

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of stent insertion for bleeding oesophageal varices

Stopping enlarged veins in the oesophagus from bleeding by inserting an expandable mesh tube

People who drink heavily or who have hepatitis C may develop liver cirrhosis (scarring). This may cause bleeding arising from swollen veins in the gullet (oesophagus), which is potentially life threatening. This procedure involves temporary insertion of a flexible, coated wire mesh tube called a stent into the oesophagus. The stent is expanded to the width of the gullet so that it presses against the veins with the aim of stopping the bleeding. The stent is removed within 2 weeks.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2010.

Procedure name

- Stent insertion for bleeding oesophageal varices

Specialty societies

- British Society of Gastroenterology
- British Association for the Study of the Liver
- Association of Upper Gastrointestinal Surgeons.

Description

Indications and current treatment

Oesophageal varices are enlarged veins within the lower oesophageal wall and the oesophagogastric junction. They develop in patients with portal hypertension, often as a result of liver cirrhosis. Oesophageal varices tend to lead to episodes of variceal bleeding and each episode typically constitutes a life-threatening medical emergency, carrying a substantial risk of mortality. Patients with previous oesophageal bleeding episodes are at risk of subsequent bleeding episodes.

The management of bleeding oesophageal varices is complex and constitutes a medical emergency. Blood transfusion is usually required. Vasoactive medications, such as glypressin, may be given to reduce the portal venous pressure and help reduce bleeding. Balloon tamponade is usually attempted using a Blakemore-Sengstaken tube. Endoscopic variceal band ligation or sclerotherapy may be used. In patients with refractory bleeding, further treatment options may include radiologically-placed transjugular intrahepatic portosystemic shunts (TIPSS) and shunt or devascularisation surgery.

The aim of using a stent is to apply standardised pressure to the bleeding oesophageal varices to induce haemostasis.

What the procedure involves

A coated metal stent is used (different from the stents commonly used in the treatment of malignant oesophageal strictures). Usually after a diagnostic endoscopy, the stent-delivery system is inserted. A stent is inserted and a gastric balloon is inflated to ensure correct positioning. The position of the stent may be confirmed endoscopically, fluoroscopically, or by chest X-ray.

After stabilisation the patient's upper body is placed in a slightly upright position (approximately 30°) to reduce the risk of reflux and aspiration.

The stent is left in position for up to 2 weeks, and then removed with a second endoscopic procedure and a foreign body extractor which grasps the proximal loop of the stent. This triggers a mechanism of automatic elongation (and narrowing) of the stent, which allows its extraction. The stent lumen allows physiological drainage of saliva, and oral ingestion of fluids/food is possible.

Further procedures, such as TIPSS or surgery may be done to reduce the risk of further bleeds

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to stent insertion for bleeding oesophageal varices. Searches were conducted of the following databases, covering the period from their commencement to 5 January 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with variceal bleeding in the oesophagus.
Intervention/test	Endoscopic insertion of stents.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 67 patients from 3 case series^{1,2,3} and 3 case reports^{4,5,6}. There is some overlap in the patients included in the first two case series of 34 and 20 patients.

Table 2 Summary of key efficacy and safety findings on stent insertion for bleeding oesophageal varices

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Zehetner J (2008)¹ Case series Austria Recruitment period: Jan 2003 to Aug 2006 (reported as Aug 2007 in abstract) Study population: patients with bleeding oesophageal varices n = 34 Age: 56 years (mean) (39 patients) Sex: 84.6% (33/39) male Patient selection criteria: patients where bleeding could not be managed using standard therapy. Technique: implantation of self-expanding metal stent (using SX-ELLA Stent Danis) for mean duration of 5 days (range: 1 to 14 days). Follow-up: 60 days Conflict of interest/source of funding: not reported	Number of patients analysed: 34 <u>Success of implant:</u> Implantation stopped bleeding in all patients. <u>Further management of patients after stent removal:</u> Endoscopic band ligation: 32.4% (11/34) Radiologic TIPSS insertion: 23.5% (8/34) Laparoscopic azygoportal disconnection: 14.7% (5/34) <u>Recurrence:</u> No re-bleeding occurred. <u>30 days mortality rate:</u> 26.5% (9/34) patients. <u>60 days mortality rate:</u> 29.4% (10/34) patients. Overall, 2 patients died of hepatic failure within 24 hours of implantation and 7 patients died of hepatic and multi-organ failure after stent removal.	Migration of stent to the stomach: 20.6% (7/34). All stents repositioned successfully 24–48 hours later in all cases. Slight ulceration at the distal end of the stent location in the oesophagus: 1patient All stents removed without complication.	Follow-up issues: • A further 5 patients underwent stent implantation but the paper only reports results for 34 patients where the SX-ELLA stent was used. • Completeness of follow-up is unclear. Study design issues: • Single centre study. • Bleeding conformed endoscopically before intervention. • Position of the stent confirmed by immediate X-ray and daily follow-up X-rays. • Liquid food and water allowed 2 hours after stent implantation. • Unclear if outcomes were independently assessed. Study population issues: • Cause of bleeding: liver cirrhosis due to alcoholism: 76.5% (26/34), immunological or cryptogenic cirrhosis: 11.8% (4/34) and virus-induced liver cirrhosis: 11.8% (4/34). • Child-Pugh grade of liver cirrhosis (based on blood markers and the appearance of the liver – graded A to C, C is the most severe): grade B: 38.2% (13/34) and grade C: 61.8%(21/34) • Patients with at least 1 prior bleeding episode: 70.6% (24/34).

