



The role of stenting in patients with variceal bleeding

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ABSTRACT

Uncontrolled acute variceal hemorrhage due to failure of standard endoscopic therapy increases the risk of decompensation of liver disease and multiorgan failure leading to death. In this article, we aim to provide a structured and comprehensive review of the management of variceal bleeding by the use of self-expanding metal stent(s) (SEMS). The intricacies of the appropriate patient and stent selection, technicality of stent placement, deployment, and follow-up will be discussed. Furthermore, certain stent models with unique delivery system that eliminates the need of endoscopic or radiographic guidance will be reviewed. While patients with uncontrolled acute variceal hemorrhage are at a very high risk of adverse events, SEMS complications and the steps to prevent them will also be discussed. As a vast majority of these cases represent advanced liver disease, liver transplant is ultimately required, thus, making SEMS an effective bridge to definitive therapy.

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1. Introduction

Life-threatening uncontrolled acute variceal hemorrhage (AVH) either due to primary or secondary failure of endoscopic therapy has limited management options due to local or systemic factors. Ongoing bleeding has the potential to further decompensate liver disease and/or result in multiorgan failure leading to death. In this review, we will discuss the candidacy, the technical details, safety, and efficacy of the endoscopic stent deployment to manage resistant variceal bleeding. We will also discuss novel stent design and future developments in this area of endoscopic management.

2. Candidates for endoscopic stenting to manage variceal hemorrhage

AVH presents commonly as hematemesis in a patient with a prior history of portal hypertension and as the severity of the liver disease increases so does the risk of AVH. The most common location of gastrointestinal varices, the usual source of AVH, is esophageal varices. In cirrhotic patients, up to 35%–80% develop varices and one-third will experience an episode of AVH [1,2]. The model for end-stage liver disease score is often used as a predictor for bleeding varices and mortality risk in patients with cirrhosis of the liver. Patients with a

model for end-stage liver disease score over 14 are 50% more likely of having two or more bleeding episodes [3–5].

The first-line endoscopic management strategy for bleeding varices is endoscopic variceal ligation (EVL). D'Amico et al. noted that in 10%–20% of patients the standard therapy of combining pharmacologic and endoscopic measures fails to stop the initial hemorrhage [6]. Acute torrential bleeding from postbanding ulceration is another subgroup where EVL is more likely to fail due to mucosal noncompliance. When variceal bleeding cannot be controlled by EVL, other hemostatic measures must be attempted, which include the Sengstaken-Blakemore tube, self-expanding metal stents (SEMS), and/or transjugular intrahepatic portosystemic shunting (TIPS). Due to infrequent use, insertion and maintenance of Sengstaken-Blakemore tube is challenging and resource-intensive. TIPS may also be contraindicated in these patients due to cardiovascular and neurologic derangements. For these patients, placement of fully covered stent could be an alternate endoscopic approach to tamponade the source of bleeding. As a proof of concept, in a 2012 case series, insertion of the SEMS led to immediate bleeding control in 100% (9/9) of patients [7]. These SEMS can be left in place for up to two weeks to manage refractory uncontrolled esophageal bleeding or as a bridge to definitive therapy and have a lower rate of complications when compared to other modalities used to tamponade the bleeding, such as the Sengstaken-Blake-more tube.

Upon suspicion or presentation of AVH, cirrhotic patients require intensive care with frequent monitoring (Figure 1). Hemodynamic stabilization with a cautious transfusion strategy, correction of any existing coagulopathy and hemostatic dysfunction, control of portal pressure with splanchnic vasoconstrictors, and prophylactic antibiotic therapy is the foundation of medical therapy before SEMS

Abbreviations: AVH, acute variceal hemorrhage; BT, balloon tamponade; EVL, endoscopic variceal ligation; MELD, model for end-stage liver disease; SEMS, self-expanding metal stent(s); TIPS, transjugular intrahepatic portosystemic shunt

