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Q: Does my patient with acute variceal hemorrhage need a transjugular intrahepatic portosystemic shunt?

A 48-year-old man with a history of alcohol-associated cirrhosis presents with hematemesis. His Model for End-stage Liver Disease (MELD) score is 17, and his Child-Pugh class is C (score 12). He undergoes upper endoscopy and is found to have nonbleeding esophageal varices with a positive nipple sign. The varices are banded. This is his first episode of bleeding varices. Should this patient with variceal hemorrhage undergo transjugular intrahepatic portosystemic shunt (TIPS) insertion before discharge?

A: Preemptive TIPS insertion should be considered within 72 hours of initial endoscopy in this patient as he is at high risk for rebleeding (Child-Pugh class C [score ≥ 10 points]). Preemptive TIPS insertion would reduce his rebleeding risk, and preemptive TIPS has been shown to improve overall mortality in patients with variceal hemorrhage.

Variceal hemorrhage is a common decompensating event and a dreaded complication in patients with cirrhosis.¹ Varices are portosystemic collateral vessels that form in the gastrointestinal tract because of clinically significant portal hypertension.² This is typically defined as a hepatic venous pressure gradient of 10 mm Hg or greater.³ In patients with cirrhosis, varices most commonly form in the distal esophagus and the proximal stomach.²

■ VARICEAL HEMORRHAGE MANAGEMENT

Variceal hemorrhage is associated with a 6-week mortality rate of up to 15%.³ If not appropriately treated at the time of initial presentation, variceal hemorrhage

can recur in up to 60% of patients.³ Treatment goals in acute variceal hemorrhage include adequate hemostasis and prevention of rebleeding, the combination of which has been shown to reduce 6-week mortality.⁴ In more than 90% of cases, variceal hemorrhage can be controlled with endoscopic and pharmacologic interventions.⁴ Endoscopic variceal ligation and medications that reduce portal venous pressure, such as nonselective beta-blockers, are used in both primary and secondary prophylaxis strategies for variceal hemorrhage management.³

Placement of a TIPS, which reduces the hepatic venous pressure gradient by diverting blood from the portal venous system to the systemic circulation, is another potential treatment strategy for variceal hemorrhage.³ It can be used as salvage therapy to control bleeding when endoscopic management fails and as a means of secondary prophylaxis in selected patients.^{2,3} Because TIPS insertion is an invasive procedure with potential serious side effects, it is not routinely considered as a primary prophylactic strategy to prevent variceal hemorrhage.²

■ HOW IS A TIPS PLACED?

A TIPS is an endovascular shunt that connects the portal vein to the systemic circulation; TIPS insertion is usually performed by an interventional radiologist.² Under fluoroscopic guidance, the hepatic vein is accessed through the jugular vein.² Once the hepatic vein is cannulated, a needle is used to puncture the portal vein and an expandable polytetrafluoroethylene-covered stent

doi:10.3949/cjcm.91a.24014

TABLE 1
Child-Pugh classification

| Finding | Points | | |
|--------------------------------|--------|--------------|--------------|
| | 1 | 2 | 3 |
| Total bilirubin (mg/dL) | < 2 | 2–3 | > 3 |
| Serum albumin (g/dL) | > 3.5 | 2.8–3.5 | < 2.8 |
| International normalized ratio | < 1.7 | 1.7–2.3 | > 2.3 |
| Ascites | Absent | Mild | Moderate |
| Hepatic encephalopathy | None | Grade 1 or 2 | Grade 3 or 4 |

Class A = 5 or 6 points; class B = 7–9 points; class C = ≥ 10 points

Adapted from reference 7.

is deployed, creating a direct connection between the portal vein (portal circulation) and the hepatic vein (systemic circulation). This effectively produces a portocaval shunt and reduces the hepatic venous pressure gradient.²

During the procedure, the pressure gradient is measured before and after TIPS insertion to ensure that the portal venous system has been successfully decompressed with placement of the shunt.² The target post-TIPS hepatic venous pressure gradient is less than 12 mm Hg or a 50% decrease in the pre-TIPS gradient.²

Once placed, the permanent endovascular TIPS does not require routine intervention except in the event of dysfunction.

■ WHEN TO CONSIDER TIPS INSERTION AFTER ACUTE VARICEAL HEMORRHAGE

Once the presence of a variceal hemorrhage is confirmed, TIPS insertion should be considered in the following scenarios.