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Hubmann R (2006)² Case series Austria Recruitment period: Nov 2002 to May 2005 Study population: patients with acute variceal haemorrhage. n = 20 Age: 52 years (mean) Sex: 90% (18/20) male Patient selection criteria: patients not successfully managed by prior pharmacological or endoscopic therapy. Technique: implantation of self-expanding metal stent for a duration of 2 to 14 days. Sedation used where necessary; 3 patients had stents inserted under intubation. Stents inserted with a guidewire and radiographic assistance in the first 5 cases, and in the remaining patients without guidewire (Ella-Danis stent) but with endoscopic visualisation. Follow-up: 60 days Disclosure of interest: none	Number of patients analysed: 20 <u>Success of implant:</u> Stent placement was successful and uncomplicated in all patients. Haemorrhage stopped immediately after implantation of the stent. In the 19 patients with oesophageal bleeding only (no gastric bleeding) circulation stabilised within 2 hours of implantation. <u>Recurrence:</u> No recurrence of bleeding from the oesophagus while the stent was in place or during the 30-day follow-up after stent extraction. <u>Further management of patients after stent removal:</u> TIPSS: 25% (5/20) Laparoscopic azygoportal disconnection: 25% (5/20) Endoscopic or interventional procedures: 20% (4/20) Embolotherapy with sclerosing agents in combination with coils: 20% (4/20) Radiographic interventional procedure: 5% (1/20) <u>60 days mortality rate:</u> 10% (2/20) of patients due to hepatic and multi-organ failure at day 3 and day 5.	Stent migration into the stomach: 25% (5/20) of patients. 3 of these 5 stents were those used in the first 5 patients. This did not result in recurrent bleeding and repositioning was carried out with repeat endoscopy. Small oesophageal ulceration at 6 days: 1 patient. Stent removal was performed easily without any complications.	Reported in table 2 in the original overview Overlap: patients recruited after Jan 2003 are likely to also be reported in Zehetner 2008. Follow-up issues: - Completeness of follow-up is unclear. Study design issues: - The stent design was changed after the first 5 patients were treated. - Unclear if outcomes were independently assessed. - All the stents were extracted using standard endoscopy and a foreign body extractor. - Liquid food and water allowed 2 hours after stent implantation. Study population issues: - In 17 patients the stent was implanted within 3 hours of the onset of bleeding where patients were rapidly transferred to the endoscopic unit. - All patients had concomitant use of vasoactive drugs. - Cause of bleeding: liver cirrhosis due to alcoholism: 55% (11/20), immunological or cryptogenic cirrhosis 15% (3/20) and gastric ulcer combined with oesophageal varices: 5% (1/20). - Mean number of previous bleeding episodes despite endoscopic interventions: 2.4. - Previous treatment: band ligation: 90% (18/20), sclerotherapy 25% (5/20) and balloon tamponade: 30% (6/20). - Child-Pugh grade: Grade B: 40% (8/20) and Grade C: 60% (12/20).

