

Acute Gastrointestinal Bleeding: Part II.

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ABSTRACT

Objective: To review the management of acute gastrointestinal bleeding in the critically ill patient in a two part presentation.

Data sources: Articles and a review of studies reported from 1991 to 2001 and identified through a MEDLINE search of the English language literature on acute gastrointestinal bleeding.

Summary of review: Oesophageal varices are a common source of upper gastrointestinal bleeding in patients who have portal hypertension. Management requires resuscitation and treatment of associated coagulation disturbances along with intravenous octreotide (50 µg followed by 50 µg/hr for 48 hr) before endoscopy is performed. Octreotide is more effective than vasopressin in controlling acute variceal haemorrhage and has fewer side effects compared with glypressin.

To provide haemostasis, endoscopic variceal sclerosis has largely been replaced by variceal ligation using an overtube and small elastic 'o' rings to band the bleeding variceal channels. If bleeding continues then balloon tamponade and intravenous fibrinolytic inhibitors (e.g. tranexamic acid 3 - 6 g i.v. daily) are used for 24 hr before endoscopy (with variceal ligation) is repeated. If the variceal bleeding is resistant to repeated banding, portal decompression using transjugular intrahepatic portosystemic shunt or surgical shunt should be considered. While beta adrenergic blockers (e.g. propranolol) are indicated to reduce the incidence of rebleeding, they are contraindicated in a patient with actively bleeding oesophageal varices.

Conclusions: Acute oesophageal variceal bleeding can often be managed successfully using octreotide and variceal ligation. If bleeding continues then transjugular intrahepatic portosystemic shunt or surgical shunt should be considered. (**Critical Care and Resuscitation 2001; 3: 117-124**)

Key Words: Acute gastrointestinal bleeding, oesophageal and gastric varices, somatostatin analogs and derivatives, transjugular intrahepatic portosystemic shunt, liver cirrhosis

BLEEDING OESOPHAGEAL VARICES

The anastomosis between splanchnic and systemic venous systems occur at the gastroesophageal junction (via thin-walled submucosal oesophageal veins channeling blood to the azygous and hemiazygous veins), in the retroperitoneal space between the kidneys and spleen, between the mesenteric and gonadal veins, and around the umbilicus, diaphragm and rectum (Figure 1). Portal venous pressures normally range from 5 to 10 mmHg and portal hypertension is present if the direct portal vein pressure is greater than 12 mmHg.¹ In patients who have bleeding oesophageal varices, the portal venous pressures range from 12 to 40 mmHg,² with the risk of oesophageal variceal bleeding low when the differences

in portal vein and inferior vena cava pressures are less than 12 mmHg.³ In one study, the risk of bleeding from varices was essentially zero if the hepatic venous pressure gradient was reduced to below 12 mmHg.⁴

Portal hypertension is often classified according to the site of obstruction to portal blood flow. For example, presinusoidal (which may be prehepatic, e.g. portal and splenic vein thrombosis,⁵ or intrahepatic, e.g. schistosomiasis, myelofibrosis, leukaemic infiltration, sarcoid), sinusoidal (e.g. cirrhosis), and postsinusoidal (e.g. Budd-Chiari syndrome). Sixty percent of patients with cirrhosis develop oesophageal varices, and 66% of these bleed (i.e. 40% of confirmed cirrhotic patients develop variceal haemorrhage⁶), usually from vessels in

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the lower 5 cm of the oesophagus.⁷ Portal hypertension may also cause gastric bleeding from portal hypertensive gastropathy (a condition which can cause diffuse gastric mucosal bleeding and may follow sclerotherapy⁸) or gastric varices.

