next step is transjugular intrahepatic portosystemic shunt (TIPS).

The complete eradication of esophageal varices requires multiple sessions of EVL as with sclerotherapy. At the subsequent sessions after initial ligation, bands can be applied as needed to any persistent varices. Usually varices are considered eradicated when they have either disappeared or cannot be grasped and banded by the ligator (Fig. 1.11).

The optimal time interval between sessions has not been clarified. The interval between each EVL sessions was various according to studies, from 1 week to 2 months. However, since the most rebleeding events after EVL occur in the interval between the initial session and the time when variceal obliteration is achieved, too long interval between sessions seems to be inappropriate [9]. A guideline suggests that in patients who bleed from varices and were treated with EVL or those who underwent EVL for primary prophylaxis, EVL should be repeated every 1–2 weeks until obliteration of varices, and the first surveillance EGD recommended 1–3 months after obliteration and then every 6–12 months to check for variceal recurrence [3].

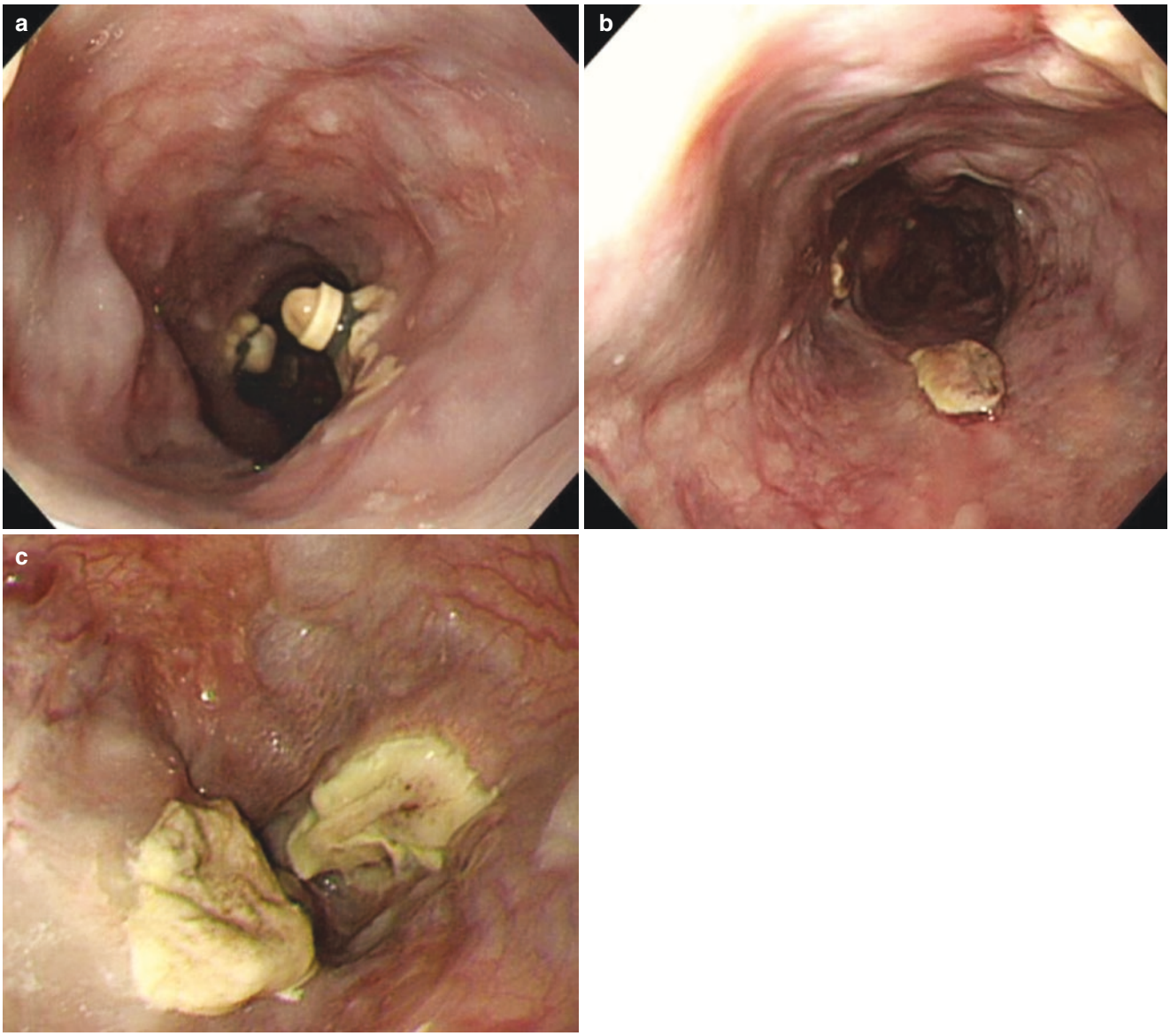

Fig. 1.10 Esophageal ulcers after band ligation. (**a**) Necrotic change of banded varices a few days after EVL. (**b**, **c**) Shallow ulcers following the sloughing of necrotic variceal tissues

