GHASSOUB RIFAI, MD
Department of Gastroenterology and Hepatology, Digestive Disease Institute, Cleveland Clinic

ZADE AKRAS
Department of Gastroenterology and Hepatology, Digestive Disease Institute, Cleveland Clinic

IBRAHIM A. HANOUNEH, MD
Minnesota Gastroenterology, Minneapolis, MN

ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Bleeding esophageal varices: Who should receive a shunt?

A: A transjugular intrahepatic portosystemic shunt (TIPS) has been shown in randomized controlled trials to be effective for:

- Secondary prevention of variceal bleeding
- Controlling refractory ascites in patients with liver cirrhosis.

In addition, findings from retrospective case series have suggested that it helps in cases of:

- Acute variceal bleeding refractory to endoscopic therapy
- Gastropathy due to portal hypertension
- Bleeding gastric varices
- Refractory hepatic hydrothorax
- Hepatorenal syndrome
- Budd-Chiari syndrome
- Veno-occlusive disease
- Hepatopulmonary syndrome.

Here, we discuss the indications for a TIPS in cirrhotic patients with esophageal variceal bleeding.

CIRRHOSIS CAN LEAD TO PORTAL HYPERTENSION, BLEEDING

Cirrhosis of the liver alters the hepatic architecture. Development of regenerating nodules and deposition of connective tissue between these nodules increase the resistance to portal blood flow, which can lead to portal hypertension.[1]

Esophageal variceal bleeding is a complication of portal hypertension and a major cause of death in patients with liver cirrhosis. Combined treatment with vasoactive drugs, prophylactic antibiotics, and endoscopic band ligation is the standard of care for patients with acute bleeding. However, this treatment fails in about 10% to 15% of these patients. A TIPS creates a connection between the portal and hepatic veins, resulting in portal decompression and homeostasis.[2]

doi:10.3949/ccjm.84a.15149

PRE-TIPS EVALUATION

Patients being considered for a TIPS should be medically assessed before the procedure. The workup should include the following:

- **Routine blood tests,** including blood type and screen (indirect Coombs test), complete blood cell count, basic metabolic panel, liver function tests, prothrombin time, and partial thromboplastin time
- **Doppler ultrasonography of the liver** to ensure that the portal and hepatic veins are patent
- **Echocardiography** to assess pulmonary arterial pressure and right-side heart function
- **The hepatic venous pressure gradient,** which is measured at the time of TIPS placement, reflects the degree of portal hypertension. A hepatic vein is catheterized, and the right atrial pressure or the free hepatic venous pressure is subtracted from the wedged hepatic venous pressure. The gradient is normally 1 to 5 mm Hg. A gradient greater than 5 mm Hg indicates portal hypertension, and esophageal varices may start to bleed when the gradient is greater than 12 mm Hg. The goal of TIPS placement is to reduce the gradient to less than 12 mm Hg, or at least by 50%.

Heart failure is a contraindication

Pulmonary hypertension may follow TIPS placement because the shunt increases venous return to the heart. Additionally, systemic vascular resistance decreases in patients who have a shunt. This further worsens the hyperdynamic circulatory state already present in patients with cirrhosis. Cardiac output increases in response to these changes. When