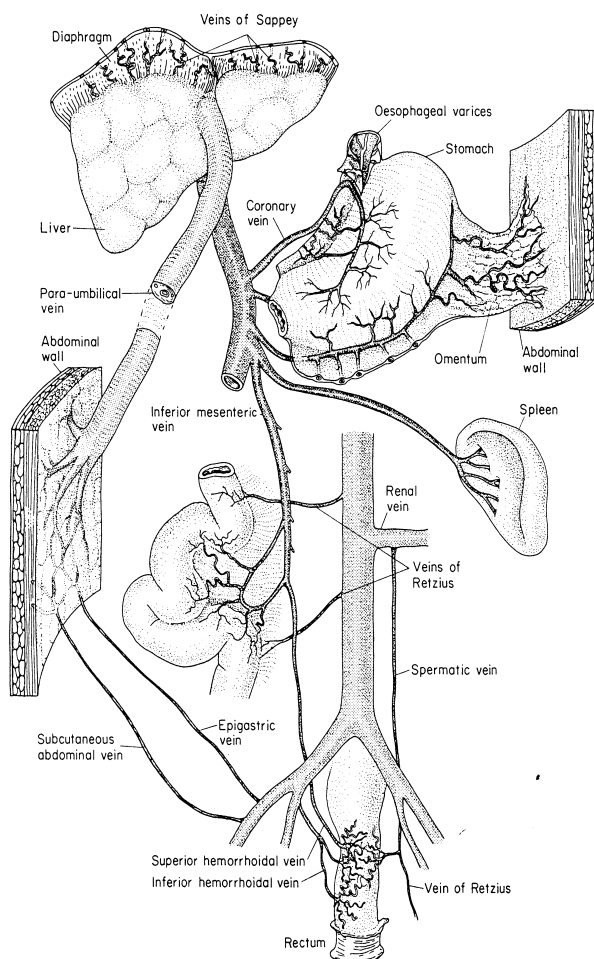


Figure 1. Sites of portosystemic circulation in cirrhosis of the liver

Treatment

While asymptomatic oesophageal varices do not require treatment,^{7,9} variceal bleeding requires therapy to control the acute bleeding episode as well as to reduce the incidence of rebleeding, as rebleeding occurs in 70% or more of cirrhotics who have survived their first variceal haemorrhage.¹⁰ Endoscopy should be performed in all patients who have upper gastrointestinal bleeding and oesophageal varices, as a non-variceal source of bleeding (e.g. gastric erosions, or chronic ulceration) may be found in up to 50% of patients.¹¹ The percentage of patients in whom bleeding is controlled, and the mortality associated with the various treatments for acute variceal haemorrhage are listed in Table 1.^{7,10,12-17}

Resuscitation

This involves blood transfusion, correction of coagulation abnormalities (e.g. fresh frozen plasma, platelets) and correction of vitamin deficiencies that may cause coagulation abnormalities (e.g. Vitamin K, folic acid). As variceal haemorrhage is associated with a high incidence of severe bacterial infections (e.g. Gram-negative septicæmia), all patients should have blood cultures taken and given i.v. ciprofloxacin 200 mg 12-hourly (or oral norfloxacin 400 mg 12-hourly) for 7 days.¹⁸

Endoscopic variceal sclerosis (sclerotherapy)

Sclerotherapy has often been used for both acute oesophageal variceal haemorrhage (once resuscitation is complete and temporary haemostasis has been achieved, which may require intravenous octreotide, vapreotide, vasopressin, or balloon tamponade¹⁹) and rebleeding prevention.^{20,21} It has a greater success rate than balloon tamponade in controlling acute oesophageal variceal haemorrhage (e.g. 90% for sclerotherapy, compared with 40 - 80% for balloon tamponade) and the 6-month survival rate is better (e.g. 84% for sclerotherapy compared with 45% for balloon tamponade).⁶ It also has a lower incidence of portal-systemic encephalopathy when compared with transjugular intrahepatic portosystemic shunts.²² The combination of sclerotherapy and octreotide (25 µg/hr for 5 days) is more effective than sclerotherapy alone in controlling acute variceal bleeding.²³

Sclerotherapy is performed during endoscopy, using a sclerosant (e.g. alcohol, ethanolamine) injected into the varix (if the varix is actively bleeding), or adjacent submucosa (if the varix is not actively bleeding). This may be repeated at weekly intervals, causing intraluminal thrombosis, fibrous organisation and progressive variceal obliteration.²⁴

While gastric varices decrease in the majority of patients after eradication of oesophageal varices,²⁰ sclerosis is ineffective in controlling acute bleeding from gastric varices or from portal hypertensive gastropathy.²⁵

Prophylactic sclerotherapy in patients who have oesophageal varices which have not bled is of no benefit,^{9,20,21,26} and in one report was associated with an increase in mortality.²⁷ While another study reported prophylactic endoscopic ligation of oesophageal varices that had never bled was more effective than propranolol in the prevention of variceal bleeding,²⁸ propranolol is still preferred for primary prevention of non-bleeding oesophageal varices.²⁹