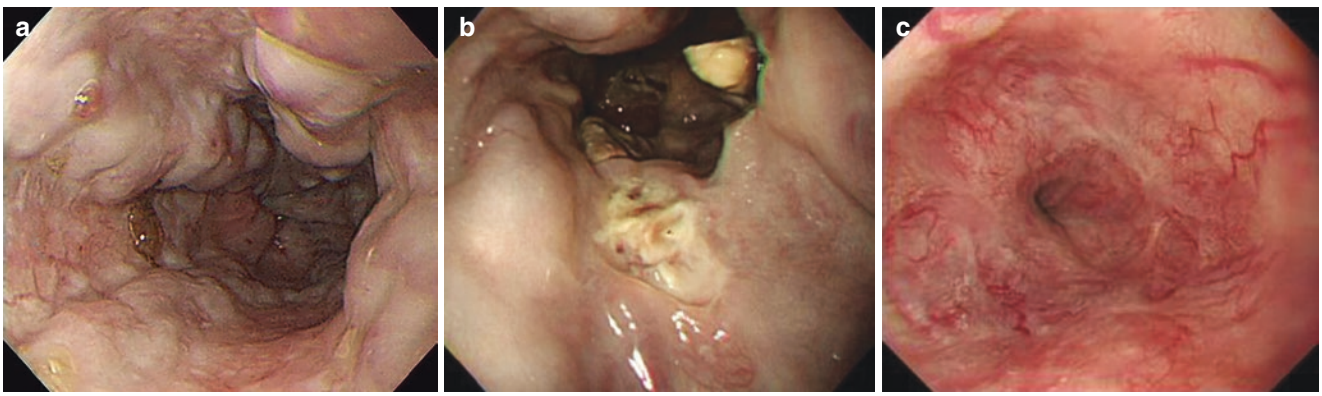

Fig. 1.11 A case of the complete eradication of esophageal varices by multiple sessions of EVL. (**a**) Initial large esophageal varices before EVL. (**b**) Multiple ulcers by EVL. (**c**) Multiple scars are left in the esophagus after complete healing of previous ulcerations by band ligation. The esophageal varices are completely eradicated

After apparent eradication is achieved, the patients must be followed with regular endoscopic examination in every 3–6 months. The main drawback of EVL is possibly a relatively frequent recurrence of varices. Fortunately, those recurrent varices can usually be treated with repeated ligation, and the recurrence after EVL did not lead to a higher risk of rebleeding or require more endoscopic treatments. Concomitant treatment with a nonselective beta-blocker should be considered as this can further decrease the rate of rebleeding. The combination of EST and EVL does not appear to be better than EVL alone.

1.8 Predictions

1.8.1 Predictive Factors for Variceal Hemorrhage

The factors that predispose to, and precipitate, variceal hemorrhage are still not clear. The important factors are pressure within the varix, variceal size, tension on the variceal wall, and severity of the liver disease [10].

1.8.2 Predictive Factors of Serious Outcome

Important predictors of serious adverse outcome are the values of hepatic venous pressure gradient (HVPG), measured within 24 h after stabilization of hemodynamic, exceeding 20 mmHg, impaired renal function, infection, hypovolemic shock, active bleeding during endoscopy, and early relapse with the need for transfusion of more than four doses of packed red blood cells.

1.9 Complication

1.9.1 Complications of EIS

Several local and systemic complications may arise after EIS, and there are early (within the first 1 day after injection) and late (a few days or weeks) complications of EIS. Complications of EIS include fever, retrosternal discomfort or pain, dysphagia, injection-induced bleeding, esophageal ulceration with delayed bleeding, esophageal perforation, mediastinitis, pleural effusion, pericarditis, bronchoesophageal fistula, adult respiratory distress syndrome, distant embolism, and infectious complications, such as bacteremia (up to 35%), distal abscess, and spontaneous bacterial peritonitis [11]. The main cause of these hazardous complications is usually an extensive wall necrosis induced by an incorrect injection technique, too much sclerosant being injected, or a high concentration of the sclerosant [12]. One disadvantage of the procedure is the increase of HVPG, which may be the cause of early recurrent bleeding.

