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# NARRATIVE REVIEW

Charles J. Kahi, Section Editor

## North American Practice-Based Recommendations for Transjugular Intrahepatic Portosystemic Shunts in Portal Hypertension



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Complications of portal hypertension, including ascites, gastrointestinal bleeding, hepatic hydrothorax, and hepatic encephalopathy, are associated with significant morbidity

and mortality. Despite few high-quality randomized controlled trials to guide therapeutic decisions, transjugular intrahepatic portosystemic shunt (TIPS) creation

<sup>a</sup>Authors share co-first authorship. <sup>b</sup>Authors share co-senior authorship.

**Abbreviations used in this paper:** AKD, acute kidney disease; AKI, acute kidney injury; BCS, Budd–Chiari syndrome; CKD, chronic kidney disease; CTP, Child–Turcotte–Pugh; ePTFE, expanded polytetrafluoroethylene; GFR, glomerular filtration rate; GV, gastric fundal varices; HE, hepatic encephalopathy; HF, heart failure; HH, hepatic hydrothorax; HRS, hepatorenal syndrome; IR, interventional radiology; IVC, inferior vena cava; LT, liver transplantation; LV, left ventricular; LVP, large-volume paracentesis; MELD, model for end-stage liver disease; POPH, portopulmonary hypertension; PSG, portosystemic gradient; PVT, portal vein thrombosis; RA, refractory ascites; RAP, right atrial pressure; RCT,

randomized controlled trial; RV, right ventricular; sCr, serum creatinine; SPSS, spontaneous portosystemic shunts; TFS, transplant-free survival; TIPS, transjugular intrahepatic portosystemic shunt; TR, tricuspid regurgitation; VHD, valvular heart disease.

Most current article

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has emerged as a crucial therapeutic option to treat complications of portal hypertension. In North America, the decision to perform TIPS involves gastroenterologists, hepatologists, and interventional radiologists, but TIPS creation is performed by interventional radiologists. This is in contrast to other parts of the world where TIPS creation is performed primarily by hepatologists. Thus, the successful use of TIPS in North America is dependent on a multidisciplinary approach and technical expertise, so as to optimize outcomes. Recently, new procedural techniques, TIPS stent technology, and indications for TIPS have emerged. As a result, practices and outcomes vary greatly across institutions and significant knowledge gaps exist. In this consensus statement, the Advancing Liver Therapeutic Approaches group critically reviews the application of TIPS in the management of portal hypertension. Advancing Liver Therapeutic Approaches convened a multidisciplinary group of North American experts from hepatology, interventional radiology, transplant surgery, nephrology, cardiology, pulmonology, and hematology to critically review existing literature and develop practice-based recommendations for the use of TIPS in patients with any cause of portal hypertension in terms of candidate selection, procedural best practices and, post-TIPS management; and to develop areas of consensus for TIPS indications and the prevention of complications. Finally, future research directions are identified related to TIPS for the management of portal hypertension.

*Keywords:* TIPS Procedure; Cirrhosis; End-Stage Liver Disease; Complications; Consensus Statement; Guidance Document; Ascites; Variceal Bleeding.

Portal hypertension, defined as increased pressure in the portal venous system, can lead to major clinical complications including ascites, gastrointestinal hemorrhage, hepatic hydrothorax (HH), and hepatic encephalopathy (HE), all associated with significant morbidity and mortality.<sup>1</sup> Although medical therapies and liver transplantation (LT) are effective treatments in many scenarios, transjugular intrahepatic portosystemic shunt (TIPS) creation is a crucial therapeutic option ([Supplementary Figure 1](#)).

In North America, the decision to perform TIPS is determined by specialists in gastroenterology and hepatology who treat patients with portal hypertension, but TIPS creation is performed by interventional radiology (IR). This is in contrast to other parts of the world (eg, Europe) in which hepatologists primarily perform TIPS. Although TIPS creation is effective for management of complications of portal hypertension,<sup>2-7</sup> it is associated with several risks, including deterioration in liver function, new onset or worsening HE,<sup>8</sup> and changes in cardiopulmonary and renal hemodynamics ([Supplementary Figure 1](#)).<sup>9</sup> Over the past decade there have been important advancements in TIPS devices, procedural techniques, and immense growth in the literature supporting the role of TIPS in the management of portal

hypertension.<sup>10,11</sup> However, there are few high-quality randomized controlled trials (RCTs) of TIPS use. New indications for TIPS placement also have emerged, including treatment of portal vein thrombosis (PVT), which require rigorous assessment. As a result, practices and outcomes vary greatly across institutions and significant knowledge gaps exist.

The goals and objectives of the Advancing Liver Therapeutic Approaches consensus conference were to convene a multidisciplinary group of North American experts from hepatology, IR, transplant surgery, nephrology, cardiology, pulmonology, and hematology to critically review existing literature and develop practice-based recommendations for the use of TIPS in persons with any cause of portal hypertension in terms of candidate selection, procedural best practices, and post-TIPS management across 7 key topic areas: general considerations for TIPS, TIPS in the management of ascites/HH, TIPS in the management of variceal bleeding, novel indications for TIPS, cardiopulmonary considerations of TIPS including management of hepatopulmonary syndrome, renal considerations of TIPS including management of hepatorenal syndrome (HRS), and HE and TIPS.

