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Endoprosthetics for bleeding esophageal varices

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ABSTRACT

Refractory esophageal hemorrhage and early rebleeding following endoscopic therapy remain challenging conditions to treat and are associated with a high mortality. Techniques such as balloon tamponade (BT) and transjugular intrahepatic portosystemic shunt (TIPS) are highly effective at controlling refractory bleeding, but they can be associated with a high rate of complications and, in the case of TIPS, may not be immediately available outside specialist centers. Recently, removable self-expanding metal stents (SEMSs) have been introduced in clinical practice for the management of esophageal variceal bleeding. SEMSs control bleeding by tamponade of varices in the distal esophagus and can remain in situ for a number of days, thus preventing early rebleeding. The use of SEMSs does not require the transfer of the patient to a specialist center, and unlike TIPS, it is not associated with deterioration in liver function. The use of SEMSs has been described in small series of patients with refractory bleeding. These series report high rates of hemostasis with low complication rates, suggesting that SEMSs may have an important role in the management of refractory bleeding either as an alternative to BT or where TIPS is contraindicated. SEMSs may also have a role in treating complications of therapy for bleeding esophageal varices, such as postbanding ulceration and BT-induced esophageal tears. The aim of this review is to summarize the published data on the efficacy of SEMSs and suggest future studies that may clarify its role in the management of esophageal variceal hemorrhage.

1. Introduction

Variceal hemorrhage in patients with cirrhosis is a life-threatening condition with an expected mortality of approximately 20% at 6 weeks [1]. Mortality rates have decreased over recent years because of the widespread use of vasoactive drugs, prophylactic antibiotics, variceal banding, and tissue adhesives; however, the treatment of refractory bleeding and prevention of early rebleeding is a significant unmet clinical need [2-5].

Transjugular intrahepatic portosystemic shunts (TIPSs) and balloon tamponade (BT) are effective modalities for the control of refractory variceal bleeding but both are subject to important limitations. TIPSs are associated with a risk of hepatic encephalopathy of up to 48% when applied as salvage therapy and can cause deterioration in liver function, limiting its use in patients with advanced liver disease [6]. BT, usually with a Sengstaken-Blakemore tube, is highly effective when treatment fails (control of bleeding $>80\%$) but is not recommended for use for more than 24 hours and is associated with risks related to misplacement, mucosal ischemia, and aspiration pneumonia [7-9].

Even after control of the initial bleeding, there remains a significant risk of rebleeding, usually observed within the first 4 days and almost always before 11 days [10]. Risk factors for early rebleeding are active bleeding at endoscopy, severe liver disease (Childs-Pugh class C), and a wedged hepatic venous pressure gradient >20 mm Hg. Mortality in patients with early rebleeding is especially high, and treatment with early TIPS for patients with these risk factors has been proposed. Two small randomized controlled trials have now been performed, which demonstrated that early application of TIPS in patients with a high predicted risk of rebleeding reduces early rebleeding and mortality. However, the number of patients enrolled in these studies is small, and given the limited access to TIPS outside specialist centers, provision of this therapy to all high-risk patients would be logistically difficult [11,12]. Given the limitations of TIPS and BT, there appears to be an unmet need for a therapy in patients with refractory bleeding from esophageal varices which can be easily and effectively applied even outside specialist centers and which can prevent early rebleeding in high-risk patients regardless of underlying liver function. The use of self-expanding metal stents (SEMSs) represents a novel approach to this unmet need.

2. Rationale and application of SEMSs in esophageal variceal bleeding

The use of SEMSs is potentially attractive in the management of variceal bleeding for the following reasons. Firstly, they can

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provide rapid control of bleeding by tamponade of varices in the distal esophagus without risk of deterioration of liver function. Secondly, they can stay in place for a number of days, thus preventing early rebleeding and allowing the institution of effective secondary prophylaxis to avoid rebleeding on stent removal. Thirdly, they facilitate the early introduction of nutrition and medication via the oral or the nasogastric route as they do not obstruct the esophagus or interfere with swallowing. Finally, as SEMSs are used widely for other indications in gastroenterology (malignant obstruction and fistulae), their use in variceal bleeding is not restricted to specialist centers, and therefore the technique can be widely and easily applied.

The development of SEMSs for variceal bleeding was facilitated by the introduction of removable stents, and early experiences used a number of different stent designs. However, most experience has now been gained with the use of the SX-ELLA Danis stent (Ella CS, Hradec Kralove, Czech Republic).

The SX-ELLA Danis stent is a removable, covered self-expanding mesh-metal stent, designed specifically for the treatment of esophageal variceal bleeding. It is 135-mm long and has a diameter of 25 mm, allowing tamponade of bleeding vessels in the distal esophagus. It can be deployed without endoscopic or radiological fluoroscopic guidance, although most stents are placed over an endoscopically inserted guidewire. The stent has atraumatic edges and markers that are radiologically opaque, allowing its position to be easily confirmed. Flaring of the proximal and distal ends of the stent prevents migration. Insertion of the SX-ELLA Danis stent is not technically challenging. Following identification of the bleeding esophageal varices, a stiff guidewire is deployed into the stomach endoscopically and the endoscope is removed. The stent introducer system is then introduced into the stomach over the guidewire. Once the stent introduction system is fully inserted into the stomach, a balloon is deployed from the distal end and then inflated with 100 mL of air. The balloon at the distal end has a pressure safety valve designed to prevent inflation if it is malpositioned. Following inflation of the balloon, traction is applied to the stent introduction system, causing the balloon to impact at the gastroesophageal junction. The stent is then deployed by retraction of the outer sheath of the delivery system. The use of the balloon effectively anchors the delivery system in the correct position, allowing deployment of the stent with the distal end at the gastroesophageal junction without the use of fluoroscopy. Following deployment, the balloon is deflated and the delivery system is removed. The upper gastrointestinal tract is then examined endoscopically to confirm adequate position and control of bleeding (Figure 1).