1.9.2 Complications of EVL

Esophageal ulcers develop at all each ligation site after all successful ligations. So, esophageal ulcers after EVL are not classified as complication. However, ulcers following EVL are less severe than with sclerotherapy, which often induce deeper ulcers and are thus prone to causing mediastinal inflammation and/or esophageal wall scarring. Combined data from a number of studies suggest that complications with EVL are substantially lesser than with EST, presumably because of the shallower tissue injury (cumulative complication rate of 11% versus 25%) [13]. The incidence of bacteremia and infectious sequelae after EST was five to ten times higher than after EVL. The complications of EVL include esophageal laceration or perforation (mostly due to trauma of the overtube), transient dysphagia, retrosternal pain, transient accentuation of portal hypertensive gastropathy, transient bacteremia, bleeding from post-EVL ulcer, and rarely esophageal stricture.

1.10 Primary Prophylaxis

It is estimated that esophageal varices may be noted in 50% of cirrhotic patients. Variceal bleeding may lead to high incidence of mortality and rebleeding. Therefore, primary prophylaxis of first bleeding from esophageal varices is important in patients with high-risk esophageal varices.

Most guidelines recommend endoscopic examinations in patients with evidence of cirrhosis to confirm presence of high-risk esophageal varices. If cirrhotic patient has no varices, follow-up endoscopy is advised at intervals of 2 years. If mild varices without red color signs, nonselective beta-blockers (NSBB) are the first option. NSBB (e.g., propranolol or nadolol), when given in doses to reduce the pulse rate by 25%, have been shown to prevent or delay the first episode of variceal bleeding.

If patient has large varices, either NSBB or EVL can be considered. However, EIS is not recommended for primary prophylaxis because it can increase the mortality rate. Endoscopic variceal ligation (EVL) eradicates esophageal varices with fewer complications than EIS and is as effective as the use of beta-blockers.

EVL reduced the rate of first variceal bleed by 43% compared with beta-blocker use, although there was no effect on mortality [14]. There was a small risk of initiating a variceal bleeding episode during prophylactic banding. The superiority of EVL over beta-blocker therapy has been questioned, although the two treatments probably have at least equivalent efficacy.

In most cases, it is recommended that prophylactic EVL be reserved for patients who cannot tolerate or have contraindications to beta-blocker use.

1.11 Summary

The management of cirrhotic patients with active esophageal variceal bleeding requires a multidisciplinary approach. Combination of endoscopic therapy with vasoconstrictors improves initial control of bleeding and 5-day hemostasis. Fortunately, the mortality of acute esophageal variceal hemorrhage has decreased to about 10% in recent years. Endoscopic therapy plays a pivotal role in management of all three aspects of variceal bleeding such as preventing first variceal bleeding, treatment of acute variceal bleeding, as well as prevention of variceal rebleeding.

Appendix: Quiz

What is the diagnosis and the best treatment option for this patient with cirrhosis?

Question: A 55-year-old man with liver cirrhosis induced by alcohol was admitted to University Hospital with a 5-day history of intermittent melena. Upon admission, his vital signs were as follows: blood pressure of 110/70 mmHg, heart rate of 70/min, respiratory rate of 18/min, and body temperature of 36.8 °C. Head and neck examinations were unremarkable except for anemic conjunctiva. His abdomen was distended with shifting dullness and the spleen was palpable. Initial laboratory data were as follows: WBC 1400/mm^3, Hb 8.1 g/dL, platelet 63,000/mm^3, BUN 35 mg/dL, creatinine 1.2 mg/dL, albumin 2.9 g/dL, AST 126 IU/L, ALT 45 IU/L, ALP 147 IU/L, total bilirubin 1.8 mg/dL, INR 1.45, and AFP 2.4 ng/dL. The hepatitis B and C marker was negative. Initial diagnosis was Child's B liver cirrhosis. The patient was treated with intravenous (IV) pantoprazole, IV terlipressin, and IV third-generation cephalosporin and was transfused with fresh frozen plasma and packed red blood cells. Emergency esophagogastroduodenoscopy revealed the presence of grade 2 esophageal varices (Fig. 1.12). Abdominal computed tomography (CT) showed liver cirrhosis with massive ascites, splenomegaly, and esophagogastric varices with portosystemic collaterals (Fig. 1.13).