## Methods

A consensus-building process was conducted consistent with standards described in the Appraisal of Guidelines for Research and Evaluation II<sup>12</sup> and used a modified Delphi approach to achieve consensus ([Supplementary Methods section](#)).<sup>13</sup> Practice-based recommendations were developed by 30 Advancing Liver Therapeutic Approaches group members with extensive experience in the management of portal hypertension and the use of TIPS, who participated in the consensus conference held on October 23, 2020. The target users are gastroenterologists, hepatologists, and subspecialty physicians who refer for TIPS and/or provide care for patients undergoing TIPS.

PubMed, EMBASE, and Cochrane were queried for English language articles published between January 1, 1990, and July 1, 2020. The target population was persons with any cause of portal hypertension undergoing TIPS. Terms were chosen through input from participants and by consultation with a medical librarian ([Supplementary Methods section](#)). We considered peer-reviewed articles in the following order of relevance: RCTs, systematic reviews and meta-analyses, and observational studies. For select topics in which studies were limited, case reports were included. Between August 2020 and October 2020, literature for each topic was discussed iteratively by workgroups of physicians with expertise in the identified topics. The level of evidence for all consensus statements was graded using the Oxford Centre for Evidence-based Medicine Levels of Evidence.<sup>14</sup>

## Results

The literature search yielded 2116 articles, with 703 reports remaining after titles and abstracts were screened for relevance (Supplementary Methods section). An additional 81 articles not captured by the literature search were included on the basis of panel agreement of relevance.

A total of 105 clinical statements were developed for assessment throughout the 2 iterations of the Delphi survey. All panelists completed all survey items. After 2 iterations of the Delphi survey, 87 statements met the standardized definition for consensus (Supplementary Methods section and Supplementary Table 1). The recommendations are outlined in Tables 1, 2, and 3. The following text provides brief rationale supporting these recommendations. Expanded rationale, where indicated, are available in the Supplementary Discussion section.

## Discussion

### General Considerations for Transjugular Intrahepatic Portosystemic Shunt

Table 1 summarizes the recommendations concerning TIPS planning, procedural best practices, and care of the TIPS recipient independent of the indication for TIPS.

**Pre-transjugular intrahepatic portosystemic shunt considerations.** *Question 1. Who should be involved in the decision to place a transjugular intrahepatic portosystemic shunt?* A team-based approach to TIPS is critical in all stages of TIPS planning and management (Figure 1).<sup>15,16</sup> Initial consideration for decision on TIPS candidacy should involve the patient and caregiver, as well as a gastroenterologist or hepatologist and a proceduralist with competency in TIPS. Complex cases should include consultation with additional specialties (eg, transplant surgery, nephrology, and so forth) as appropriate.

*Question 2. What services should be readily available at centers where transjugular intrahepatic portosystemic shunt is performed and what referral pathways should be established for a higher level of care?* Centers that offer TIPS creation should ensure availability of multidisciplinary services to provide high-quality care for this high-risk population (Figure 1).<sup>16</sup> Centers should have access to expertise in IR, gastroenterology/hepatology, cardiology, surgery, nephrology, and critical care medicine. In complex cases, including patients meeting criteria for referral for transplant or requiring specific technique expertise (eg, PVT), referral to centers with additional expertise is recommended.

*Question 3. Is there a model for end-stage liver disease threshold above which elective transjugular intrahepatic portosystemic shunt should not be considered?* A multidisciplinary approach, rather than an absolute model for end-stage liver disease (MELD) cut-off value, is recommended to assess TIPS candidacy. The MELD score is the strongest predictor of 90-day mortality after TIPS when

compared with MELD-Na and other scoring systems (eg, Child–Turcotte–Pugh (CTP) score, and so forth) (Supplementary Discussion section).<sup>17–22</sup> The MELD score performs better in patients with TIPS for variceal bleeding compared with patients with refractory ascites (RA).<sup>23–25</sup> Studies have examined additional risk factors for poor outcomes with mixed results, including older age and specific numeric MELD score cut-off values.<sup>24–30</sup> Variability in patient population and study design limit the ability to determine firm cut-off values.<sup>4,31–34</sup> Determination of TIPS candidacy using the MELD score should take into consideration the relative risk and benefit of TIPS creation, considering the TIPS indication, patient comorbidities, and alternative treatment options.

*Question 4. What evaluation is required before transjugular intrahepatic portosystemic shunt creation?* Cross-sectional imaging and echocardiography provide important information for TIPS planning. Cross-sectional imaging should include portal venous phase imaging to adequately define portal veins, hepatic veins, and the liver parenchyma to permit planning of TIPS creation. Comprehensive echocardiography before TIPS is recommended to assess the risk for cardiac decompensation after TIPS (details in cardiopulmonary considerations in transjugular intrahepatic portosystemic shunt).<sup>15</sup> Emergent TIPS indications may not allow a complete anatomic and cardiac evaluation; however, a liver ultrasound with Doppler and a limited 2-dimensional echocardiogram still should be considered.

