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Best Use of the Transjugular Intrahepatic Portosystemic Shunt Procedure for the Management of Portal Hypertension

Lisa B. VanWagner, MD, MSc
Assistant Professor of Medicine
Gastroenterology & Hepatology and Preventive Medicine
Comprehensive Transplant Center
Northwestern University Feinberg School of Medicine
Chicago, Illinois

G&H What are the traditional treatments for portal hypertension, and how effective are they?

LVW Cirrhosis is a major cause of portal hypertension, which has consequences that include ascites, hepatic hydrothorax, esophageal varices, hepatic encephalopathy (HE), and hepatorenal syndrome, and can lead to substantial morbidity and mortality. Over the past several decades, there have been major improvements in the clinical management of most of the complications of portal hypertension, leading to substantial gains in patient outcomes. However, several challenges still remain. One is that the effectiveness of drugs or interventions for portal hypertension can be assessed in 2 different ways: indirectly by looking at clinical outcomes such as the incidence of a person having a variceal bleed, or directly by looking at the hepatic venous pressure gradient (HVPG), which is an indirect measure of the pressure in the portal vein. The effectiveness of treatment for portal hypertension is often defined as achieving a HVPG of less than 12 mm Hg or a 20% reduction from baseline. That threshold has been associated with a significant decrease in the incidence of complications and, in particular, sustained long-term reduction in the risk of first variceal bleeding.

Traditional treatments for portal hypertension can be grouped into 2 categories. One consists of the pharmacologic therapies that have been studied, including nonselective beta blockers, angiotensin receptor blockers, the somatostatin analog octreotide, nitric oxide, and statins. However, of that list of drugs, only nonselective beta blockers are part of the current guideline-recommended treatment for the prevention and management of portal hypertension, in particular patients with variceal bleeding. In terms of effectiveness, nonselective beta blockers have been shown to decrease the HVPG and have been linked to a decrease in clinical outcomes. In addition, nonselective beta blockers decrease the incidence of first variceal hemorrhage, and they reduce variceal rebleeding rates when used in conjunction with endoscopic band ligation. In patients with compensated cirrhosis, nonselective beta blockers can even prevent clinical decompensation. When the other portal hypertension medications previously listed have been studied, they have either not been effective in human trials; have been harmful, in particular with kidney function; or have not been linked to clinical outcomes and only reduce the HVPG.

The other category of treatments for portal hypertension consists of portosystemic shunting procedures, which are highly effective at reducing portal pressure. In the past, these have been surgical procedures involving portacaval, mesocaval, or splenorenal shunts to divert blood away from the liver and reduce portal pressure. However, the transjugular intrahepatic portosystemic shunt (TIPS) procedure is much less invasive and is now considered the standard of care for most patients with cirrhosis. With the advent of the TIPS procedure, surgical procedures are now reserved for patients who have noncirrhotic causes of portal hypertension and might have a technical or anatomic limitation for the TIPS procedure. The TIPS procedure is the treatment of choice when choosing a procedural approach to treating portal hypertension.

G&H How is the TIPS procedure performed?

LVW The TIPS procedure is performed by an interventional radiologist via the internal jugular vein, which is located in the neck. Essentially, an artificial liver shunt, or a tube, is placed between the portal vein (the vein that feeds blood to the liver) and then between that vein and the hepatic vein (the vein that drains blood from the liver) in order to allow better blood flow through the liver.

G&H What are the study data surrounding the use of the TIPS procedure?

LVW The TIPS procedure is currently approved for 4 specific indications—acute or recurrent variceal hemorrhage, refractory ascites, refractory hepatic hydrothorax, and gastropathy—with fairly good data to support its use. Outcomes after the procedure are excellent, but depend on good patient selection and the indication for which the procedure is being performed. For example, the TIPS procedure improves transplant-free survival in patients with refractory ascites.

The TIPS procedure has also been used in a variety of other settings, including revascularization of the portal vein, Budd-Chiari syndrome, severe portal hypertensive gastropathy, hepatopulmonary syndrome, and hepatorenal syndrome type 2. However, the data are not as strong in these settings to support routine use of the procedure.

G&H Which patients with portal hypertension are candidates for the TIPS procedure (eg, in terms of Model for End-Stage Liver Disease score and symptoms), and what are the contraindications?