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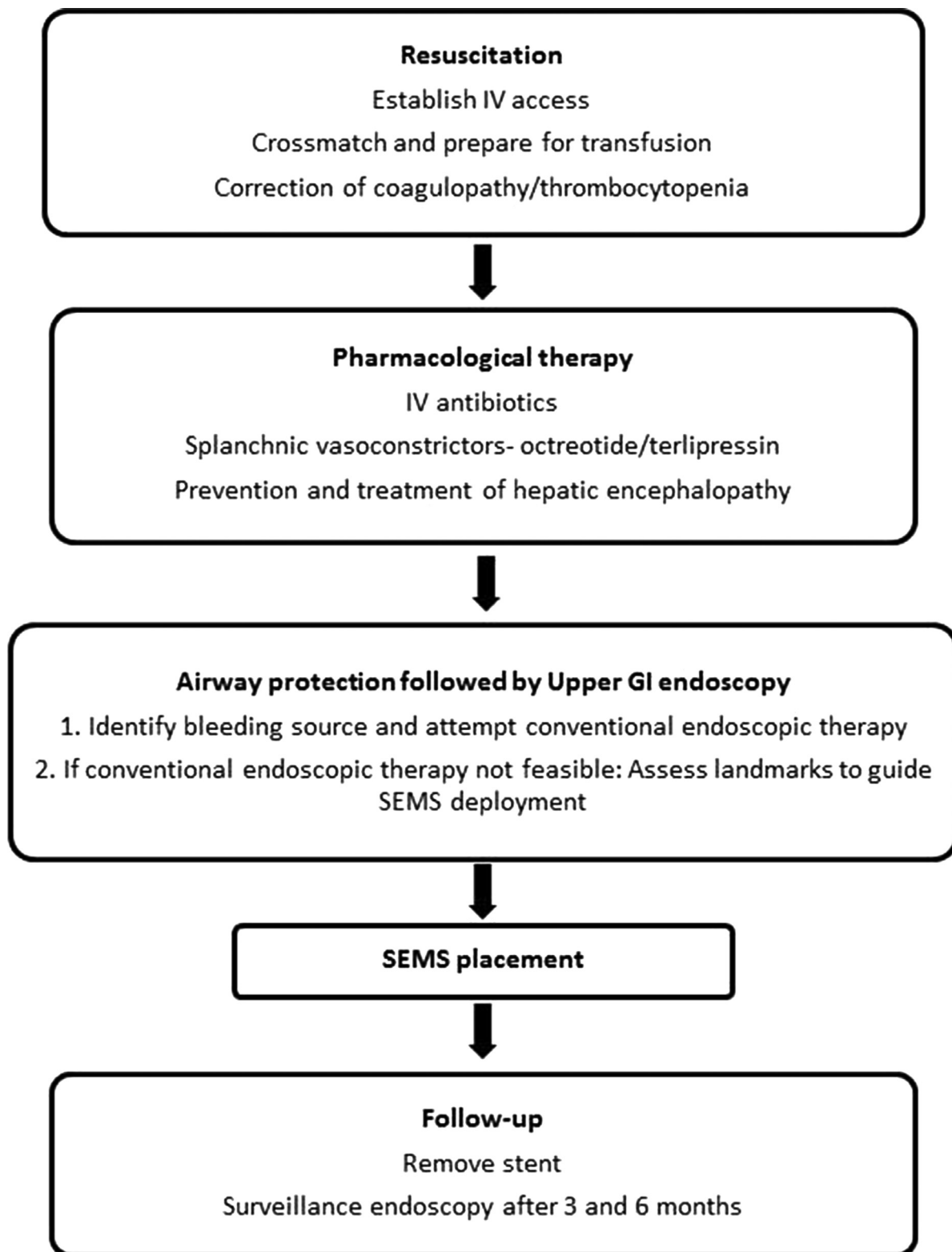


Fig. 1. Medical management of acute variceal hemorrhage before the placement of stent.

placement. These therapies are initiated as soon as the diagnosis of AVH is suspected and before endoscopy. Initial medical management is focused on volume restitution to maintain hemodynamic stability and tissue perfusion. Overtransfusion may increase the portal venous pressure, which can precipitate rebleeding or aggravate ongoing bleeding. Better survival rates are seen with the restrictive replacement of blood volume, where the hemoglobin level is maintained

between 7 and 8 g/dL [8]. Thrombocytopenia and coagulopathy predispose the patient to increased procedural and postprocedural bleeding. Transfusion of fresh frozen plasma and platelets (when platelet levels are below $50,000/\text{mm}^3$) can be considered in cirrhotic patients with AVH; although the Baveno committee makes no such recommendation [9,10]. Antibiotic prophylaxis is crucial as it prevents bacterial infection such as spontaneous bacterial peritonitis,