*Question 5. What are absolute contraindications to elective transjugular intrahepatic portosystemic shunt creation?* The absolute contraindications to TIPS creation include American College of Cardiology/American Heart Association stage C or D heart failure (HF) (ie, echocardiographic evidence of systolic ± diastolic dysfunction combined with clinical features of HF),<sup>35</sup> American Heart Association/American College of Cardiology stage C or D untreated valvular heart disease (VHD) (ie, asymptomatic severe VHD with or without decompensation of the left or right ventricle or symptomatic VHD),<sup>36</sup> moderate-severe pulmonary hypertension, uncontrolled systemic infection, refractory overt HE, and anatomic barriers to shunt creation (eg, multiple hepatic lesions).<sup>15,16</sup>

*Question 6. Should all patients undergo evaluation for liver transplantation before transjugular intrahepatic portosystemic shunt creation?* In patients undergoing elective or emergent TIPS, there is insufficient evidence to recommend universal preprocedure LT evaluation. Although patients with cirrhosis and RA or variceal bleeding undergoing TIPS have indications for a LT evaluation, not all will be LT candidates.<sup>37</sup> TIPS should not be delayed to consider a LT evaluation.

**Transjugular intrahepatic portosystemic shunt procedural considerations.** *Question 7. Who should perform transjugular intrahepatic portosystemic shunt creation?* TIPS should be performed by a credentialed, board-certified interventional radiologist or a certified provider with equivalent training and procedural competency, acknowledging that training pathways vary

**Table 1.** Clinical Consensus Statements for TIPS Planning, Procedural Best Practices, and Care of the TIPS Recipient Independent of Indication for TIPS

Question	Statement	Level of evidence
Pre-TIPS considerations		
Question 1. Who should be involved in the decision to place a TIPS and what other preprocedure consultations are recommended?	Before TIPS creation, we recommend that a gastroenterologist or hepatologist should be involved in the initial decision to place an emergent or nonemergent TIPS with subsequent consultation by an interventional radiologist or other proceduralist with competency in TIPS. If center expertise is not available, we recommend referral to an expert center. Additional specialty consultations (eg, transplant surgery, cardiology, critical care, hematology, nephrology) may be considered on a case-by-case basis.	5
Question 2. What services should be readily available at centers where TIPS is performed and what referral pathways should be established for a higher level of care?	For all patients undergoing TIPS creation, we recommend that TIPS should occur at a center with available IR, gastroenterology/hepatology, cardiology, pulmonary surgery, hematology, nephrology, and critical care services to provide an adequate level of support for patient management before and after TIPS. In patients requiring a higher level of care, such as possible liver transplant candidates, or in whom the need for further IR expertise is indicated (eg, extensive portal vein thrombosis), we recommend referral to centers with adequate experience in these areas.	5
Question 3. Is there a MELD threshold above which elective TIPS should not be considered?	In patients with cirrhosis undergoing TIPS, a multidisciplinary approach, rather than an absolute MELD cut-off value, is recommended to assess TIPS candidacy.	2a
Question 4. What imaging and/or preprocedural evaluation is required before TIPS creation?	<p>Q4a. In patients undergoing elective TIPS, we recommend the following:</p> <ul style="list-style-type: none"> <li>• Contrast-enhanced multiphasic cross-sectional imaging (CT/MRI) to assist with TIPS planning.</li> <li>• Comprehensive echocardiography to assess for abnormalities in cardiac structure, function, and right ventricular systolic pressure.</li> </ul> <p>Q4b. In patients with cirrhosis undergoing emergent TIPS, best clinical judgement should be applied. We suggest at least a liver ultrasound with Doppler to evaluate the patency of the portal venous system and consideration of a limited (bedside) echocardiogram, evaluating left ventricular ejection fraction and right ventricular systolic pressure.</p>	2a  3
Question 5. What are absolute contraindications (medical and anatomic) to elective TIPS creation?	The absolute contraindications to elective TIPS include the following: <ul style="list-style-type: none"> <li>• Severe congestive heart failure (ACC/AHA stage C or D HF)</li> <li>• Severe untreated valvular heart disease (AHA/ACC stage C or D VHD)</li> <li>• Moderate–severe pulmonary hypertension (based on invasive measurements) despite medical optimization</li> <li>• Uncontrolled systemic infection</li> <li>• Refractory overt HE</li> <li>• Unrelieved biliary obstruction</li> <li>• Lesions (eg, cysts) or tumors in the liver parenchyma that preclude TIPS creation</li> </ul>	2a
Question 6. Should all patients being considered for TIPS undergo evaluation for liver transplantation before TIPS creation?	In patients with cirrhosis undergoing elective or emergent TIPS, there is insufficient evidence to recommend universal preprocedure liver transplant evaluation.	5

