Outcomes of Transjugular Intrahepatic Portosystemic Shunts for Ascites

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Abstract

Keywords

- portal hypertension
- refractory ascites
- transjugular intrahepatic portosystemic shunt
- hepatic hydrothorax
- liver transplant
- interventional radiology

Refractory ascites represents a devastating complication of portal hypertension. Transjugular intrahepatic portosystemic shunt (TIPS) is an efficacious option for patients for whom transplant is not an immediate option. Techniques to optimize the hepatic venous pressure gradient and the use of covered stents have reduced rates of hepatic encephalopathy and stent occlusion, respectively. Patients with a Model for End-Stage Liver Disease score less than 15, serum creatinine less than 2 mg/dL, and serum bilirubin less than 2 mg/dL are particularly suited for TIPS placement. TIPS is also effective for hepatic hydrothorax and for massive ascites in the posttransplant setting, although future investigations are necessary to elucidate risk factors and establish the effect on transplant-free survival.

Objectives: Upon completion of this article, the reader will be able to describe the current role of TIPS in the treatment of patients with intractable ascites.

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Portal hypertension is a hemodynamic abnormality resulting from impedance of blood outflow from the portal venous system.^{1–3} The incidence of portal hypertension is unknown, although in Western countries gastroesophageal varices are found at presentation in 50 to 78% of patients with cirrhosis.^{4–6} Advanced liver cirrhosis can further complicate portal hypertension through hyperdynamic circulation from increased cardiac output and decreased peripheral vascular resistance.⁷

Complications of portal hypertension include ascites, hepatorenal syndrome,^{8–12} variceal bleeding, and spontaneous bacterial peritonitis.^{8,9} Ascites is the most common presentation of decompensated ascites.¹³ Refractory ascites is defined by an inability to mobilize ascites despite maximal doses of diuretics,¹⁴ and carries significant morbidity.¹⁰ The 2-year survival rate after the development of ascites is only 50%.^{15,16} Spontaneous bacterial pneumonitis, the most common infectious complication of ascites and cirrhosis, has been associated with mortality rates as high as 87 to 95%.^{16,17}

Transjugular Intrahepatic Portosystemic Shunt for Ascites

The International Ascites Club guidelines recommend modest salt restriction and diuretics for mild to moderate ascites; however, medically refractory ascites requires more complex management.¹⁸ Therapeutic options for refractory ascites include frequent paracentesis, transjugular intrahepatic portosystemic shunt (TIPS), and transplant.^{11,12,19} TIPS may be an attractive option for patients given long transplant waitlists, transplant morbidity, and the impact of frequent paracentesis and hospitalization on patient well-being.

Serum sodium and creatinine levels are improved by TIPS.^{20,21} Early investigations demonstrated lower ascites recurrence and hepatorenal syndrome risk with TIPS as compared with repeated paracentesis.^{22–27} TIPS is more effective at controlling ascites than large-volume paracentesis (LVP)²⁸; TIPS essentially relieves the obstruction of blood flow within the liver, allowing for ascites resolution, while LVP represents only a temporary fix.

The most frequent complications of TIPS include hepatic encephalopathy (HE), shunt stenosis/obstruction, cardiopulmonary disease from increased blood return to the heart, and hemolytic anemia.¹⁸ In comparison with LVP, TIPS is associated with reduced ascites recurrence and improved transplant-free survival, at the expense of increased rates of HE.^{21,29–31} Recently, techniques have been refined facilitating narrow-diameter dilatation of the stent and more precise manipulation of the hepatic venous pressure gradient (HPVG),³² hypothetically reducing the risk of HE.

Improved outcomes following TIPS placement rely on selection of appropriate patients for which postprocedural mortality is expected to be low. Factors associated with increased mortality include Child class C cirrhosis, Model for End-Stage Liver Disease (MELD) score greater than 25, HPVG less than 8 mm Hg,³³ international normalized ratio (INR) greater than 2,³⁴ total serum bilirubin greater than 3 mg/dL, and platelet count of less than 75×10^9 per liter.³⁵ Factors associated with improved survival are MELD score less than 15,³⁶ serum creatinine less than 2 mg/dL, and serum bilirubin less than 2 mg/dL.³⁷ Serum sodium, bilirubin, and creatinine levels may also predict the likelihood of encephalopathy; however, exact predictors remain nebulous.³⁸

Covered TIPS has led to reassessment of post-TIPS outcome risk factors. Polytetrafluoroethylene is believed to reduce the liver parenchymal ingrowth that results in shunt insufficiency. The use of expanded polytetrafluoroethylene (ePTFE)-coated TIPS is widespread despite a lack of controlled studies.^{36,39,40} Nevertheless, the 2009 American Association for the Study of Liver Diseases (AASLD) guidelines update recommends use of ePTFE-covered TIPS to decrease the incidence of shunt dysfunction and portal hypertension recurrence.⁴¹ In a randomized study of 80 patients, 32 of whom had refractory ascites, patients with ePTFE-covered TIPS had significantly lower rates of shunt dysfunction and clinical relapse when compared with patients with uncovered TIPS.^{42,43} The effect of ePTFE-covered TIPS on survival is controversial⁴⁴; in most studies, covered TIPS demonstrates no greater rate of HE with some studies suggesting a trend toward lower rates of HE with covered TIPS.^{45,46} This finding may be related to reduced dilatation of covered TIPS,⁴⁵ presumably because operators avoid aggressive balloon dilatation, feeling confident stents will maintain patency with narrower luminal diameters.