Complications of sclerotherapy include dysphagia, retrosternal pain, fever, rebleeding, bacteraemia, mediastinitis, pleural effusions, empyema, paraoesophageal

Table 1. Treatment of acute variceal bleeding in alcoholic cirrhosis

Treatment	% control of acute haemorrhage	% rebleed	Hospital mortality (%)	
			Child's A	C
No therapy	40	70	10	80
Sclerotherapy	95	30	3	50
Somatostatin 250 µg/h	60	40	5	60
Vasopressin 0.4 u/min	50	50	7	60
Balloon tamponade	40-80	40-60	15	80
Percutaneous portacaval shunt	95	10	3	50
Emergency portacaval shunt	90	10	15	95

abscess, aspiration, pneumonia, ARDS, portal vein thrombosis, spinal cord paralysis, oesophageal ulceration, oesophageal perforation, and oesophageal strictures.^{20,30}

Endoscopic variceal ligation

Endoscopic variceal ligation, by the application of small elastic 'o' rings over variceal channels, is a technique which has recently been introduced to manage oesophageal variceal bleeding. The method appears to have results that are at least equal to sclerotherapy, with lower rates of rebleeding, lower mortality and fewer serious complications.³¹⁻³³ However, the major disadvantage of variceal ligation is the need to withdraw the endoscope and load bands individually. This requires the passage of an over-tube which is uncomfortable and may traumatise the oesophagus,³⁴ although newer devices have been developed which allow up to six-band ligations without the need for reloading or an overtube.³⁵

A recent meta-analysis of studies comparing endoscopic ligation with sclerotherapy for treatment of oesophageal variceal bleeding concluded that ligation should be considered the endoscopic treatment of choice for patients with oesophageal variceal bleeding.³⁶ Also the combination of endoscopic ligation and octreotide (50 µg bolus followed by 50 µg/hr for 5 days) is more effective than endoscopic ligation alone in controlling acute variceal bleeding.³⁷

Vasopressin

Intravenous vasopressin at 20 units (U) in 200 mL of 5% dextrose in 20 min followed by 0.2 - 0.8 U/min for 24 hr, will often reduce portal pressure and allow temporary control of variceal haemorrhage in 50% of patients.⁶ However, rebleeding is frequent. As intra-arterial vasopressin at 0.05-0.4 U/min is no more effective than intravenous vasopressin,^{38,39} and as it is associated with a greater number of complications,² the intravenous route is usually preferred. The side-effects of vasopressin include diarrhoea, colic, hypertension,

bowel ischaemia and coronary ischaemia. Bowel and coronary ischaemia and hypertension may be reduced by simultaneously infusing glyceryl trinitrate at 40 - 400 µg/min (or one tablet sublingually every hour for 6 hr^{7,40}); however, it does not improve the efficacy of vasopressin.¹² In one study, 2 mg intravenously, 6-hourly of the synthetic analog Glypressin (which is slowly broken down to lysine-vasopressin in the circulation), had a higher success rate in controlling acute variceal haemorrhage when compared to vasopressin at 0.4 U/min.⁴¹ However, the prolonged vasomotor side-effects of glypressin may be disadvantageous when compared with vasopressin.¹²

Somatostatin and somatostatin analogues (octreotide, lanreotide and vapreotide)

Somatostatin and analogues (e.g. octreotide, vapreotide) reduce portal pressure, are more effective in controlling acute variceal haemorrhage than vasopressin and are associated with fewer adverse effects.^{42,43} Octreotide (50 µg intravenously followed by 25-50 µg/hr for 48 hr, i.e. 500 µg of octreotide in 50 mL of 5% dextrose at 2.5 - 5 mL/hr) has been found to be equally as effective as emergency sclerotherapy⁴⁴ and balloon tamponade in management of variceal bleeding.⁴⁵ In one randomised controlled trial in patients with cirrhosis and variceal bleeding, vapreotide (50 µg i.v. bolus followed by 50 µg per hour for five days) begun before endoscopic therapy (e.g. sclerotherapy or band ligation) was more effective than endoscopic therapy alone.⁴⁶ However, in another randomised, controlled trial and a meta-analysis of two trials failed to show a clinical benefit of somatostatin in the emergency treatment of bleeding oesophageal varices.⁴⁷