Uncontrolled bleeding

Salvage TIPS should be pursued if hemostasis cannot be achieved during endoscopy.^{3,5} In this setting, TIPS insertion is considered an emergency procedure. Even though it is successful in controlling bleeding in more than 80% of cases, 6-week mortality remains high as patients experience increased rates of liver failure, renal failure, and infection.⁶ In a retrospective analysis of 83 patients treated with a salvage TIPS, 6-week survival was 100% in those with an arterial lactate level of 2.5 mmol/L or less and a MELD score of 15 or less, but 5% in those with a lactate level of 12 mmol/L or higher and a MELD score of 30 or higher.⁶ Hence, salvage TIPS is not recommended in patients with a Child-Pugh score of 14 or higher, a MELD score greater than 30, or an arterial lactate level greater than 12 mmol/L unless liver transplantation is an option.⁵

Recurrence of bleeding within 5 days

If a patient with variceal hemorrhage rebleeds within 5 days of an index bleed, they are considered to have failed first-line management and salvage TIPS is recommended.^{3,5}

High risk for rebleeding

Preemptive TIPS insertion should be done within 72 hours of variceal hemorrhage in patients considered to be at high risk for rebleeding, with high risk defined as Child-Pugh class C (≥ 10 points) cirrhosis and Child-Pugh class B (7–9 points) cirrhosis with active bleeding at the time of endoscopy (Table 1).^{2,3,5,7}

The efficacy of this intervention was demonstrated in the landmark multicenter, randomized controlled trial by García-Pagán et al⁸ in 2010. Sixty-three patients with Child-Pugh class C or class B cirrhosis with active variceal bleeding on endoscopy were randomized to TIPS placement within 72 hours of diagnostic endoscopy vs standard of care (endoscopic therapy plus nonselective beta-blockers). The 1-year probability of remaining free of failure to control bleeding and of variceal rebleeding was 97% in the preemptive TIPS group vs 50% in standard-of-care group (number needed to treat = 2.1).⁸ Survival at 6 weeks and 1 year was significantly higher in the preemptive TIPS group than in the standard-of-care group (number needed to treat = 3.3 and 4, respectively). Moreover, there was not a significant difference in serious adverse events among the 2 groups.⁸

Several studies since 2010 have shown the survival benefit of preemptive TIPS. In an individual-patient data meta-analysis of 8 studies and 1,389 patients,⁹ preemptive TIPS significantly improved 1-year survival compared with standard of care in patients with acute variceal hemorrhage (hazard ratio 0.43, 95% confidence interval 0.32–0.60, number needed to treat = 6), providing strong evidence in support of preemptive TIPS. The recently published Baveno VII guidelines⁵ state that acute-on-chronic liver failure, hepatic encephalopathy, and hyperbilirubinemia at admission should not be contraindications to preemptive TIPS.

Preemptive TIPS has primarily been studied in patients with bleeding from esophageal varices. There is limited evidence from an underpowered study showing improved rebleeding-free survival in patients with gastric fundal variceal hemorrhage.¹⁰

Secondary prophylaxis

Elective TIPS insertion is recommended in patients in whom first-line secondary prophylaxis measures

Suspicion of acute variceal bleed in a patient with cirrhosis who presents with an upper gastrointestinal bleed



Start preendoscopic management

Resuscitation

- Conservative transfusion strategy with a target hemoglobin of 7 to 8 g/dL
- Fresh frozen plasma and platelet transfusions are not recommended as they do not correct coagulopathy and can lead to volume overload

Location

- Intensive care unit or step-down unit
- If patient is actively vomiting or has altered mentation, intubation before endoscopy is required

Initial medical management

- Start vasoactive drugs (somatostatin, octreotide, or terlipressin) and continue for 2 to 5 days
- Start antibiotic prophylaxis with intravenous ceftriaxone 1 g daily for 5 days
- Start intravenous proton pump inhibitors empirically, as peptic ulcer disease is common in patients with cirrhosis



Perform endoscopy within 12 hours of presentation



Variceal hemorrhage confirmed or suspected

- Bleeding from a varix or presence of a "white nipple" (a sign of recent bleeding)
- Presence of varices and blood present in the stomach, or varices present without blood in the stomach if esophagogastroduodenoscopy was performed 24 hours after the hemorrhage



Evaluate for indications for TIPS

- Uncontrolled bleeding → **salvage TIPS**
- Rebleeding within 5 days → **salvage TIPS**
- High risk for rebleeding: Child-Pugh class C or class B (see **Table 1**) plus active bleeding → **preemptive TIPS**
- Secondary prophylaxis → **elective TIPS**
 - First-line prophylaxis failed
 - First gastric variceal bleed
 - Recurrent ascites

Assess for contraindications to TIPS

- Heart failure
- Severe hepatic encephalopathy
- Pulmonary hypertension
- Uncontrolled sepsis



Indication for TIPS not present or contraindication to TIPS present

- Start a nonselective beta-blocker, preferably carvedilol
- Perform serial endoscopic variceal ligation until eradication

Figure 1. Initial management of patients with cirrhosis presenting with signs of acute variceal hemorrhage.

TIPS = transjugular intrahepatic portosystemic shunt

Based on information from reference 2.