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Wright G (2010)³ Case series UK Recruitment period: Mar 2007 to Jul 2008 Study population: patients with refractory variceal bleeding n = 10 Age: 49.4 years (mean) (calculated by IP analyst) Sex: 90% (9/10) male Patient selection criteria: patients with cirrhosis with contraindications for TIPSS insertion or balloon tamponade. Technique: implantation of self-expanding metal stent (using SX-ELLA Stent Danis) for a median duration of 9 days (6 patients). Follow-up: 42 days Disclosure of interest: none	Number of patients analysed: 10 <u>Success of implant:</u> Stent placement was successful in 90% (9/10). Placement failed in the first patient in the series due to failure of the gastric balloon to inflate. In another patient a second attempt was necessary following gastric balloon rupture. Immediate control of bleeding: 77.8% (7/9) <u>Survival at 42 days:</u> 50% (5/10) 2 patients died of exsanguination, 1 patient died of multi-organ failure 2 days after stent insertion which failed to control bleeding, and 2 patients died of progressive multi-organ failure (bleeding controlled) at day 17 and day 11. <u>Recurrence:</u> Early re-bleeding: 1 patient (due to resumption of alcohol use after discharge and successfully treated with insertion of TIPSS)	Minor ulceration of the oesophagus caused by stent insertion: 1 patient. Stent removal was performed easily without major complications in 6 patients. One removal was performed under fluoroscopic control.	Follow-up issues: - Completeness of follow-up is unclear. Study design issues: - Single centre study - Cirrhosis conformed by biopsy or combination of typical biochemical and radiographic abnormalities. - All patients underwent daily chest X-ray to check for stent migration. - Unclear if outcomes were independently assessed. Study population issues: - Cause of cirrhosis: alcohol: 60% (6/10), alcohol + hepatitis C: 20% (2/10) and cryptogenic and primary biliary cirrhosis: 10% (1/10). 2 patients also had hepatocellular carcinoma. - Mean number of previous endoscopies before stenting: 1.3 (range 0 to 3).

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Dechene A (2009)⁴ Case report Germany Recruitment period: not reported Study population: patient with hilar cholangio-carcinoma and subsequent thrombosis of the intrahepatic portal vein who presented with acute upper gastrointestinal haemorrhage from distal oesophageal grade III varices. n = 1 Age: 59 years Sex: male Patient selection criteria: see above Technique: implantation of self-expanding metal stent (using SX-ELLA Stent Danis) for 6 days Follow-up: 13 days Disclosure of interest: Not reported	Number of patients analysed: 1 Implantation of the stent immediately stopped the bleeding (confirmed endoscopically 1 day later).	Acute bronchial obstruction reported on day 6 caused by stent related compression of the left main bronchial wall (confirmed by CT scan). Successfully treated by removing the stent. The patient died due to liver failure on day 13.	Patient had previous unsuccessful variceal band ligation and required intubation and artificial ventilation due to respiratory failure following aspiration of regurgitated blood. Artificial ventilation was maintained after stent insertion because of aspiration pneumonia.

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Matull W-R (2008)⁵ Case report UK Recruitment period: not reported Study population: patient with known alcoholic cirrhosis who presented with oesophageal tear and variceal haemorrhage (confirmed by endoscopy) following insertion of a Sengstaken-Blakemore tube. n = 1 Age: 44 years Sex: male Patient selection criteria: see above Technique: implantation of self-expanding metal stent (using SX-ELLA Stent Danis) for 7 days Follow-up: 20 days Disclosure of interest: none	Number of patients analysed: 1 Implantation of the stent in the intensive care unit (paper does not indicate if bleeding stopped immediately). A transjugular intrahepatic portosystemic shunt was successfully performed 36 hours later and the patient was extubated the following day. The stent was removed at day 7 under fluoroscopy, and a nasogastric tube for parenteral nutrition was inserted. Oral intake reintroduced 11 days after stent removal and the patient was discharged 2 days later.	Not reported.	Patient had previous unsuccessful endoscopic therapy for variceal haemorrhage.

Abbreviations used: CT, computed tomography; TIPSS, transjugular intrahepatic portosystemic shunt			
Study details	Key efficacy findings	Key safety findings	Comments
Mishin I (2010)⁶ Case report Moldova Recruitment period: not reported Study population: patient with a diagnosis of postviral liver cirrhosis (Child Pugh – grade C) and portal hypertension for 3 years. Patient had a 1 hour history of haematemesis and melena on admission n = 1 Age: 49 years Sex: male Patient selection criteria: see above Technique: implantation of self-expanding metal stent (using SX-ELLA Stent Danis) for 8 days Follow-up: discharge (10 days) Disclosure of interest: not reported	Number of patients analysed: 1 8 days after latest endoscopic band ligation treatment the patient was admitted with massive rebleeding. Emergency endoscopy indicated post endoscopic band ligation ulcer in the middle third of the oesophagus. The stent was implanted immediately and haemostasis was obtained. Endoscopic and radiological examination confirmed the correct position of the stent. The patient was resuscitated with 2 units of red blood cells and 3 units of plasma. The endoscopic examination was repeated at 8 hours to confirm hemostasis and stent placement. Oral intake was started 24hours after stent placement. The stent was removed with no complications or rebleeding after 8 days and the patient was discharged at 10 days.	Not reported.	The patient had previously had 2 episodes of oesophageal bleeding and 3 sessions of endoscopic band ligation treatment.