Medical and endoscopic treatments fail in 10% to 15% of patients

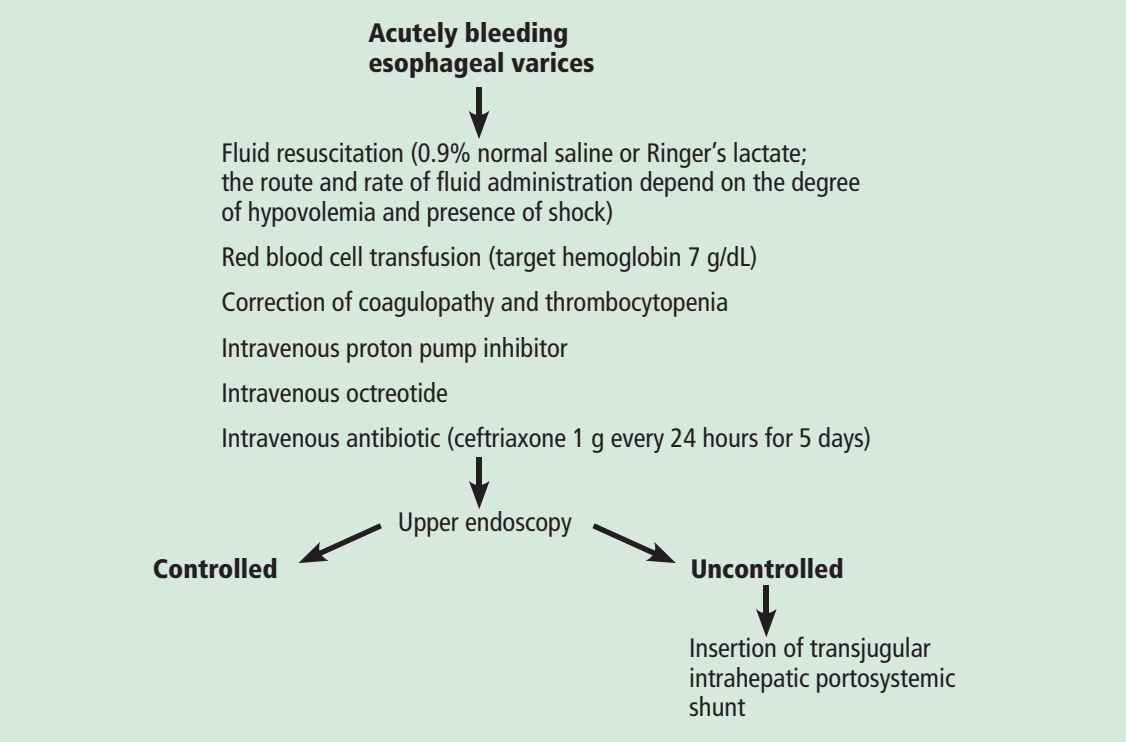

FIGURE 1. Algorithm for managing acutely bleeding esophageal varices.

Absolute contraindications to TIPS: heart failure, severe tricuspid regurgitation, severe pulmonary hypertension

the heart's ability to handle this "volume overload" is exceeded, pulmonary venous pressures rise, with increasing ventilation-perfusion mismatch, hypoxia, and pulmonary vasoconstriction; pulmonary edema may ensue.

Congestive heart failure, severe tricuspid regurgitation, and severe pulmonary hypertension (mean pulmonary pressures > 45 mm Hg) are therefore considered absolute contraindications to TIPS placement.[3,4] This is why echocardiography is recommended to assess pulmonary pressure along with the size and function of the right side of the heart before proceeding with TIPS insertion.

Other considerations

TIPS insertion is not recommended in patients with active hepatic encephalopathy, which should be adequately controlled before insertion of a TIPS. This can be achieved with lactulose and rifaximin. Lactulose is a laxative; the recommended target is 3 to 4 bowel movements daily. Rifaximin is a poorly absorbed antibiotic that has a wide spectrum of coverage, affecting gram-negative and gram-positive aerobes and anaerobes. It wipes out the gut bacteria and so decreases the production of ammonia by the gut.

Paracentesis is recommended before TIPS placement if a large volume of ascites is present. Draining the fluid allows the liver to drop down and makes it easier to access the portal vein from the hepatic vein.

WHEN TO CONSIDER A TIPS IN ESOPHAGEAL VARICEAL BLEEDING

Acute bleeding refractory to endoscopic therapy

A TIPS remains the only choice to control acute variceal bleeding refractory to medical and endoscopic therapy (**Figure 1**), with a success rate of 90% to 100%.[5] The urgency of TIPS placement is an independent predictor of early mortality.

Esophageal variceal rebleeding

Once varices bleed, the risk of rebleeding is higher than 50%, and rebleeding is associated with a high mortality rate. TIPS should be considered if nonselective beta-blockers and surveillance with upper endoscopy and

banding fail to prevent rebleeding, with many studies showing a TIPS to be superior to pharmacologic and endoscopic therapies.[6]

A meta-analysis in 1999 by Papatheodoridis et al[6] found that variceal rebleeding was significantly more frequent with endoscopic therapies, at 47% vs 19% with a TIPS, but the incidence of hepatic encephalopathy was higher with TIPS (34% vs 19%; $P < .001$), and there was no difference in mortality rates.