Table 1. Continued

Question	Statement	Level of evidence
TIPS procedural considerations		
Question 7: Who should perform TIPS creation?	We recommend that TIPS creation should be performed by a credentialed, board-certified interventional radiologist or a certified provider with equivalent training and procedural competency <sup>a</sup>	5
Question 8. Which type of stent is recommended for TIPS creation?	For patients undergoing TIPS placement, we recommend the use of an ePTFE-lined stent graft (1b) with controlled expansion, which allows the surgeon to tailor the amount of portosystemic shunting based on the indication, target gradient, and patient comorbidities (2b).	1b and 2b
Question 9. Should coagulopathy be corrected before TIPS placement?	Because of insufficient evidence, we do not recommend a specific target INR or platelet threshold when placing a TIPS in a patient with cirrhosis.	2b
Question 10. Should periprocedural antibiotics be used routinely in TIPS creation?	There are no studies to show that the routine use of antibiotics during TIPS placement decreases infectious complications and their use should depend on patient and local risk factors.	5
Question 11. Should TIPS creation be performed using general anesthesia or is deep or conscious sedation appropriate?	The use of general anesthesia, deep sedation, or conscious sedation all may be appropriate for TIPS placement and their use will vary depending on the patient risk factors and local practices.	5
Question 12. Is the use of intravascular ultrasound recommended to assist with the portal vein puncture?	For patients undergoing TIPS creation, although there is insufficient evidence to recommend the universal use of intravascular ultrasound guidance, it may facilitate efficient portal access in certain situations. Its use will depend on equipment availability and surgeon preference.	3b
Question 13. What is the optimal location from which to measure the systemic venous pressure at the time of TIPS creation (hepatic vein, IVC, right atrium)?	We recommend the use of the free hepatic vein or IVC pressure as the systemic pressure when measuring the portosystemic gradient before and after TIPS placement.	2a
Question 14. Are there specific technical factors that should be considered to ensure that TIPS placement does not adversely influence liver transplant candidacy?	Q14a. In patients undergoing TIPS placement who are potentially eligible for liver transplant, we recommend positioning the stent as to not interfere with the portal and hepatic vein anastomoses, presuming that this does not detrimentally affect TIPS function or patency. This positioning includes leaving a segment of unstented main portal vein and not extending the TIPS stent into the right atrium. Q14b. Liver transplant candidacy should not be impacted by placement of TIPS.	5 2a
Care of the post-TIPS patient		
Question 15. What is the recommended duration of intensive postprocedure monitoring?	After TIPS creation, we recommend that all patients undergo in-hospital overnight observation at minimum. The level of care during post-TIPS observation should be dictated by the patient's condition, indication for TIPS, and intraprocedural technical complexity.	5
Question 16. What early laboratory testing and/or imaging is recommended after TIPS creation and at what interval?	Q16a. In all patients undergoing TIPS creation, routine laboratory tests (complete blood count, comprehensive metabolic panel, and PT/INR) should be obtained on the day after TIPS creation. Hemoglobin/hematocrit laboratory tests may be obtained on the same day of TIPS creation, depending on institution and/or surgeon discretion. Q16b. Predischarge imaging is not indicated in most patients undergoing TIPS creation.	5 5

Table 1. Continued

Question	Statement	Level of evidence
Question 17. Should TIPS venography and intervention be based on ultrasound, clinical findings, or both?	Q17a. In patients who have undergone TIPS creation for management of varices, either Doppler ultrasound findings suggesting TIPS dysfunction or persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry $\pm$ intervention. Ultrasound findings suggesting TIPS dysfunction include alterations in intrahepatic portal vein direction of flow, abnormal flow velocities within the TIPS, and persistent (eg, >6 weeks after TIPS) or recurrent ascites.	2b
	Q17b. In patients who have undergone TIPS creation for management of ascites and/or hepatic hydrothorax, persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry $\pm$ intervention. Medical decision making should be individualized in patients with well-controlled ascites and/or hepatic hydrothorax and ultrasound findings suggesting TIPS dysfunction.	2b
	Q17c. In select patients, scheduled TIPS venography with intervention is suggested in the early (1–2 months) post-TIPS period. An example of such a scenario would be TIPS creation in a patient with portal vein thrombosis.	5
Question 18. What are the optimal techniques for increasing or decreasing TIPS flow when intervention is required?	Q18a. In patients in whom further decrease in portal pressure is desired, we recommend stepwise dilatation of TIPS to its maximum diameter. If it is already at maximum diameter, other interventions to decrease portal pressure (eg, nonselective $\beta$ -blockers, parallel TIPS creation) should be evaluated.	5
	Q18b. In patients in whom an increase in portal pressure is desired, there is insufficient evidence to recommend a specific technique to reduce portosystemic shunting through a TIPS.	5
Question 19. Who should see patients with TIPS in follow-up evaluation?	In patients who have undergone TIPS creation, we recommend that a gastroenterologist or hepatologist and a competent proceduralist (eg, interventional radiologist) should follow-up the patient to ensure ongoing management of chronic liver disease, postprocedural complications, and to determine any need for potential device revision.	5

ACC, American College of Cardiology; AHA, American Heart Association; CT, computed tomography; ePTFE, Polytetrafluoroethylene; HE, hepatic encephalopathy; HF, heart failure; INR, international normalized ratio; IR, interventional radiology; IVC, inferior vena cava; MELD, model for end-stage liver disease; MRI, magnetic resonance imaging; PT, prothrombin time; TIPS, transjugular intrahepatic portosystemic shunt; VHD, valvular heart disease.