Fibrinolytic inhibitors

Tranexamic acid (1 g 8-hourly oral or i.v) has been used to successfully reduce the bleeding of portal gastropathy and gastric antral vascular ectasia in cirrhotic patients.⁴⁸

Beta-adrenergic blockers

Beta-adrenergic blockers reduce portal venous pressure by two mechanisms: by decreasing cardiac output (by blocking β_1 receptors) and by producing splanchnic vasoconstriction (through β_2 receptor blockade and unopposed α -adrenergic activity on splanchnic vessels). Predictably, nonselective beta-adrenergic blockers (e.g. propranolol, nadolol, timolol) are more effective than selective beta-adrenergic blockers in reducing portal venous pressure. Propranolol is contraindicated in a patient with actively bleeding oesophageal varices. However, it reduces the incidence of variceal rebleeding (by decreasing the splanchnic blood flow and therefore portal pressure) and should be used after the first bleed at 40 - 360 mg/day (mean 160 mg/day) to reduce the resting pulse rate by 25%,⁴⁹⁻⁵¹ in the well compensated cirrhotic patient (e.g. Child's class A), who has no contraindications for propranolol use.^{1,6}

While some studies comparing chronic sclerotherapy with beta-blockers have shown that the two treatments are equivalent with respect to rebleeding and mortality, and that combination therapy with sclerotherapy and beta-blockers showed no advantage,⁵² a recent study comparing sclerotherapy with a combination of a beta-blocker and a vasodilator (nadolol 80 mg daily initially and adjusted to decrease the heart rate by 25% or no less than 55 per minute, and isosorbide-5-mononitrate added after the nadolol had been adjusted and increased up to 40 mg 12-hourly, unless side effects appeared), demonstrated that the combination drug therapy significantly decreased the risk of rebleeding with a trend towards improved survival.⁵³

Currently, (following endoscopic band ligation) a non-selective beta-blocker (e.g. propranolol or nadolol) with, or without, isosorbide dinitrate, are advocated as the treatment of choice in the prevention of rebleeding.⁵⁴

Other drugs

Pentagastrin, and metoclopramide constrict the lower oesophageal sphincter and have been reported to control acute variceal bleeding in more patients than in a control group.⁷ Isosorbide-5-mononitrate has been suggested as an alternative to beta-blockers for variceal haemorrhage prophylaxis, particularly in patients intolerant to beta-blockade.³⁴

Balloon tamponade

Balloon tamponade should be reserved for acute variceal bleeding uncontrolled by sclerotherapy, octreotide, or vasopressin.¹³ The incidence of rebleeding after removing the balloon is about 50%.¹³ The Linton-Nachlas tube has a single lumen which is inflated in the gastric fundus and compresses the varices at the gastric

side of the oesophagogastric junction (Figure 2). The Sengstaken-Blakemore tube has an oesophageal balloon as well as a gastric balloon, for both oesophageal and gastric compression (Figure 2). The Minnesota tube has four lumens; two are used to inflate the oesophageal and gastric balloons; the remaining lumens allow for gastric and oesophageal aspiration. The Minnesota tube is often the preferred tube for balloon tamponade management.

Technique. Before inserting the tube, the balloons are checked for leaks. The gastric balloon is inflated progressively by 100 mL amounts of air, and the press-

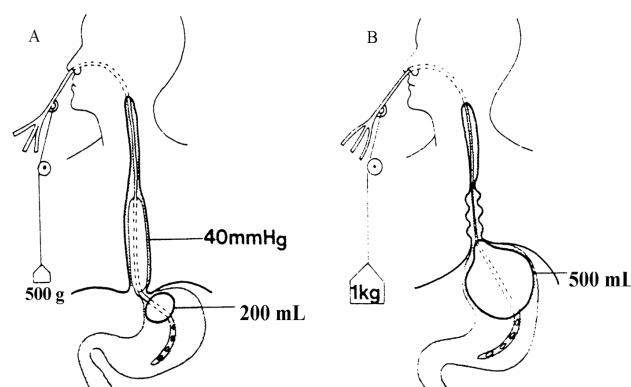


Figure 2. A diagrammatic representation of the Sengstaken-Blakemore tube (A) in position and the Linton-Nichlas tube (B) in position (Modified from Burcharth F and Malmstrom J. *Surg Gynecol Obstet* 1976;142:529-531).