reduces the incidence of early-rebleeding, and increases survival [11,12]. The appropriate antibiotic therapy is customized to the local antimicrobial susceptibility patterns and individual patient characteristics. Conventionally, oral norfloxacin is the main therapy, administered at a dose of 400 mg, twice daily, for seven days. Intravenous (IV) ciprofloxacin or IV ofloxacin is the alternative when oral intake of norfloxacin is not possible. In cases of advanced cirrhosis and quinolone-resistance, IV ceftriaxone (1 g/24 hours for 7 days) is the drug of choice [13]. Avoid antibiotic prophylaxis in the subgroup of Child-Pugh A cirrhosis as the risk of bacterial infection and mortality is very low in these patients [14]. To prevent and treat hepatic encephalopathy, lactulose is administered. In suspected variceal bleeding, vasopressor therapy is promptly started to control the bleeding by reduction of portal venous pressure. The intravenous vasoactive agents lead to better hemostasis and a shorter hospital stay. They are also associated with lower transfusion requirements and reduced incidence of mortality and rebleeding [15]. Terlipressin, somatostatin, vasopressin, or octreotide are the available vasoactive agents, but in the United States, only octreotide is approved for use. Sodium levels must be monitored with terlipressin use as it has been linked to hyponatremia [16]. It is recommended that the therapy be used in combination with endoscopic intervention and continued for 5 days [10]. Medical management is followed by endoscopy to confirm the site and severity of AVH and perform the endoscopic intervention. Guidelines recommend that following hemodynamic resuscitation, endoscopy should be performed within 12 hours of presentation [10]. Delayed endoscopy (past 12 hours of initial presentation) is linked to an increased risk of death and rebleeding [17]. Pre-endoscopy infusion of erythromycin is done after ruling out QT prolongation.

3. Stent selection for tamponade of variceal hemorrhage

The SEMS used to manage refractory esophageal variceal bleeding are typically required emergently; they need to be effective and placed for a few days to one week to achieve the desired effect without resulting in an injury that could exacerbate the bleeding. Therefore, appropriate stent selection is critical.

3.1. Characteristics of an ideal stent

The integration of specific technical features in the stent design and deployment mechanism potentiates its suitability for arresting variceal hemorrhage without causing injury. Ability to deploy over a wire, fully covered profile to prevent embedding of the stent, smooth margins to prevent esophageal injury, tailored dimensions, radial strength, and expansion profile are key considerations. The stent architecture must be configured to the anatomy of the esophagus and the luminal alteration caused by tortuous or large varices. The stent must be flexible, easily-implantable, and conform to the esophageal peristaltic movements. Postdeployment, the stent must exert an effective radial force on the esophageal wall to fully compress the varices and stop the bleeding. Predictable expansion with minimal foreshortening and negligible recoil are important features. Controlled expansion minimizes the chances of pressure necrosis and wall rupture. It should be repositionable and removable past the cessation of the bleed. Radiographic visibility is less important during these emergency stent placements but it allows for precise tracking. A wide distal flange can reduce the chances of stent migration to the stomach. All these characteristics contribute to the efficiency and safe usage of a stent.

3.2. Suitability of conventional stents and development of novel stents for variceal tamponade

The initial stents utilized to arrest variceal bleeding were the conventional covered SEMS. Traditionally, these models were being used

for palliative therapy of inoperable esophageal malignancies until Hubmann et al. demonstrated their usage in acute variceal bleeding [18]. In this pilot study, the Choo stent (diameter 18 mm, length 140 mm, NES-18-080-070, M.I. Tech Co., Ltd) and the Ella-Boubella-Danis stent (diameter 20 mm, length 95 mm, Ella-CS, Hradec Kralove, Czech Republic) were used in 2 and 3 patients respectively and lead to immediate hemostasis in all of the 5 patients [19,20].

The Choo stent is a covered nitinol stent shaped like a dumbbell. Its segmented body helps conform to the esophageal peristaltic movements and the dumbbell ends prevent stent migration. The body of the stent bears radiopaque markers for positional verification and the lasso at both ends allows repositioning. The Boubella Danis stent is a polyethylene covered, stainless steel stent, and features gold markers for guiding placement and retrieval loops at both ends for repositioning or removal. An antimigration segment is present at the proximal end. It has a unique rocket style delivery system wherein the olive tip automatically detaches at the time of stent release and falls into the stomach. The olive tip then passes through the gastrointestinal tract without any complications.