<sup>a</sup>According to radiology professional society guidelines, TIPS placement must be performed by a physician with board certification or accredited training as well as sufficient experience with TIPS procedures. In the absence of certification or accredited training, TIPS placement can be performed by a competent proceduralist defined as one who has performed a sufficient number of TIPS procedures under supervision (minimum threshold, 5), in addition to other endovascular techniques (ie, minimum of 10 angiograms, 5 angioplasties, 10 stent placements, and 5 embolizations), has achieved expected procedure completion thresholds, and has obtained appropriate privileges at their center.<sup>38</sup>

worldwide.<sup>16,38</sup> According to radiology professional society guidelines, TIPS placement must be performed by a physician with board certification or accredited training as well as sufficient experience with TIPS procedures. In the absence of certification or accredited training, TIPS placement can be performed by a competent proceduralist defined as one who has performed a sufficient number of TIPS procedures under supervision (minimum threshold, 5), in addition to other endovascular techniques (ie, minimum of 10 angiograms, 5 angioplasties, 10 stent placements, and 5 embolizations), has

achieved expected procedure completion thresholds, and has obtained appropriate privileges at their center.<sup>38</sup>

*Question 8. What type of stent is recommended for transjugular intrahepatic portosystemic shunt creation?* Numerous studies have shown improved patency, ascites control, and rebleeding prevention with the use of expanded polytetrafluoroethylene (ePTFE)-covered stent grafts vs bare metal stents at the time of TIPS creation.<sup>39–46</sup> The use of a specialized purpose-designed stent graft appears to yield superior patency compared with shunts created with off-label use of bare metal

**Table 2.** Clinical Consensus Statements for TIPS by Indication

Question	Statement	Level of evidence
TIPS in ascites or HHT		
Question 1. What is the optimal technical approach to TIPS creation among patients with cirrhosis and refractory ascites?	Q1a. For patients with cirrhosis and diuretic refractory or resistant ascites undergoing elective TIPS, we recommend the use of an ePTFE-covered controlled expansion stent.	2b
	Q1b. For patients with cirrhosis and diuretic refractory or resistant ascites undergoing elective TIPS, we recommend a staged approach to TIPS creation with an initial procedural stent dilation to 8 mm followed by clinical assessment, and then subsequent progressive stent dilation to 9 mm and then 10 mm at 6-week intervals if needed to optimize clinical response.	2b
Question 2. Is TIPS associated with better outcomes (mortality, ascites control) than serial LVP for the treatment of refractory ascites?	Q2a. For carefully selected patients with cirrhosis and refractory ascites, TIPS is recommended over LVP to prevent recurrent ascites.	1a
	Q2b. For carefully selected patients with cirrhosis and refractory ascites, TIPS is recommended over LVP to improve transplant-free survival.	1a
Question 3. Is there a threshold of liver dysfunction above which TIPS for refractory ascites should be contraindicated and how should it be defined?	Among patients with cirrhosis and refractory ascites, increased bilirubin, increased MELD score, and CTP class C cirrhosis are associated with increased post-TIPS complications including mortality. There is insufficient evidence to recommend a cut-off value above which any of these measures should be considered a contraindication to TIPS.	1a
Question 4. What is the impact of age on candidacy for TIPS for refractory ascites?	Among patients with cirrhosis and refractory ascites, advanced age is associated significantly with post-TIPS complications including severe hepatic encephalopathy and death. There is insufficient evidence to recommend a cut-off age that should be considered a contraindication to TIPS.	1a
Question 5. What is the role of TIPS in patients with ascites that is not refractory?	In patients not fulfilling a strict definition of refractory ascites but requiring at least 3 LVP for tense ascites in a year despite optimal medical therapy, we recommend that TIPS creation should be considered.	1a
Question 6. What is the role of TIPS in HHT? Is patient selection similar for patients with ascites vs patients with HHT?	For patients with HHT requiring recurrent thoracentesis, we recommend that TIPS should be considered.	2b
Question 7. Is prior liver transplantation a contraindication to TIPS for refractory ascites? Is TIPS a better treatment than surgical shunt, serial LVP, or splenic artery embolization in liver transplant recipients with refractory ascites?	Unlike TIPS for ascites and HHT in cirrhosis, there is insufficient evidence to support any recommendation regarding therapy (TIPS and other modalities) in liver transplant recipients with refractory ascites.	2b
Question 8. What is the expected timeline for the TIPS to be effective for reduction of ascites/HHT?	In the setting of TIPS creation for ascites or hepatic hydrothorax, we recommend using a staged approach by starting with the TIPS stent with the smallest diameter with concomitant use of diuretics as tolerated. Reassessment for need to further dilate the TIPS stent should be performed every 6 weeks.	2b

stent/stent graft constructs.<sup>47</sup> Use of a controlled-expansion stent that allows for incremental and reliable expansion of stent diameter is recommended to optimize the amount of portosystemic shunting based on the indication, patient risk factors, and target gradient, while potentially mitigating the risk of HE.<sup>10</sup>

Underdilation of a self-expanding stent with a fixed diameter as a method of decreasing HE risk is not recommended because the stent will passively expand over time to its nominal diameter.<sup>48,49</sup>

*Question 9. Should coagulopathy be corrected before transjugular intrahepatic portosystemic shunt creation?*