LVW Interestingly, the Model for End-Stage Liver Disease (MELD) score was developed to predict 90-day mortality after a TIPS procedure; thus, the MELD score is a fairly accurate predictor of mortality with the procedure. Historically, a MELD score greater than 15 was thought to be a poor marker of potential mortality after the TIPS procedure, but newer data now suggest acceptable outcomes with MELD scores up to around 20. The most important consideration when looking at the MELD score in a TIPS candidate is what is driving the score. A high bilirubin level, typically greater than 3.5 mg/dL, has historically been linked to poorer outcomes in patients.

In terms of symptoms, those are linked to the indication for which the TIPS procedure is being performed. Thus, if the TIPS procedure is being done for ascites, then the symptom would be abdominal distension; if the TIPS procedure is being done for bleeding, the symptom would be vomiting of blood or the presence of blood in stool.

Relative contraindications include a high bilirubin level; severe intrinsic kidney disease (stage 4 or above), as the disease could potentially be worsened by the shunt or the contrast dye used in the TIPS procedure; and a MELD score greater than 20. Absolute contraindications include severe refractory HE, severe pulmonary hypertension, heart failure, and significant right ventricular dysfunction that could be exacerbated, causing death after the TIPS procedure.

G&H At what point in the management plan should the TIPS procedure be considered?

LVW For many of the complications of portal hypertension, the TIPS procedure is often considered late in the disease course. At that point, patients may have worsening synthetic liver function and, therefore, higher MELD scores or bilirubin, which makes the procedure riskier. Data are accumulating now that support the use of the TIPS procedure much earlier in the disease course, particularly for patients with diuretic-intolerant or -resistant ascites and even among patients who have had a first variceal bleeding episode, especially in patients considered to be high risk. Guidelines define high-risk patients as patients with Child-Pugh class C cirrhosis, Child-Pugh class B cirrhosis with active bleeding, or a MELD score greater than 18 who required at least 4 units of a red blood cell transfusion with their bleeding episode. These are the patients in whom clinicians should be actively thinking about using the TIPS procedure as an early intervention for managing complications of portal hypertension.

G&H What impact does the TIPS procedure have on ascites?

LVW It has been shown in several studies that the TIPS procedure is a very effective alternative to large-volume paracentesis for patients with refractory ascites. One study demonstrated that the TIPS procedure led to complete ascites resolution in approximately 50% to 75% of patients and a substantial reduction in large-volume paracentesis frequency in 90% to 100% of patients. A recent meta-analysis of patients with refractory ascites showed a significant survival benefit with the TIPS procedure compared to large-volume paracentesis. The 1-year transplant-free survival rate was approximately 93% in the TIPS group vs 52% in patients who continued to undergo large-volume paracentesis.

G&H Does the TIPS procedure have an impact on other areas, such as cardiac function or quality of life?

LVW One of the hemodynamic consequences of undergoing the TIPS procedure is that there is increased venous return to the right heart, which can lead to an elevation in end-diastolic volume. Therefore, the TIPS procedure is contraindicated in patients with congestive heart failure, severe pulmonary hypertension, and, potentially, severe tricuspid regurgitation.

In terms of quality of life, I am only aware of one study, which was published approximately 15 years ago in *Hepatology*, that specifically looked at this issue. The authors used data from the North American Study for the Treatment of Refractory Ascites, which was a multicenter trial of 109 patients who were randomized to the TIPS procedure or repeat large-volume paracentesis for the treatment of refractory ascites. Both groups had similar changes in quality of life, driven by the need for hospitalizations—because of HE in the TIPS group and because of the requirement for repeat procedures in the large-volume paracentesis group. To my knowledge, there has not been an updated study that has specifically looked at quality of life in patients with ascites, nor specifically on cardiac function and quality of life, or variceal bleeding and quality of life.

G&H Could you discuss any TIPS-related complications and ways to prevent or manage them?

LVW The biggest concern after a TIPS procedure is HE. Most data in the literature suggest that the rate of hospitalization for HE within 1 year after the TIPS procedure is likely around 24%. However, most HE can be treated with medications such as lactulose and rifaximin. Currently, guidelines do not recommend any prophylaxis for HE in patients who are undergoing the TIPS procedure who do not already have a history of the condition.

Nevertheless, data were presented at last year's Liver Meeting from a group in France that showed that preventive rifaximin at a dose of 600 mg twice a day vs placebo starting 15 days prior to the TIPS procedure and continuing for 6 months was associated with a lower risk of HE and a higher rate of transplant-free survival. It will be interesting to see if clinicians start adapting the use of rifaximin potentially as a way to prevent HE because it is the main complication after the TIPS procedure and it affects quality of life in patients.