Overall survival has been reported to be 58% at 1 year with bare metal stents and Child–Pugh scores less than 10.⁴⁷ Transplant-free survival, a separate measure in the literature to account for organ survival, has been reported to be as high as 71% with ePTFE-covered stents in patients with ascites or variceal bleeding.⁴² In a retrospective study unpublished at

the time of publication of this article, the authors have found a transplant-free survival of 74.5% at 1 year in a population of 100 patients with refractory ascites. Cost-effectiveness has yet to be determined, although preliminary data suggest a reduction in costs with ePTFE-covered TIPS.⁴⁸ Anecdotally, in the authors practice over the past 10 years, a marked reduction in post-TIPS re-interventions has been noted, likely related to the predominant use of covered stents.

Hepatic Hydrothorax

Hepatic hydrothorax represents a unique complication of portal hypertension for which TIPS may be useful. The incidence of pleural effusion in the setting of cirrhosis is 0.4 to 12.2%.^{49,50} Hepatic hydrothorax is the accumulation of transudate in the pleural space in patients with cirrhosis, typically on the right side.^{51,52} Compared with the large volume of fluid in the abdomen in symptomatic patients with ascites (5–8 L), just 1 to 2 L of fluid in the thoracic cavity may result in severe symptomatology, including shortness of breath, cough, and hypoxemia.⁵³ Diuretic therapy is often ineffective and may even result in intravascular volume depletion.⁵⁴ Thus, alternative therapies for hepatic hydrothorax are critical.

TIPS has been described as effective for refractory hepatic hydrothorax,⁵⁰ especially for patients younger than 60 years.⁵⁵ Successful resolution of hepatic hydrothorax with TIPS has even been reported in the absence of ascites.⁵⁶ In addition, the presence of TIPS before balloon-occluded retrograde transvenous obliteration (BRTO), a technique used to treat bleeding gastric varices, significantly reduces risk of post-BRTO ascites and hepatic hydrothorax, as well as recurrent hemorrhage, although the effect on 1-year survival is negligible.⁵⁷

Future investigations of hepatic hydrothorax should assess the impact of TIPS on overall and transplant-free survival. In addition, risk factor analysis should be performed to identify the optimal patient population for TIPS placement in the setting of hepatic hydrothorax, given that the pathophysiology is distinct from refractory ascites.

Transplant versus Nontransplant

Liver transplantation represents the best treatment for end-stage liver disease. Nevertheless, complications after transplantation may arise. Ascites and hepatic hydrothorax may occur in the posttransplant setting. Small amounts of ascites may occur postoperatively and resolve after a few days; however, massive ascites has been reported, possibly related to hepatic vein outflow impedance due to caval vein stenosis.⁵⁸

The use of TIPS for refractory ascites in the transplant setting has been established.⁵⁹ TIPS may be performed even with segmental allografts.⁶⁰ TIPS does not preclude retransplantation^{61,62}; in one small series, approximately half of all patients with refractory ascites responded to TIPS. For these patients, serum INR, creatinine level, bilirubin level, and MELD scores all increased following TIPS, reflecting the natural history of worsening hepatic dysfunction.⁶³ A larger

series, where 90% of TIPS placed in transplanted livers were for refractory ascites, found equivalent technical success rates between transplanted livers and nontransplanted livers, although increased complexity was noted with some inferior vena cava piggyback anastomoses in small livers. One-year graft patency was 32%.⁶⁴

The etiologies of refractory ascites in the posttransplant setting are different from those seen with pretransplant hepatic dysfunction. Thus, TIPS placement, while still efficacious, has decreased levels of efficacy. Overall, this patient population likely has lower rates of transplant-free survival; however, TIPS may provide a therapeutic role or serve as a bridge to retransplantation. Future investigations should assess patient selection for TIPS in the posttransplant setting.

Conclusion

TIPS is a critical therapy for patients with refractory ascites. An appropriate post-TIPS HPVG, use of ePTFE-covered stents, and proper patient selection improve efficacy. TIPS is also effective for hepatic hydrothorax and for refractory ascites in the posttransplant setting. Future studies, however, are necessary to elucidate risk factors leading to increased or decreased success of ascites clearance.

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