Table 2. Continued

Question	Statement	Level of evidence
TIPS in variceal bleeding		
Question 1. When is TIPS indicated in acute variceal hemorrhage?	For acute variceal hemorrhage, we recommend TIPS creation in the following scenarios:	1c
	<ul style="list-style-type: none"> <li>• Pre-emptive TIPS in patients who have been banded successfully but who meet high-risk criteria for rebleeding. High-risk criteria are CTP class C (10–13 points) or CTP class B &gt;7 points with active bleeding at endoscopy. TIPS should be performed within 72 hours of admission in patients without contraindications to TIPS.</li> </ul>	
	<ul style="list-style-type: none"> <li>• Rescue TIPS in patients who have been banded successfully but who rebleed at any time during admission (after endoscopy).</li> </ul>	2a
Question 2. When should TIPS be used in the management of bleeding gastric fundal varices or prevention of rebleeding?	Q2a. We recommend that the initial management of bleeding gastric-fundal varices should be based on center expertise. Variceal obliteration/embolization with or without TIPS should be considered for bleeding gastric-fundal varices if unable to be managed endoscopically.	5
	Q2b. For rebleeding gastric-fundal varices after endoscopic therapy, we recommend variceal obliteration with or without TIPS creation.	2b
Question 3. What are the procedural considerations in TIPS creation for variceal hemorrhage?	Q3a. When placing a TIPS for variceal hemorrhage, we recommend a goal PSG of <12 mm Hg or 50%–60% decrease from initial. We do not recommend using shunt diameter as a procedural end point.	2b
	Q3b. In cases of TIPS creation for variceal hemorrhage, we recommend concurrent obliteration of varices.	1b
Question 4. How should patients be monitored after TIPS creation for variceal hemorrhage?	Q4a. In the setting of TIPS creation for variceal bleeding, we recommend surveillance with Doppler ultrasonography 3 months after TIPS creation and every 6 months thereafter to monitor for post-TIPS stenosis or occlusion.	5
	Q4b. If TIPS stenosis/occlusion is suspected or if patient rebleeds after TIPS creation, TIPS venogram with pressure measurements is indicated with consideration of TIPS revision.	2b
Novel indications for TIPS		
Question 1. Does preoperative TIPS creation in patients with portal hypertension reduce surgical complication and/or improve perioperative outcomes after nontransplant abdominal surgery?	Q1a. In patients with portal hypertension requiring nontransplant surgery, there is insufficient evidence to recommend that preoperative TIPS prevents bleeding complications or the need for blood transfusion during or after invasive nontransplant surgical procedures.	1b
	Q1b. In patients with cirrhosis without clinically significant ascites, there is insufficient evidence to recommend preoperative TIPS in abdominal surgery to prevent complications of ascites. In patients with cirrhosis with clinically significant ascites requiring abdominal surgery, a multidisciplinary team approach (hepatology and hepatobiliary surgery) is recommended to individualize surgical/medical management.	3b
	Q1c. There is no evidence that preoperative TIPS has an impact on postoperative mortality after invasive nontransplant surgical procedures.	3b

Table 2. Continued

Question	Statement	Level of evidence
Question 2. Does TIPS creation in patients with cirrhosis and portal vein obstruction facilitate listing for liver transplantation and/or improve outcomes after liver transplantation?	Q2a. In patients with cirrhosis and chronic, complete portal vein thrombosis, portal vein recanalization, and TIPS creation could be considered to facilitate transplant eligibility.	3b
	Q2b. Patients with cirrhosis and complete portal vein thrombosis otherwise being considered for liver transplantation or denied listing because of technical challenges associated with complete portal vein obstruction should be considered for portal vein reconstruction and TIPS. Referral to a center with specialized expertise may be necessary.	5
Question 3. Does TIPS creation prevent or reduce portal hypertensive complications in patients with noncirrhotic portal hypertension owing to extrahepatic portal vein obstruction?	Q3a. In patients with noncirrhotic portal hypertension and acute portal vein thrombosis, we recommend immediate anticoagulation. In those who fail or have a poor response to anticoagulation, we recommend that portal vein thrombectomy/thrombolysis using a transjugular approach with or without small-caliber TIPS creation should be considered.	4
	Q3b. In patients with acute noncirrhotic portal vein thrombosis who are not critically ill, evidence is insufficient to recommend TIPS vs anticoagulation alone. We recommend that a trial of anticoagulation be considered initially given the reported rates of venous recanalization.	2b
	Q3c. In patients with chronic portal hypertension secondary to noncirrhotic extrahepatic portal vein obstruction that is not responsive to anticoagulation, TIPS may be considered for the same indications as cirrhotic portal hypertension.	5
Question 4. Does TIPS creation in patients with noncirrhotic portal hypertension and without extrahepatic portal vein obstruction prevent or reduce portal hypertensive complications?	In patients with chronic idiopathic portal hypertension/portosinusoidal vascular disease TIPS may be considered for the same indications as cirrhotic portal hypertension.	5
Question 5. Does TIPS creation improve outcomes in patients with Budd–Chiari syndrome?	Q5a. Patients with Budd–Chiari syndrome should be evaluated and managed at centers with experience and expertise in hematologic evaluation, clinical management, and percutaneous intervention in this patient population. Ideally, the center also will have expertise in liver transplantation, should this be warranted at initial evaluation or during subsequent follow-up evaluation. If these resources are not available at the presenting institution, strong consideration of transfer to such an institution should be given while medical management is initiated.	5
	Q5b. In patients with Budd–Chiari syndrome who remain symptomatic or without improving liver function after initiation of appropriate medical therapy and who are not candidates for percutaneous revascularization of the hepatic venous outflow tract (short-segment obstruction), creation of a percutaneous portosystemic shunt, either TIPS or direct intrahepatic portosystemic shunt, should be strongly considered.	2b
	Q5c. In patients with Budd–Chiari syndrome undergoing TIPS, we recommend close clinical monitoring and imaging follow-up evaluation.	4

CTP, Child-Turcotte-Pugh; ePTFE, polytetrafluoroethylene; HHT, hepatic hydrothorax; LVP, large-volume paracentesis; MELD, model for end-stage liver disease; PSG, portosystemic gradient; TIPS, transjugular intrahepatic portosystemic shunt.