Despite demonstrating efficacy, these conventional stent designs were not ideal for deployment and use in variceal bleeding, hence the SX-ELLA Danis Stent (Ella-CS, Hradec Kralove, Czech Republic) was engineered. It differs from the Choo stent and the Ella-Boubella-Danis stent in having a balloon-style delivery system. The SX-ELLA Danis Stent (Figure 2a) is a self-expandable, MRI-conditional, and polyurethane-covered nitinol stent preloaded in a balloon-style delivery system. The nitinol wires are weaved in a braided fashion that imparts high flexibility and adequate axial force. It can be readily deployed without endoscopic or radiological assistance, which is advantageous in emergencies. The security pressure valve prevents accidental inflation of the gastric balloon in the esophagus. As an over distended balloon can rupture and cause esophageal perforation, it is advised not to insufflate with more than 100 mL of air. The body of the stent is braided in variable pitches maximizing its conformity to esophageal peristalsis. The shape is customized to the anatomical curves of the lower esophagus and varices. The wide distal throat is an effective antimigration measure. Radiopaque markers at the midpoint and both ends aid visualization and radiological confirmation of its position. The stent features atraumatic ends to minimize mucosal injury and the biocompatible alloy provided high durability and acid resistance. The retrieval loops at both ends permit stent repositioning and extraction. The body of the stent can be elongated or narrowed by grasping and pulling these loops. The stent is removed under endoscopic and fluoroscopic guidance using the extractor device (PEX-Ella Extractor) or by grasping forceps. The nominal (relaxed) diameter of the stent body is 25 mm, the nominal diameter of flares is 30 mm, and the length is 135 mm. The delivery system is 28 Fr (9.4 mm) / 20 F (6.6 mm) in diameter and is available in a standard length of 60 cm.

In the United States, due to lack of availability of the aforementioned stents, we use fully covered SEMS such as esophageal WallFlex (diameter 18 or 23 mm, length 100 or 120 mm, Boston Scientific, Marlborough, MA), or polyurethane-covered Nitinol Taewoong Niti-S (diameter 18 or 20 mm, length 100 or 120 mm, Cook Medical, Bloomington, IN) stents to manage acute refractory variceal bleeding. For this off-label use, we discuss the pros and cons and possible complications with the patient and/or family.

4. Technical aspects of stent used to manage refractory variceal bleeding

The acute nature of refractory variceal bleeding typically requires the placement of the stents at the bedside. Due to the emergency situation, these stents are typically placed without fluoroscopy and with or without endoscopic guidance. Unlike conventional stents, SX-Ella Danis stent has a unique stent delivery system (Figure 2b)

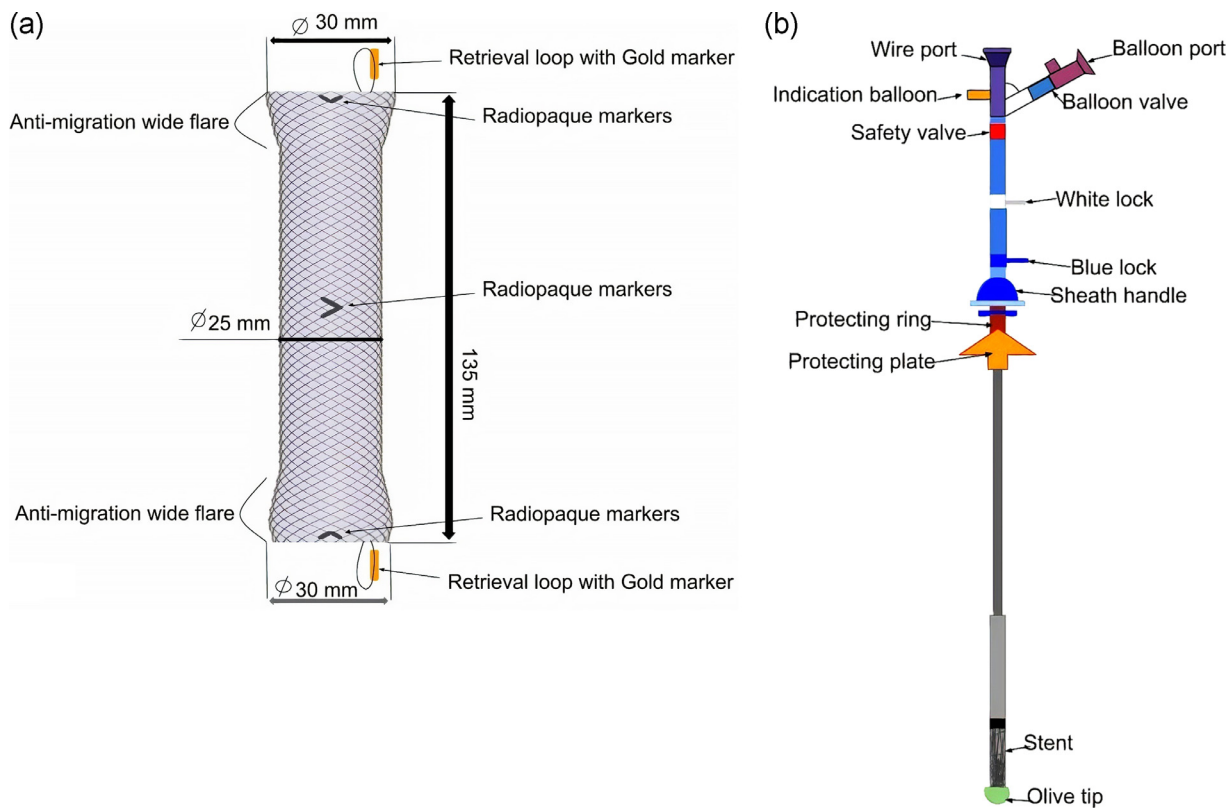


Fig. 2. Illustration showing
 a. The design and structural components of the SX-ELLA Danis stent.
 b. The unique ready-to-use delivery system with the preloaded SX-ELLA Danis stent.

and it is designed to be deployed without the need for endoscopic or radiographic guidance.