ure is recorded with each 100 mL inserted (enabling one to monitor the gastric balloon inflation pressure on insertion, to check that the balloon is not in the oesophagus). The tube is placed through the nose (as nasal insertion is tolerated better and is associated with less aspiration than oral insertion). If oral insertion of the tube is required, the patient requires endotracheal tube intubation with a cuffed tube (and therefore anaesthesia) to protect the airway. The tip of the tube is inserted up to the 60 cm mark before the gastric balloon is inflated. The gastric balloon is filled with 200-500 mL of air and gently drawn up to the fundus of the stomach. The tube is then firmly secured to the face by taping, or by traction of no greater than 1 kg (usually 500 - 1000 mL of saline is used as gravity traction). It is seldom necessary to inflate the oesophageal balloon if the gastric balloon is correctly placed.⁵⁵ The stomach should be continuously aspirated to assess bleeding control. If bleeding continues, the oesophageal balloon is inflated with air to a pressure of 40 mmHg. The positions of the balloons are checked radiologically. Pharyngeal aspiration should be continuous when the oesophageal balloon is inflated. If bleeding is controlled, the oesophageal balloon is left inflated for 24 hr only (deflating the oesophageal balloon for 30-60 min every

8 hr). The gastric-balloon tamponade can be maintained continuously for 48-72 hr, after which it is deflated and bleeding assessed before it is removed. If bleeding continues, the patient should be considered for a surgical procedure (e.g. sclerotherapy, portosystemic shunt or oesophageal transection) or a transjugular intrahepatic portosystemic shunt. The complications associated with balloon tamponade include, aspiration pneumonia, upper airway obstruction, oesophageal rupture and hiccups.

Surgical management

Surgical management may be divided into those methods which involve decompression of the splanchnic circulation (e.g. central or selective porto-systemic shunts), a direct attack on the varices (e.g. endoscopic or transhepatic sclerosis, transection by stapling, transoesophageal ligation, devascularisation) or replacement of the diseased liver (i.e. hepatic transplantation). Rebleeding after a variceal decompressive shunt usually indicates a technical failure (duplex sonography is often used to confirm shunt occlusion).

Child developed a classification to assess the hepatic reserve to tolerate a major operation and consequence of a diminished portal flow to the liver.⁵⁶ The risk of operation is good with class A, moderate with class B and poor with class C. Child's classification has subsequently been modified by including prolongation of prothrombin time, excluding the 'excellent', 'good' and 'poor' nutritional classification and classifying a patient with a score. A score of 5 or 6 is class A, 7, 8 or 9 is class B, and 10 to 15 is class C (i.e. Child-Pugh class. Table 2).⁵⁷

Central portosystemic (i.e. portacaval) shunts.

Surgical. Four prospective randomised trials comparing central portosystemic (i.e. portacaval) shunting with medical therapy for patients who have cirrhosis and confirmed variceal haemorrhage concluded that shunting prevented rebleeding. However, survival rates were not

significantly different. Central shunting seemed to alter the mode of death from exsanguination to hepatic failure and encephalopathy.⁵⁸⁻⁶¹

Percutaneous. A transjugular intrahepatic portosystemic shunt (TIPS), using a balloon-expandable stent has made the decompression of portal vein hypertension extremely simple (by reducing the difference between portal venous and inferior vena cava values to 12 mmHg), reducing the patient's postprocedure stay to a few days (Figure 3).

The procedure does not preclude liver transplantation at a later date (although difficulty in removing the stent from the inferior vena cava and portal vein thrombosis have been reported⁶²) and in skilled hands has become treatment of choice (irrespective of the patient's Child classification) in reducing portal venous pressure in the management of difficult variceal bleeding (i.e. continued oesophageal bleeding despite two sclerotherapy sessions or bleeding caused by gastric varices or portal hypertensive gastropathy).^{17,25,63,64} During the insertion of the shunt and in the presence of active bleeding, shunt venography can be performed and thrombotic emboli may be inserted directly into the bleeding varix. TIPS has also been used to treat refractory ascites.⁶⁵