1. What is the diagnosis?
   A. Esophageal ulcer.
   B. Esophageal erosion.
   C. Herpes esophagitis.
   D. Mallory-Weiss syndrome.
   E. Esophageal variceal hemorrhage.

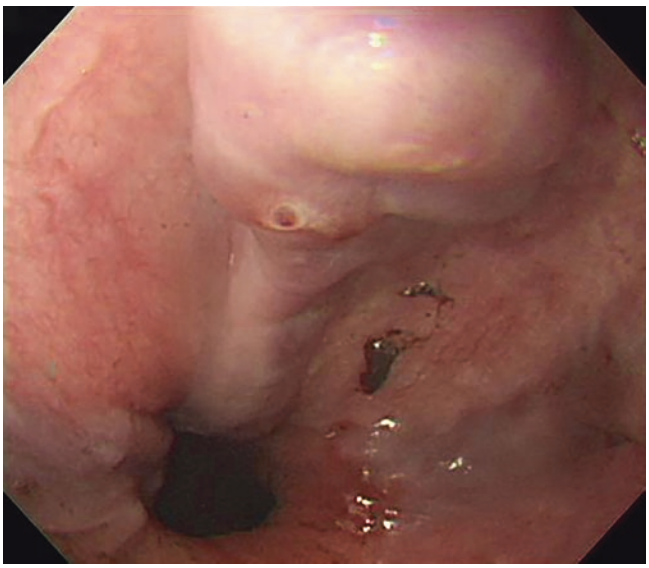

Fig. 1.12 Grade 2 esophageal varices

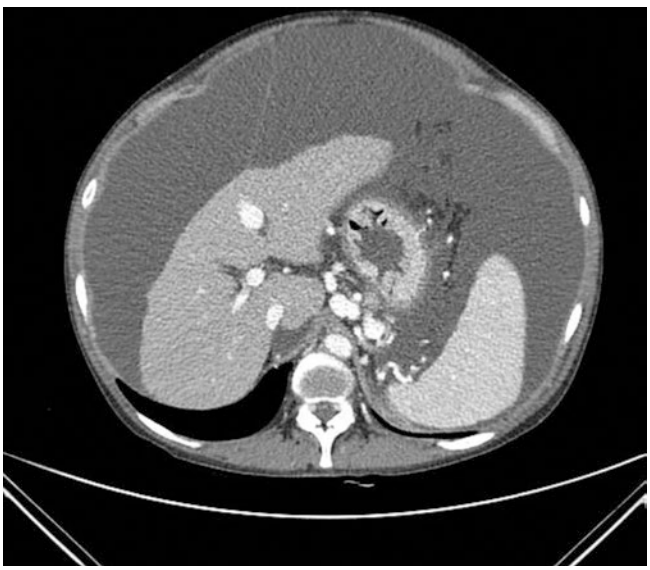

Fig. 1.13 Liver cirrhosis with massive ascites, splenomegaly, and esophagogastric varices with portosystemic collaterals

2. What is the best treatment option?
   A. Nonselective beta-blocker.
   B. Endoscopic injectional sclerotherapy.
   C. Sengstaken-Blakemore tube insertion.
   D. Transjugular intrahepatic portosystemic shunt.
   E. Endoscopic variceal ligation and nonselective beta-blocker.

Answer:

1. (E) Esophageal variceal hemorrhage.
2. (E) Endoscopic variceal ligation and nonselective beta-blocker.

Esophageal variceal hemorrhage is defined as bleeding from an esophageal varix at the time of endoscopy or the presence of large varices with blood in the stomach and no other recognizable cause of bleeding. We can see endoscopic feature of recent esophageal variceal bleeding, such as a red plug on esophageal varix, which is a blood clot and also the stigmata of recent bleeding (Fig. 1.12).

Nonselective beta-blocker (NSBB, propranolol or nadolol) + esophageal variceal ligation (EVL) combination therapy are strongly recommended as secondary prophylaxis. NSBB or EVL monotherapy is suggested as not best option but alternative option. EVL alone is used to eradicate varices if there are contraindications or intolerance to combined use with NSBB. We suggest that TIPS is used for patients who rebleed despite combined EVL and NSBB therapy. EIS cannot be recommended for prophylaxis of esophageal variceal hemorrhage in patients with cirrhosis because of iatrogenic complications such as strictures.

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