The procedure is performed in a supine or left lateral position with endotracheal intubation to protect the airway. Fluoroscopy is preferred and postprocedure patients should receive anti-nausea medications to prevent retching. For SX-ELLA Danis stent, when implanted at the bedside, local pharyngeal anesthesia is delivered with topical lidocaine spray (unless the patient is intubated). As a first step, the distance of gastroesophageal junction from the incisors is measured endoscopically. A stiff guidewire is then placed up to the gastric antrum. For Wallflex SEMS, the shaft of the delivery system is marked to match the distance from incisors to GE junction. Through the mouthpiece, the delivery system is advanced until the shaft marking reaches the mouthpiece. The endoscope is then advanced alongside the delivery system. The stent can be deployed under direct vision. If the stent is deployed across the GE junction, it typically requires proximal anchoring with a clip or endoscopic stitching. Alternatively, the stent can be deployed in its entirety in the esophagus to prevent the migration.

At this point, remove the blue lock adjacent to the sheath handle freeing the delivery system to be slid till the white lock (Figure 2b). This step unsheathes and releases the positioning balloon at the distal end of the insertion device. Then using the balloon port, inflate the balloon with 100-mL air. The 50-mL syringe provided in the procedure pack is typically used for insufflating the balloon. Then pull the delivery system outwards to fix the balloon in the gastric cardia. The fixation can be confirmed by feeling resistance as the balloon impacts the cardia on withdrawing the system. Due to the design of the delivery system, fixing the positioning balloon in the gastric cardia aligns the proximally placed stent in the lower esophagus. Holding the system in place, remove the white lock and slide the sheath handle outwards till the safety valve. As the stent is placed proximal to the

positioning balloon, doing so unsheathes the stent. Upon release, the stent decompresses and extends to its manufactured size. The last step is the removal of the delivery system. The balloon valve is unscrewed and the balloon port is removed. This deflates the balloon and the delivery system can now be safely withdrawn.

The standard procedure time is reported to be 10 minutes [21]. As the positioning balloon is only inflated during the positioning of the apparatus and is deflated during removal, there is no risk of accidental inflation of the balloon in the esophagus. The same balloon system allows the correct positioning of the system without the need for endoscopic or radiographic support. The removal of the balloon with the rest of the system bypasses the risk of balloon-related esophageal injury. For the conventional designs that require endoscopic and radiographic support, stent implantation is carried in an endoscopy suite. A guidewire is placed in the stomach under endoscopic visualization and the stent is then placed at the site of bleed. The distal esophagus is the optimal site for stent implantation. Depending on the severity of the varices, anchorage of the stent might pose a difficulty. The SX-ELLA Danis stent does not need securing. The stent can be easily repositioned using a polypectomy snare or a grabbing forceps. Balloon dilatation after stent placement is not recommended. After implantation, the stent position can be verified with chest X-ray. Endoscopic evaluation is possible through the lumen and helps assess the status of the bleed.

5. Technically successful deployment of the stent to control initial bleeding

The first step toward achieving satisfactory control of bleeding is technically correct placement of the stent at the desired location, that is, in the lower esophagus so that the stent can exert adequate tamponade on the bleeding varices and prevent them from bleeding

further. Among current literature [21–24], most studies report successful placement in over 90% cases. Considering the poor prognostic implications of uncontrolled variceal bleeding, the clinical outcome that is of perhaps the most imminent relevance is the ability of the stent to provide early and effective control of bleeding. Current literature suggests remarkable success in terms of initial hemostasis with SEMS with several small studies [7,25–27] reporting a 100% immediate bleeding control rate and many others reporting success rates higher than 80% [21–24,28–30]. Studies comparing SEMS with balloon tamponade for control of variceal bleeding suggest the much greater success of SEMS [31,32]. Comparisons [33] of SEMS with repeat endotherapy and vasoactive drugs also yield similar results affirming the greater success of SEMS in providing early control of bleeding. A recent meta-analysis [34] comparing SEMS with TIPS does suggest the greater success of TIPS in managing refractory bleeding; however, it is to be noted that TIPS is associated with a significant risk of hepatic encephalopathy and its benefits must be weighed against this risk.