Efficacy

Success of the stent

Case series of 34 and 20 patients reported that the stent stopped the bleeding in all patients in both studies^{1,2}. It is worth noting that there may be overlap between these 2 studies.

A case series of 10 patients reported successful implantation of the stent in 90% (9/10) of patients and immediate control of bleeding in 78% (7/9) of patients who had successful implantation³.

Recurrence of bleeding

Case series of 34 and 20 patients reported that no re-bleeding occurred in any patients in both studies^{1,2}.

The case series of 10 patients reported early re-bleeding in 1 patient who resumed alcohol use after discharge. The re-bleeding was successfully treated with TIPSS insertion³.

Mortality

The case series of 34 patients reported a mortality rate of 29% (10/34) at 60 days. Two patients died of hepatic failure within 24 hours of implantation and 7 patients died of hepatic and multi-organ failure after the stent was removed¹.

The case series of 20 patients reported a mortality rate of 10% (2/20) at 60 days. Both patients died due to hepatic and multi-organ failure; 1 patient died on day 3 and the other died on day 5².

The case series of 10 patients reported a mortality rate of 50% (5/10) at 42 days. Two patients died of exsanguination, 1 patient died of multi-organ failure 2 days after stent insertion which failed to control bleeding, and 2 patients died of progressive multi-organ failure (bleeding controlled) at day 17 and day 11³.

Further procedures required after stent removal

The case series of 34 patients reported that 32% (11/34) of patients required endoscopic band ligation, 24% (8/34) required radiologic TIPSS insertion and 15% (5/34) required laparoscopic azygoportal disconnection after the stent was removed¹.

A case series of 20 patients reported 25% (5/20) patients required TIPSS insertion, 25% (5/20) required laparoscopic azygoportal disconnection, 20% (4/20) required endoscopic or interventional procedures, 20% (4/20) required embolotherapy with sclerosing agents in combination with coils, and 5% (1/20) required a radiographic interventional procedure after the stent was removed².

Safety

Acute bronchial obstruction

A case report of 1 patient reported acute bronchial obstruction at day 6 caused by stent-related compression of the left main bronchial wall (confirmed by computed tomography scan). This was successfully treated by removing the stent. The patient died due to liver failure on day 13⁴.

Migration of stent to stomach

The case series of 34 patients reported migration of the stent into the stomach in 21% (7/34) of patients within 60-day follow-up. All stents were successfully repositioned within 24 to 48 hours¹.

The case series of 20 patients reported migration of the stent into the stomach in 25% (5/20) of patients. Three of the 5 migrations were in the first 5 patients in the series and repositioning was performed under repeat endoscopy².

Ulceration

The case series of 34 patients reported slight ulceration at the distal end of the stent location in the oesophagus in 1 patient within 60-day follow-up¹.

The case series of 20 patients reported a small oesophageal ulceration in 1 patient at day 6².

The case series of 10 patients reported minor ulceration of the oesophagus caused by stent insertion in 1 patient within 42-day follow-up³.

Validity and generalisability of the studies

- Only small case series and individual case reports available. Very little new evidence has been published since the current guidance was published in 2008.
- Only short-term follow-up (up to 60 days) available.

Existing assessments of this procedure

A 2010 position paper was published by the Baveno V consensus workshop on the methods used to diagnose and treat portal hypertension. The following statement was made regarding the use of self-expandable metal stents:

“Uncontrolled data suggest that self-expanding covered esophageal metal stents may be an option in refractory esophageal variceal bleeding, although further evaluation is needed” (Level 4C evidence according to the Oxford system)⁷

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Dr Stephen Pereira, Dr Steven Ryder, Dr Adrian Stanley and Dr Catharine Anne McCune (British Association for the Study of the Liver), Professor Andrew Burroughs and Mr Sean Preston (British Society of Gastroenterology)