TABLE 2
Reported rates of complications
from transjugular intrahepatic
portosystemic shunts

| Complications | Reported rate, % |
|-------------------------------------|------------------|
| Major | 3 |
| Hemoperitoneum | 0.5 |
| Biliary peritonitis | 1 |
| Stent malposition | 1 |
| Hemobilia | 2 |
| Renal failure requiring dialysis | 0.25 |
| Hepatic infarction | 0.5 |
| Hepatic artery injury | 1 |
| Liver failure | 3 |
| Minor | 4 |
| Medically controlled encephalopathy | 15–25 |
| Transient pulmonary edema | 1 |
| Fever | 2 |
| Entry-site hematoma | 2 |

Based on information from reference 19.

(eg, endoscopic variceal ligation plus nonselective beta-blockers) have failed.^{2,5} This recommendation is supported by evidence from randomized controlled trials in which patients who underwent TIPS insertion had significantly lower rates of rebleeding compared with those who did not undergo TIPS insertion.^{11,12} Of note, these trials showed no difference in survival among the TIPS vs non-TIPS groups, and the incidence of hepatic encephalopathy was higher in the TIPS group.

Current guidelines recommend TIPS insertion as the first-line form of secondary prophylaxis following an acute bleed from gastric fundal varices.^{3,5} These varices are less common than esophageal varices but tend to bleed more severely.^{2,4} Because gastric fundal variceal hemorrhage is less common, studies evaluating the role of TIPS after variceal hemorrhage in this location are limited. In a randomized controlled trial that included 72 patients with cirrhosis and acute gastric variceal bleeding, variceal rebleeding occurred less often in patients who received a TIPS for secondary prophylaxis compared with those who received cyanoacrylate injections.¹³

The Baveno VII guidelines⁵ include a new recommendation to consider TIPS insertion for first-line therapy after a variceal hemorrhage in patients with recurrent ascites, defined as 3 or more large-volume paracenteses in a year. Of note, regardless of whether variceal hemorrhage occurs, TIPS insertion should be considered in patients with recurrent ascites.⁵

Figure 1 outlines the initial management of patients with cirrhosis presenting with signs of acute variceal bleeding.²

■ CONSIDERATIONS FOR TIPS

Pre-TIPS evaluation requires contrast-enhanced cross-sectional imaging to evaluate the vasculature as part of procedure planning.² In emergent situations, bedside Doppler ultrasonography of the liver may suffice.² Because a TIPS diverts blood directly to the systemic circulation, echocardiography is needed to assess the ejection fraction, right heart function, and potential for pulmonary hypertension; severe preexisting abnormalities can precipitate circulatory dysfunction after TIPS insertion.²

Absolute contraindications to TIPS include American Heart Association heart failure stage C or D, ejection fraction of less than 50%, severe pulmonary hypertension (mean pulmonary artery pressure > 45 mm Hg), and severe tricuspid regurgitation.^{2,14} Similarly, because blood is bypassed into the systemic circulation without being filtered through the liver, a history of severe uncontrolled hepatic encephalopathy is a strong contraindication, as is uncontrolled systemic infection.² Relative contraindications are untreated severe biliary obstruction, severe uncontrollable coagulopathy, polycystic liver disease, and hepatocellular carcinoma.^{1,10,15}

There is no specific MELD score cutoff, but trials for elective and preemptive TIPS procedures have excluded patients with a Child-Pugh score of 14 or higher⁸ and a MELD score of 18 or more, as higher MELD scores are associated with a worse prognosis.¹⁶ MELD scores higher than 30, Child-Pugh scores of 14 or greater, and lactate levels above 12 mmol/L typically render salvage TIPS attempts futile.⁵

Prophylactic rifaximin can be prescribed to reduce the risk of hepatic encephalopathy, as supported by a randomized controlled trial in which rifaximin started 14 days before TIPS placement resulted in a 19% absolute risk reduction in post-TIPS hepatic encephalopathy.¹⁷

The decision to insert a TIPS should be made by a multidisciplinary team involving at least a hepatologist and interventional radiologist.

■ TIPS-RELATED COMPLICATIONS

Procedural complications include injury to the vasculature causing intraperitoneal bleeding, hemobilia, hepatic infarct, immediate TIPS thrombosis, cardiac arrhythmias, and sepsis.^{2,18} Procedure-related deaths occur in less than 1% of patients who undergo TIPS placement.² Increases in total bilirubin and international normalized ratio can be seen after TIPS insertion

but have not been associated with negative outcomes.² Long-term complications include hepatic encephalopathy, cardiac overload, and deterioration of liver function.² **Table 2** lists rates of complications related to TIPS insertion.¹⁹

POST-TIPS CARE

After TIPS insertion, if the hepatic venous pressure gradient drops below 12 mm Hg, nonselective

beta-blockers (eg, carvedilol) may be discontinued.^{2,5} Doppler ultrasonography evaluation is routinely performed within 1 to 4 weeks to screen for TIPS dysfunction and assess patency, and is repeated at regular intervals thereafter.²

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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