Other common complications of the TIPS procedure include bleeding, infection, abscess, the aforementioned heart complications, bile leak or injury, acute liver failure, or stent thrombosis or migration. All of these complications have fairly low rates of risk (approximately 1%-2%).

G&H Do patients who undergo the TIPS procedure require any special follow-up?

LVW At our center, which is a high-volume TIPS site that performs approximately 150 TIPS procedures per year, my colleagues and I perform an ultrasound of the shunt at 1 month and then every 6 months thereafter to monitor for TIPS dysfunction. Many, but not all, centers follow similar practices.

In addition, due to the rise in the recognition of cirrhotic cardiomyopathy, which is the subclinical form of cardiac dysfunction associated with cirrhosis, many centers are starting to obtain echocardiograms of the heart at predefined intervals after the TIPS procedure to monitor for cardiac dysfunction.

G&H What is the ALTA Consortium?

LVW The ALTA (Advancing Liver Therapeutic Approaches) Consortium began as an initiative by the American Society of Transplantation Liver and Intestinal Community of Practice. Other hepatologists and I were seeing an increase in the use of the TIPS procedure in our clinical practices and looked to the literature for contemporary findings, such as expected survival and outcomes. We could not find any high-quality manuscripts with significant sample sizes; the research was mainly single-center studies reporting on their experiences. Thus, a group of 9 academic centers initially joined together in 2017 to retrospectively look at our center experiences with the TIPS procedure between 2010 and 2015. We created a database with information on 1329 patients who underwent a TIPS procedure in the United States during that time frame, and then in 2018 we transitioned to a prospective registry study with the help of an investigator-initiated industry grant from W. L. Gore & Associates. We now have 12 participating centers across the United States and began active enrollment on June 10, 2019. Any adult patient who is undergoing the TIPS procedure for any reason at any of the participating centers is eligible for enrollment in the prospective study. The main goal is to collect information on the real-world usage and clinical outcomes of the TIPS procedure.

G&H Have any data been released yet from the consortium?

LVW Data have been presented at the International Liver Congress 2018, the Liver Meeting 2018, Digestive

Disease Week (DDW) 2019, and the American Transplant Congress 2019, and more data were accepted for presentation at DDW 2020. Our first 2 manuscripts have been submitted and are undergoing review.

G&H Could you discuss any of the data that have been presented?

LVW We have seen a large increase in the use of the TIPS procedure for indications that are not listed in any TIPS guidelines or guidance statements, such as for the management of portal vein thrombosis and hepatopulmonary syndrome, as well as for potentially increasing candidacy for patients with portal hypertension surrounding other endoscopic or intra-abdominal procedures. For example, if a person with portal hypertension requires gallbladder removal, which is associated with a high risk of death, it has been thought that perhaps the TIPS procedure might improve outcomes by decreasing pressures in the portal system.

As previously mentioned, historically a MELD score of 15 has been used as the cut point where the mortality risk is much higher in patients who undergo the TIPS procedure. We found that the inflection point is likely closer to approximately 19 to 20 and that people have very good outcomes after the TIPS procedure with MELD scores up until approximately 20; it is after 20 that a drop off is seen. I think we are doing a better job with the TIPS procedure and being able to manage complications and identify patients prior to the procedure so that it can be performed in more patients than it was 15 or 20 years ago.

There have been subprojects that have looked at the predictors of patients who might have ongoing renal injury after the TIPS procedure. We have seen that patients with intrinsic renal disease and, interestingly, patients with nonalcoholic steatohepatitis might have an increased incidence of renal dysfunction after the TIPS procedure. We have also looked at the use of sedative and other psychotropic medications and how it might affect the risk of HE following the procedure.

Because of the richness of the database, we have been able to look at many interesting questions and ongoing analyses on many different issues, particularly those related to cardiopulmonary and renal function and unique indications for TIPS use.

G&H Have there been any findings regarding the best approach to the TIPS procedure?

LVW As hepatologists, we tend to focus on the indications for the TIPS procedure and who should be undergoing it, and sometimes forget that there are different ways to approach it and that there are no published best practices. Thus, we do not know whether it matters where a patient undergoes the procedure—at an academic medical center or at a community hospital with people who have been trained in the procedure. I was surprised to learn from interventional radiology colleagues that there is no minimum number of TIPS procedures that needs to be performed to learn how to do the procedure; thus, there is a good deal of variation in approach. One of the goals of the ALTA Consortium is to study what happens in the TIPS procedure from an interventional radiologist's perspective, and we are working with colleagues in interventional radiology to develop standardized protocols and a standardized approach to performing the procedure.

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Suggested Reading

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