The shunt is often reviewed on a three month basis using duplex sonography, and the stent is redilated if there is greater than 50% reduction in shunt flow.²⁵ While TIPS is more effective than endoscopic treatment (i.e. sclerotherapy and/or banding ligation) plus propranolol in prevention of variceal rebleeding, it is associated with an increased incidence of hepatic encephalopathy (particularly if the portal pressure is reduced excessively) and the mortality at 12 months is no different.⁶⁶

As TIPS creates a side to side portosystemic shunt, hepatic encephalopathy and deterioration in liver function occur in up to 25% of cases,⁵² and shunt malfunction (e.g. stenosis) occurs in more than 50% after 6

Table 2. Child-Pugh classification of hepatic functional reserve

	points scored for abnormality		
	1	2	3
Encephalopathy (grade)	None	1 and 2	3 and 4
Ascites	None	Easily controlled	Poorly controlled
Total serum bilirubin ($\mu\text{mol/L}$)	< 35	35 - 50	> 50
Serum albumin (g/L)	> 35	30 - 35	< 30
INR	< 1.3	1.3 - 1.5	> 1.5
Post operative mortality	5-15%	15-30%	30-60%

months.⁶⁶ Other problems related to the procedure include perforation of the hepatic capsule with intra-abdominal haemorrhage and visceral perforation, infection, arrhythmias, thrombosis, misplaced or migrating stents, renal failure and haemolytic anaemia.⁶⁷

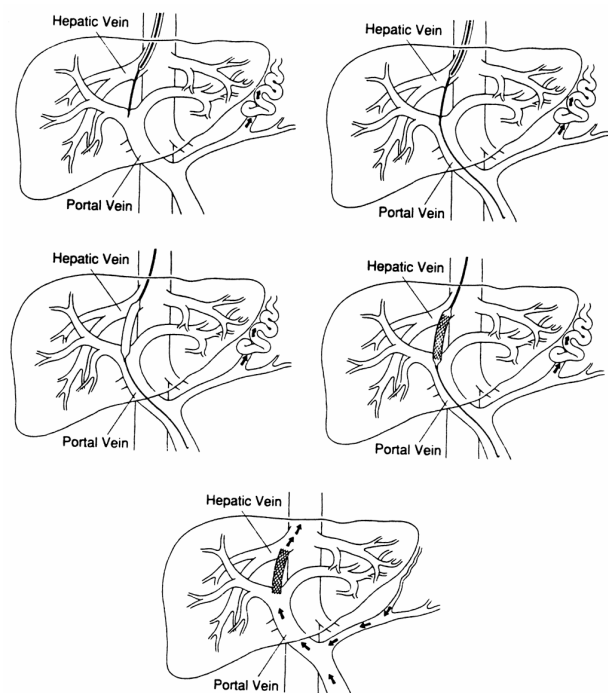


Figure 3 Transjugular intrahepatic portosystemic shunt. Top left: a needle is advanced from the hepatic to portal vein via a transjugular approach. Top right: a guidewire is advanced through the needle into the portal vein. Centre left: an angioplasty balloon is advanced over the guidewire and expanded across the hepatic parenchymal tract. Centre right: a stent mounted on the angioplasty balloon, is expanded to bridge the hepatic and portal veins. Lower final: appearance of the intrahepatic shunt with the stent in place (Reproduced, with permission, from Zemel G, et al. JAMA 1991;266:390-393).

Selective portosystemic (i.e. distal splenorenal) shunts. The creation of a distal splenorenal shunt (i.e. Warren shunt), selectively decompresses varices by separating the splanchnic circulation into two components, the portomesenteric and the gastrosplenic. The latter is decompressed into the systemic venous circulation via the left renal vein, which reduces pressure in the oesophageal varices and prevents haemorrhage. Because the portomesenteric circulation is separate and not decompressed, portal perfusion and thus hepatic function is preserved. The incidence of postshunt encephalopathy in some studies has been greatly reduced.^{68,69} This procedure does not preclude liver transplantation at a later date. The procedure is technically more difficult than the standard portacaval shunt.

However, while the procedure is associated with acceptable mortality, is efficacious in controlling haemorrhage and has minimal propensity for precipitating hepatic encephalopathy; most prospective randomised trials to date have shown no difference in mortality when compared with the central shunt procedures.^{70,71} Some trials have even shown no difference in encephalopathy rate when compared with central portosystemic shunt procedures.⁷²

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