The stent can remain in situ for 7-14 days and is easily removed endoscopically. To facilitate removal, there are retrieval loops with gold markers at both ends. Removal is via a specific extractor device (PEX-Ella extractor). During endoscopy, the proximal retrieval loop is snared with a hook connected to a guidewire supplied with the extraction device. Following removal of the endoscope, the extraction device is advanced over the guidewire. Traction is applied and the extraction device is advanced, facilitating collapse of the stent into the extraction device. Once the stent is fully constrained within the device, the PEX-Ella extractor is removed.

3. Preclinical and early experience with the use of SEMSs for variceal bleeding

Benkő et al [13] published the original animal data on the use of SEMSs in variceal bleeding. SEMSs were inserted into dogs with variceal bleeding, and esophageal histology, tissue oxygen saturation, and thermal denaturation requirements were analyzed following stent placement. Two different stent systems were used, the SX-ELLA Danis stent and the FerX-Ella-Boubella stent system. Using both stents, the authors demonstrated that stent insertion was safe, with no adverse effects noted on esophageal histology or microcirculation even after 2 weeks of deployment.

Following these initial encouraging animal data, a pilot study was performed in a cohort of 20 patients with massive bleeding from esophageal varices in whom endoscopic and medical treatment failed [14]. Of the 20 patients, 15 were treated with the specifically designed SX-ELLA-Danis stent, while the other 5 were treated with 1 of 2 standard esophageal SEMSs (Choo or Ella-Boubella-Danis stent). The SX-ELLA-Danis stents was placed with specific introducers, and placement was confirmed using chest X-ray images. In all patients except 1, the placement of the stent was satisfactory and bleeding was immediately controlled. On further endoscopic examination, the patient who continued to bleed was found to have bleeding from gastric varices. There was no rebleeding reported at follow-up after 30 days. All the stents were removed within 14 days (range: 2-14 days), with migration only documented in 2 patients. Following placement, 2 patients subsequently died of bleeding-related complications (multiorgan failure). It can be noted that, 1 patient who was treated with an SEMS had previously sustained an esophageal rupture as a complication from BT.

The original Hubmann study was subsequently extended to include 39 patients (20 of them had been included in the original report) [15]. As previously demonstrated, insertion of SEMSs in these patients was uncomplicated, and bleeding was controlled in

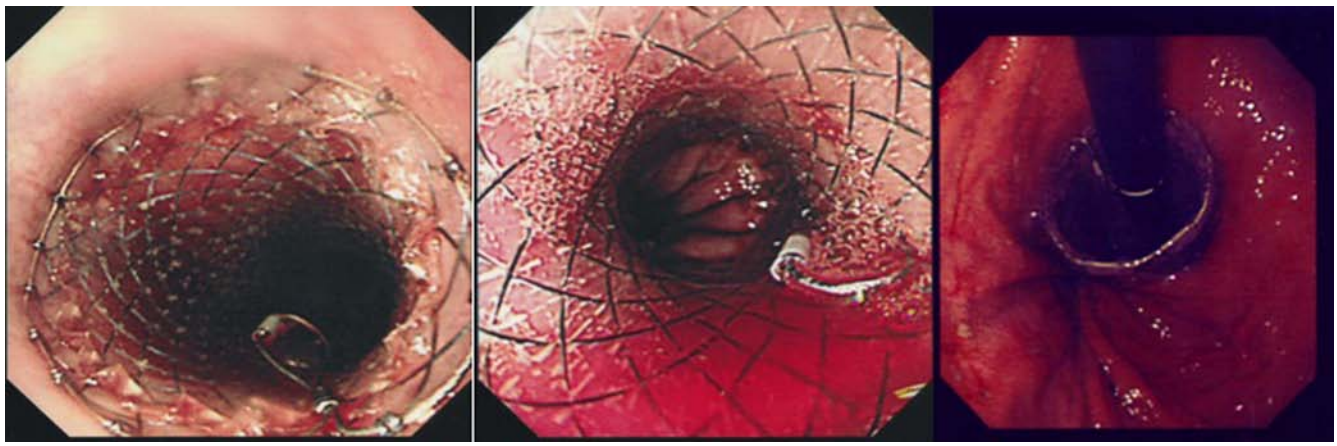

Fig. 1. Endoscopic appearances of the SX-ELLA Danis stent following deployment. The retroflexed endoscopic view demonstrates satisfactory position covering the gastroesophageal junction. The loops at either end of the stent facilitate removal or repositioning once in situ.