**Table 3.** Cardiopulmonary, Renal, and Neurologic Considerations in TIPS

Question	Statement	Level of evidence
Cardiopulmonary considerations in TIPS		
Question 1. What cardiopulmonary testing is indicated before elective TIPS?	Q1a. In patients undergoing elective TIPS creation, we recommend comprehensive echocardiographic evaluation incorporating, in addition to the assessment of LVEF, measurement of left ventricular global longitudinal strain, when feasible, and the contemporary surrogates of left ventricular diastolic function.	2b
	Q1b. In patients undergoing elective TIPS creation, we recommend assessment of right ventricular function using TAPSE and RVSP. Right ventricular strain has not become standard of care in most centers but should be measured if available.	5
	Q1c. In patients undergoing TIPS creation who have a RVSP exceeding 45 mm Hg or TAPSE less than 1.6 cm, we recommend referral to cardiology for consideration of right heart catheterization to evaluate for RV dysfunction and pulmonary hypertension before TIPS creation.	5
	Q1d. In patients undergoing TIPS creation, who have tachycardia or bradycardia on physical examination, we recommend pre-TIPS electrocardiographic assessment to evaluate for arrhythmia.	5
Question 2. Does cirrhotic cardiomyopathy or diastolic dysfunction confer a risk for post-TIPS heart failure?	Q2a. In patients undergoing elective TIPS creation, we recommend considering the presence of systolic and/or diastolic dysfunction, which may suggest cirrhotic cardiomyopathy in the absence of other cardiac history, a significant risk factor for post-TIPS heart failure.	2b
	Q2b. In patients undergoing evaluation for elective TIPS, we recommend avoiding TIPS if LVEF is <50% or if there is grade III diastolic dysfunction, given the risk of post-TIPS cardiac decompensation.	5
Question 3. Can TIPS be performed safely in patients with moderate or severe portopulmonary hypertension?	Q3a. In patients with moderate or severe POPH on treatment (ie, mean pulmonary artery pressure >35 mm Hg, pulmonary vascular resistance >3 wood units), we recommend significant caution when considering TIPS insertion because it may precipitate right-sided heart failure.	5
	Q3b. In patients undergoing elective TIPS who do not have evidence of POPH on screening, we recommend measuring the right atrial pressure at the time of planned TIPS insertion, and if >14 mm Hg we recommend considering right heart catheterization before TIPS creation to exclude POPH based on the clinical situation.	5
Question 4. Can tricuspid regurgitation severity be prohibitive of TIPS creation?	In patients being considered for elective TIPS who have moderate or severe tricuspid regurgitation despite optimization of volume overload, we recommend evaluation for the underlying cardiopulmonary etiology, which can prohibit proceeding with TIPS.	5
Question 5. Can TIPS treat HPS?	We do not recommend TIPS as a therapy for HPS, but it may be considered in patients with HPS who have an established indication for TIPS.	4
Question 6. Does stent size affect risk for post-TIPS HF in high-cardiac-risk patients?	In patients with systolic and/or diastolic dysfunction or mild POPH who are undergoing TIPS, we recommend balancing the desired portosystemic gradient with potential worsening of cardiac function by initially deploying the endoprosthesis to 8-mm diameter. If the desired gradient is achieved, no additional dilatation of the shunt should be pursued.	5