6. Follow-up

Immediately after deployment, the stent position is confirmed by a chest X-ray. A subsequent fluoroscopic or endoscopic evaluation may be required to assess the status of the bleed and plan further management. Figure 3 shows endoscopic images taken at the time of follow-up showing resolved variceal bleeding. We typically hold oral intake for 24 hours. As with any standard stent procedure, a low-residue diet is advised to avoid stent obstruction. For the in situ duration of the stent, periodic checks for possible esophageal injury and stent migration must be done. A migrated stent can be repositioned or replaced.

7. Optimal stent duration and time for removal

A meta-analysis and systemic review of relevant studies reported variations in the timing of removal of the stent [23]. The stent can be

left in place for as long as 1–14 days [35,36]. Wright and Dechene et al reported 7–14 days and Fierz et al. reported placement duration of 12 hours to 5 days [7,24,28]. Overall, a stent can remain “in situ” for a few hours to 214 days [37]. A review by Changela et al. reports a successful extraction rate of 100% [38]. The removal of SX-ELLA Danis stent is advised under endoscopic guidance using the custom PEX-Ella extractor (Ella-CS) within a maximum of 7 days following implantation [39]. The ELLA extractor system has 2 components—the overtube (diameter 28F, length 100 cm) and the extractor (length 150 cm, outer diameter 2.6 mm). Endoscopic and fluoroscopic guidance is needed at the time of removal. The extractor is introduced through the working channel of the endoscope and is inserted until the stent is visualized. Then the capturing hook at the distal end of the stainless steel cable wire is advanced till the edge of the stent. As previously described, the SX-ELLA-Danis stent bears retrieval loops at both ends. Under direct endoscopic visualization, the retrieval loop at the stent edge is captured by the hook. Thereafter, the cable wire is retracted to lock the captured hook and the loop in place. This prevents the detachment of the captured hook and the loop. Keeping the extractor in place, the scope is withdrawn, and the overtube is now advanced over the extraction cable and is locked onto it. The overtube is now slid to completely encase and capture the stent in a sheath. After this step, the extractor system is withdrawn from the body. As the stent is encased by the overtube, the extraction is atraumatic as no shearing stress is exerted on the esophageal wall in the process of withdrawing the stent through the esophagus (Figure 4). This also allows for safe retrieval of a distally migrated stent from the stomach.

8. Short- and long-term outcomes of SEMS in variceal bleeding

In 2015, the Baveno VI consensus conference report issued an evidence-based recommendation for the utilization of self-expanding covered esophageal metal stents in the management of refractory esophageal variceal bleeding [10]. A meta-analysis of 12 eligible