- Three of the six Specialist Advisers have performed the procedure at least once and the other three Specialist Advisers have never performed this procedure (one has taken part in patient selection or referred a patient for the procedure at least once).
- Two Specialist Advisers consider this to be the first in a new class of procedure, one considers it to be a minor variation on an existing procedure and the other three Specialist Advisers consider this to be a novel procedure of uncertain safety and efficacy.
- Comparator: oesophageal variceal band ligation and balloon tamponade using Sengstaken–Blakemore tube insertion.
- Adverse events reported in the literature or from their own experience include stent migration, mucosal trauma on withdrawal, perforation of oesophagus, oesophageal pressure ulceration, fistula formation, failure to control bleeding, worsening of bleeding, failure of removal of device and aspiration pneumonia.
- Theoretical adverse events include uncontrolled bleeding, oesophageal ulceration, oesophageal perforation, malpositioning, dysphagia and aspiration.
- Efficacy outcomes include cessation of bleeding, survival, prevention of aspiration pneumonia, and avoidance of using blood products and re-bleeding.
- Five of the Specialist Advisers reported uncertainty regarding the efficacy and safety of the procedures due to limited quantity of published evidence. One Adviser stated that randomised trials are needed.

- One Specialist Adviser reported efficacy concerns in terms of the frequency of poor deployment of the stent for technical or operator reasons.
- Training and facilities: requires standard endoscopy facilities. Staff should be competent in therapeutic endoscopy and stent placement. One Adviser reported that many clinicians would be able to train to do this procedure with ease. One Specialist Adviser states that unlike transjugular intrahepatic portosystemic shunt, this procedure could theoretically be available in every centre that performs upper GI endoscopy.
- One Specialist Adviser reported that the stent can be deployed with or without endoscopy and that if placed correctly allows the patient to eat and drink. He also stated that a Sengstaken tube can be very uncomfortable for patients.
- One Specialist Adviser reported that efficacy is high in carefully selected patients e.g. patients who are unsuitable for TIPSS or patients who have a complication as a result of balloon tamponade. It remains unclear if stenting can replace balloon tamponade.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure. .

References

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3. Wright G, Lewis H, Hogan B et al. (2010) A self-expanding metal stent for complicated variceal hemorrhage: experience at a single center. *Gastrointestinal Endoscopy* 71:71-78.
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5. Matull W-R, Cross TJS, Yu D et al. (2008) A removable covered self-expanding metal stent for the management of Sengstaken-Blakemore tube--induced esophageal tear and variceal hemorrhage... including commentary by Brandt LJ. *Gastrointestinal Endoscopy* 68:767-769.
6. Mishin I, Ghidirim G, Dolghii A et al. (2010) Implantation of self-expanding metal stent in the treatment of severe bleeding from esophageal ulcer after endoscopic band ligation. *Dis Esophagus* 2010:E35-E38.
7. de Franchis R. (2010) Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 2010:762-768.

Appendix A: Additional papers on stent insertion for bleeding oesophageal varices

There were no additional papers identified.

Appendix B: Related NICE guidance for stent insertion for bleeding oesophageal varices

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for stent insertion for bleeding oesophageal varices

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	5/01/2010	January 2011
Database of Abstracts of Reviews of Effects – DARE (CRD website)	5/01/2010	N/A
HTA database (CRD website)	5/01/2010	N/A
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	5/01/2010	January 2011
MEDLINE (Ovid)	5/01/2010	1950 to December Week 3 2010
MEDLINE In-Process (Ovid)	5/01/2010	January 03, 2011
EMBASE (Ovid)	5/01/2010	1980 to 2010 Week 52
CINAHL (NLH Search 2.0)	5/01/2010	N/A
BLIC (Dialog DataStar)	02/07/2010	-
Zetoc	5/01/2010	N/A

Trial sources searched on 02/07/2010:

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 25/06/2010 to 02/07/2010:

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) – MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Esophagus/
2	(oesophag* or esophag*).tw.
3	or/1-2
4	Varicose Veins/
5	vari*.tw.
6	or/4-5
7	Hemorrhage/
8	Gastrointestinal Hemorrhage/
9	Blood/
10	(bleed* or blood* or haemorr* or hemorr*).tw.
11	or/7-10
12	3 and 6 and 11
13	"Esophageal and Gastric Varices"/
14	((oesophag* or esophag*) adj3 tamponad*).tw.
15	or/12-14
16	Stents/
17	stent*.tw.
18	danis.tw.
19	(SX adj3 ELLA).tw.
20	or/16-19
21	15 and 20
22	Animals/ not Humans/
23	21 not 22