Hepatic encephalopathy occurs in 15% to 25% of patients after TIPS procedures. Risk factors include advanced age, poor renal function, and a history of hepatic encephalopathy. Hepatic encephalopathy can be managed with lactulose or rifaximin, or both (see above). Narcotics, antihistamines, and benzodiazepines should be avoided. In rare cases (5%) when hepatic encephalopathy is refractory to medical therapy, liver transplant should be considered.

A surgical distal splenorenal shunt is another option for patients with refractory or recurrent variceal bleeding. In a large randomized controlled trial,[7] 140 cirrhotic patients with recurrent variceal bleeding were randomized to receive either a distal splenorenal shunt or a TIPS. At a mean follow-up of 48 months, there was no difference in the rates of rebleeding between the two groups (5.5% with a surgical shunt vs 10.5% with a TIPS, $P = .29$) or in hepatic encephalopathy (50% in both groups). Survival rates were comparable between the two groups at 2 years (81% with a surgical shunt vs 88% with a TIPS) and 5 years (62% vs 61%).

Early use of TIPS after first variceal bleeding

In a 2010 randomized controlled trial,[8] 63 patients with cirrhosis (Child-Pugh class B or C) and acute variceal bleeding who had received standard medical and endoscopic therapy were randomized to receive either a TIPS within 72 hours of admission or long-term conservative treatment with nonselective beta-blockers and endoscopic band ligation. The 1-year actuarial probability of remaining free of rebleeding or failure to control bleeding was 50% in the conservative treatment group vs 97% in the early-TIPS group ($P < .001$). The 1-year actuarial survival rate was 61% in the conservative treatment group vs 86% in the early-TIPS group ($P < .001$).

The authors[8] concluded that early use of TIPS in patients with cirrhosis and Child-Pugh scores of 7 to 13 who were hospitalized for acute variceal bleeding was associated with significant reductions in rates of treatment failure and mortality.

REFERENCES

1. **Brenner D, Rippe RA**. Pathogenesis of hepatic fibrosis. In: Yamada T, Alpers DH, Laine L, Kaplowitz N, Owyang C, Powell DW, editors. Textbook of Gastroenterology. 4th edition. Philadelphia, PA: Lippincott Williams & Wilkins; 2003.
2. **Bhogal HK, Sanyal AJ**. Using transjugular intrahepatic portosystemic shunts for complications of cirrhosis. Clin Gastroenterol Hepatol 2011; 9:936–946.
3. **Garcia-Tsao G, Sanyal AJ, Grace ND, Carey WD; Practice Guidelines Committee of American Association for Study of Liver Diseases; Practice Parameters Committee of American College of Gastroenterology**. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Am J Gastroenterol 2007; 102:2086–2102.
4. **Azoulay D, Castaing D, Dennison A, Martino W, Eyraud D, Bismuth H**. Transjugular intrahepatic portosystemic shunt worsens the hyperdynamic circulatory state of the cirrhotic patient: preliminary report of a prospective study. Hepatology 1994; 19:129–132.
5. **Rodríguez-Laiz JM, Bañares R, Echenagusia A, et al**. Effects of transjugular intrahepatic portasystemic shunt (TIPS) on splanchnic and systemic hemodynamics, and hepatic function in patients with portal hypertension. Preliminary results. Dig Dis Sci 1995; 40:2121–2127.
6. **Papatheodoridis GV, Goulis J, Leandro G, Patch D, Burroughs AK**. Transjugular intrahepatic portosystemic shunt compared with endoscopic treatment for prevention of variceal rebleeding: a meta-analysis. Hepatology 1999; 30:612–622.
7. **Henderson JM, Boyer TD, Kutner MH, et al; DIVERT Study Group**. Distal splenorenal shunt versus transjugular intrahepatic portal systemic shunt for variceal bleeding: a randomized trial. Gastroenterology 2006; 130:1643–1651.
8. **García-Pagán JC, Caca K, Bureau C, et al; Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group**. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med 2010; 362:2370–2379.

ADDRESS: Ibrahim A. Hanouneh, MD, Minnesota Gastroenterology, P.A., PO Box 14909, Minneapolis, MN 55414; ibrahim.hanouneh@mngastro.com