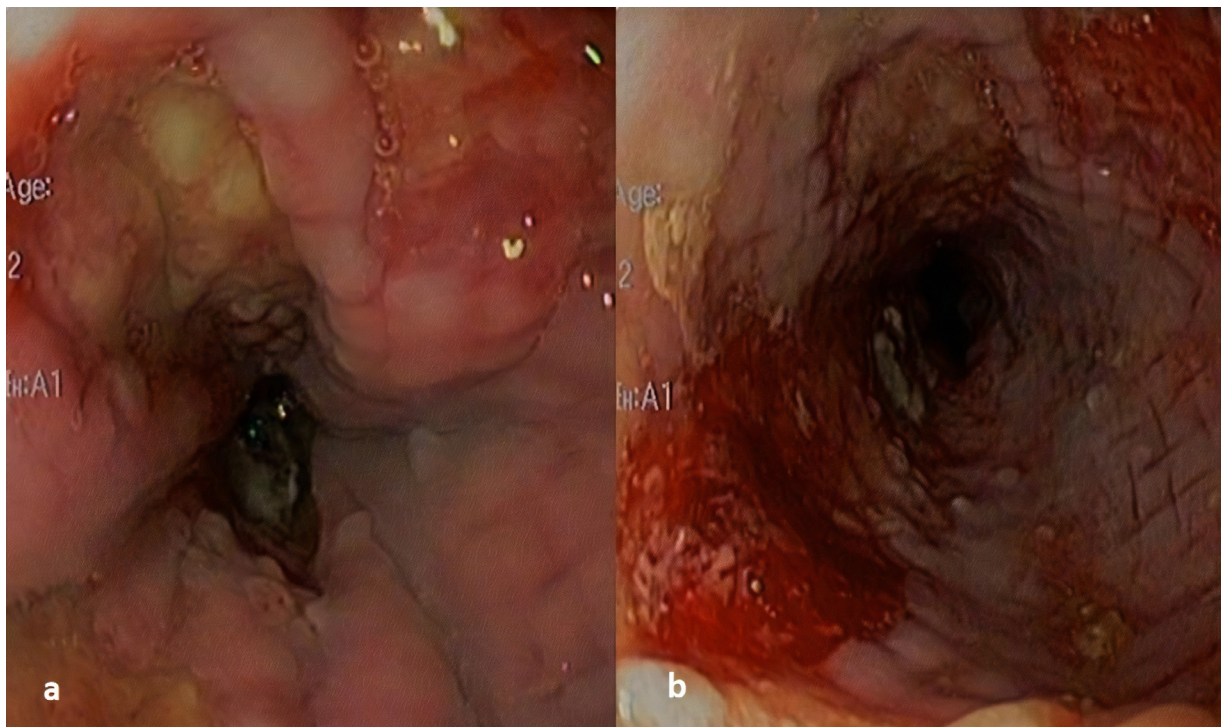


Fig. 3. Endoscopic view at the follow-up showing
 a. The distal esophagus with resolved variceal bleeding.
 b. Healed varices in the distal esophagus and the imprints of the removed stent.

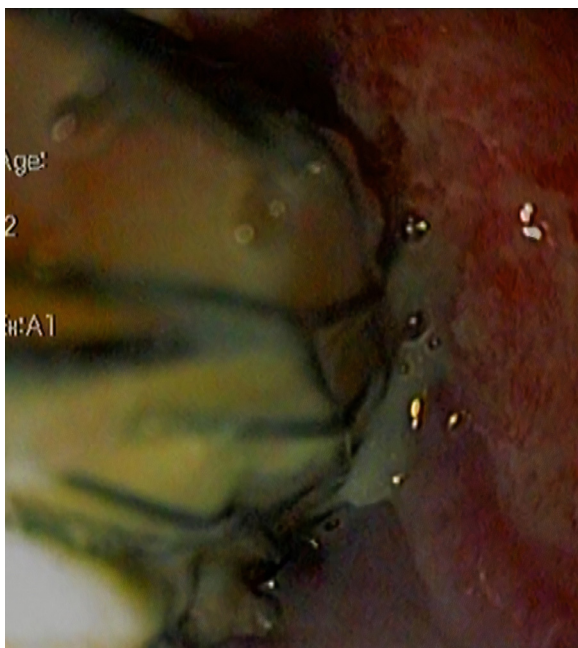


Fig. 4. Endoscopic image showing the stent retrieval by pulling the purse-string suture to constrain the proximal flare of the stent to prevent stent-related injury to the esophagus and varices.

studies evaluating SEMS placement for acute refractory esophageal variceal hemorrhage reported pooled clinical success (absence of bleeding within 24 hours of SEMS placement) rate of 96% (95% confidence interval, 0.90–1.00) and technical success (guidewire-assisted endoscopic SEMS deployment) rate of 97% (95% confidence interval, 0.91–1.00) [23]. These results strongly support SEMS placement as a technically and clinically successful management option. Functionally, SEMS exert a direct compressive force on the local varices, in effect, instantaneously constrict the venous blood flow and establish durable tamponade at the bleed site. This reflects in a prospective study by Zehetner et al., where immediate hemostasis was noted in all of the 34 patients that underwent stent placement [35].

The metal most widely used in the construction of SEMS is the highly conformable and elastic nickel-titanium alloy nitinol [40]. A mesh of weaved nitinol wires is shaped in a tubular form to yield high flexibility. Additionally, owing to the elasticity of nitinol, SEMS are capable of expanding to their manufactured size upon release from the delivery system [41]. The nitinol-SEMS are compressed to a size that can be accommodated in the delivery system and passed through the working channel of the endoscope. During implantation, the stent is positioned at the target site, the sheath is retracted, and the stent is released. At the body temperature, the stent expands upon release and conforms to the anatomical curves of the esophagus. The inward forces exerted by the resisting esophageal wall are balanced by the chronic outward forces exerted by the stent. The steady mechanical compression results in an immediate tamponade at the variceal bleed site. The alloy also confers MRI compatibility [42].

9. Adverse events

Adverse events associated with the placement of SEMS include stent migration (28%), rebleeding (16%), and ulcers; however, there was no significant difference in mortality compared to balloon tamponade. To combat some of these complications, endoscopists have developed novel techniques to minimize risk to the patient, such as anchoring the stent to the mucosal wall to prevent migration. Stent manufacturers have also developed atraumatic edges, to prevent ulcers, and radiological markers at both ends and at the midpoint to

easily assess its position by a plain chest X-ray. Retrieval loops with gold markers at both stent ends allow the endoscopic extraction of the stent without causing excessive trauma to the delicate mucosal wall. Some complications from SEMS placement may not be from the stent itself but from the procedure itself, such as aspiration from the placement at the gastroesophageal junction or compression of the left main bronchus due to the anatomical association of the esophagus and the bronchus.

9.1. Rebleeding, migration, and ulceration

While several studies do report a significant risk of rebleeding within the first 6 weeks of stent placement, it is to be noted that when SEMS are used as a bridge to more definitive therapy (like TIPS or orthotopic liver transplant) instead of being used as definitive therapy themselves, this risk is markedly reduced. The most commonly reported adverse event has consistently been stent migration. Most migrations, however, are managed with relative ease either by repositioning the existing stent or replacing it with a new one. Notable rates of ulceration upon stent removal have also been reported but this is easily managed with conservative measures, for example, proton pump inhibitors.

9.2. Mortality

Significantly high mortality rates are reported in patients who undergo esophageal stenting for refractory variceal bleeding but it is important to note that only a small fraction of this rate is due to failure to control the bleeding itself. The high mortality rate is more likely a function of the severe underlying liver disease than a direct effect of the variceal bleeding/rebleeding, stenting of the esophagus, or its associated complications.

10. Advantages, stent as definitive therapy and contraindications

Stent implantation provides immediate stabilization. It is tolerated well by the patient and oral intake can be resumed immediately after the procedure. The lumen permits the physiological drainage of the saliva and suction of gastric contents, therefore, minimizing aspiration-related events. Airway protection by endotracheal intubation is not required. External manipulation by an agitated patient cannot remove or dislocate the stent. Immediate and repeated endoscopic evaluation is possible which helps assess the status of the bleed. While esophageal stenting may be used as definitive therapy in itself, sustained high portal venous pressures and risk of rebleeding often necessitate additional management with TIPS. As a vast majority of these cases represent advanced hepatic disease, orthotopic liver transplant is also often required. Both of these factors make esophageal stents an effective bridge to more definitive therapy and help improve patient outcomes. Contraindication to stent placement is a malignancy in the esophagus, larynx, trachea, bronchi, and stomach. Stents must be avoided in cases of foreign body-related bleeding, esophagorespiratory fistula, and history of radiation therapy to the chest.

11. Current and future status

Despite the recommendation by the Baveno committee and multiple studies demonstrating the safety and efficacy of SEMS in the management of variceal bleeding, its utilization remains experimental and on a case-by-case basis. The SX-ELLA Danis stent investigated in the majority of the studies on SEMS placement is currently not FDA-approved for use in the United States. In such an instance, esophageal SEMS that are FDA-approved but not necessarily indicated for AVH can be used off-label after the patient's consent. SEMS

is preferable in agitated patients at risk of external manipulation and accidental removal of the tube.

Faster control of the bleeding is made possible through better delivery systems and improved deployment techniques. In acute scenarios, the reduced procedure time is life-saving. Chances of iatrogenic esophageal injury are minimal at the hands of an experienced endoscopist. Training and practice also improve the speed and safety of stent deployment and extraction. Optimizing the stent design and delivery reduces stent migration, therefore, making SEMS usage more attractive. The longer in-place duration of SEMS temporizes until more definitive treatment can be instituted. Liver functions improve and the condition of the patient stabilizes. This, in turn, makes it safer to proceed to more definitive treatment.

To substantiate the place of SEMS in the management of variceal bleeding, specific investigative studies are needed. Outcomes studies can uncover if the patients fare better when they undergo SEMS placement before TIPS as compared to BT. Escorsell et al. noted higher adverse events for BT as compared to SEMS [32]. This makes SEMS safer to use in refractory bleeding due to lesser complication rates. Further randomized controlled trials comparing SEMS with other endoscopic modalities are required. In most of the studies, SEMS placement is done when conventional endoscopic and medical treatments had failed. Its use as a first-line treatment is reported in very few studies. Therefore, large scale studies assessing its first-line usage in the earlier course of the bleeding are needed. In settings where TIPS or transplant surgery is not available or is otherwise contraindicated, SEMS can become a definitive measure. Ultimately, for accepted widespread use, SEMS must demonstrate cost-effectiveness on a large scale and comparative basis. Future studies can, therefore, support and popularize the use of SEMS in variceal bleeding. SEMS could then be preferred for stabilizing measures until rescue-TIPS or be used as the first-line therapy.

Author contributions

Study concept and design: NB; Review of literature: FC, ZHR, MO; Initial draft: FC, ZHR, MO; Critical revision of manuscript: NB. All authors approved the final draft submitted.

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