Table 3. Continued

Question	Statement	Level of evidence
Question 7. Is there a need for post-TIPS echocardiographic surveillance?	In patients with systolic and/or diastolic dysfunction, pulmonary hypertension, or moderate to severe valvular disease, we recommend echocardiographic surveillance at 3 months post-TIPS or earlier, if indicated. Surveillance beyond 3 months can be considered if there is echocardiographic worsening at 3 months (compared with baseline) or if there is clinical indication.	5
Renal considerations in TIPS		
Question 1. What is the best marker to assess kidney function before or after TIPS?	Q1a. In patients with cirrhosis undergoing TIPS, kidney function should be assessed before the procedure either through measurement of serum creatinine or GFR (estimated or measured). A change in GFR may better capture changes in kidney function, although there is insufficient evidence to recommend one equation over another. Q1b. The optimal method to assess kidney function in cirrhosis patients with sarcopenia or chronic kidney disease is not known.	5 5
Question 2. Is there an absolute cut-off value for kidney function for which TIPS is contraindicated?	There is insufficient evidence to recommend an absolute serum creatinine, CKD stage, or presence/absence of renal replacement therapy for which TIPS creation is contraindicated.	5
Question 3. What can be done periprocedurally to reduce the incidence of kidney complications after TIPS? What secondary or tertiary preventive measures can be considered to avoid AKI, acute kidney disease, or de novo or progressive CKD after TIPS?	Q3a. In patients undergoing TIPS creation for ascites, albumin infusion should be considered in all patients undergoing concurrent paracentesis, and especially for those in whom >5 L are removed, to prevent paracentesis-induced circulatory dysfunction and AKI. Q3b. LVP with albumin infusion may be performed either within 24 hours before, or concomitantly during, TIPS creation. Q3c. Adequate hydration and judicious use of iodinated contrast are rational strategies to help reduce the risk of contrast-related injury. Q3d. In patients with AKI/CKD before TIPS or in those who develop AKI after TIPS creation, kidney function should be followed up closely within 1 week of discharge after TIPS creation.	1a 5 2b 5
Question 4. What is the role of TIPS for HRS?	Q4a. There is insufficient evidence to recommend for or against the use of TIPS for treatment of HRS; however, the presence of HRS is not an absolute contraindication for TIPS creation in the presence of other indications (eg, refractory ascites, variceal bleeding). Q4b. Mortality in patients with HRS undergoing TIPS appears to be driven by liver function (ie, serum bilirubin, INR), therefore, careful patient selection is recommended.	2a 4
Hepatic encephalopathy and TIPS		
Question 1. When counseling patients, what is the overall risk of overt hepatic encephalopathy after TIPS and what patient-specific factors contribute to the development of overt HE?	We recommend counseling patients that TIPS is associated with a risk of overt HE in approximately 25%–50% of recipients (1b). Patient-specific risk factors for the development of post-TIPS overt HE include prior history of overt HE, advanced age, advanced liver dysfunction (CTP class C), hyponatremia, renal dysfunction, and sarcopenia (2a).	1b, 2a

Table 3. Continued

Question	Statement	Level of evidence
Question 2. What social factors should be considered a contraindication to elective TIPS as it relates to overt HE?	We recommend avoiding elective TIPS in patients with cognitive impairment and limited family or social support.	3
Question 3. What is the role for formal evaluation for covert or minimal HE before elective TIPS?	In patients being considered for elective TIPS, testing for covert or minimal HE could be considered for prognostication and discussion with the patient.	2
Question 4. What TIPS stent diameter should be considered with regard to limiting post-TIPS HE?	In patients undergoing elective TIPS for ascites, we recommend starting with a smaller-diameter controlled-expansion stent to potentially reduce rates of HE.	4
Question 5a. Is there a role for collateral embolization at the time of TIPS?	In patients undergoing elective TIPS for ascites and/or hepatic hydrothorax, embolization of SPSS >6 mm may be considered to reduce the risk of post-TIPS hepatic encephalopathy.	4
Question 5b. Is there a role for TIPS with shunt embolization in the management of refractory HE related to presumed clinically significant portosystemic shunting?	In select patients with large (>6 mm) SPSS and refractory HE, we recommend that shunt embolization be considered. For select patients who develop portal hypertensive-associated complications (ascites, varices) after shunt embolization, we recommend that small-caliber TIPS creation could be considered.	4
Question 6a. What is the role for medical prophylaxis to prevent HE after TIPS?	In patients without a history of overt HE undergoing TIPS, we do not recommend medical prophylaxis to prevent HE after TIPS.	3
Question 6b. What is the recommended medical therapy to treat overt HE after TIPS?	We recommend medical management of post-TIPS overt HE based on current guidelines with the use of lactulose and rifaximin.	1
Question 6c. What is the role for TIPS stent reduction/occlusion as the treatment of persistent or refractory HE?	We recommend consideration of TIPS stent diameter reduction in patients with persistent or refractory HE post-TIPS.	2b

AKI, acute kidney injury; CKD, chronic kidney disease; CTP, Child-Turcotte-Pugh; GFR, glomerular filtration rate; HE, hepatic encephalopathy; HF, heart failure; HPS, hepatopulmonary syndrome; HRS, hepatorenal syndrome; INR, international normalized ratio; LV, left ventricular; LVEF, left ventricular ejection fraction; LVP, large volume paracentesis; POPH, portopulmonary hypertension; RVSP, right ventricular systolic pressure; SPSS spontaneous portosystemic shunt; TAPSE, tricuspid annular plane systolic excursion; TIPS, transjugular intrahepatic portosystemic shunt.

It is unclear whether correction of coagulopathy to a specific target international normalized ratio or thrombocytopenia decreases complications or improves survival after TIPS.<sup>50</sup> International normalized ratio and platelet count are poor measures of bleeding risk in patients with cirrhosis and routine transfusion of blood products before invasive procedures does not portend lower procedural bleeding risk.<sup>51-55</sup> However, these studies primarily include patients undergoing paracentesis and liver biopsy, and it is unclear if the results can be extrapolated to patients undergoing TIPS creation, which carries a higher bleeding risk. Plasma fibrinogen levels less than 100 mg/dL are associated with an increased bleeding risk in critically ill patients with cirrhosis, but causal relationships are not established.<sup>50</sup> The role of correction to levels greater than 100 mg/dL and reduction of bleeding risk during TIPS creation is unknown.<sup>50</sup>

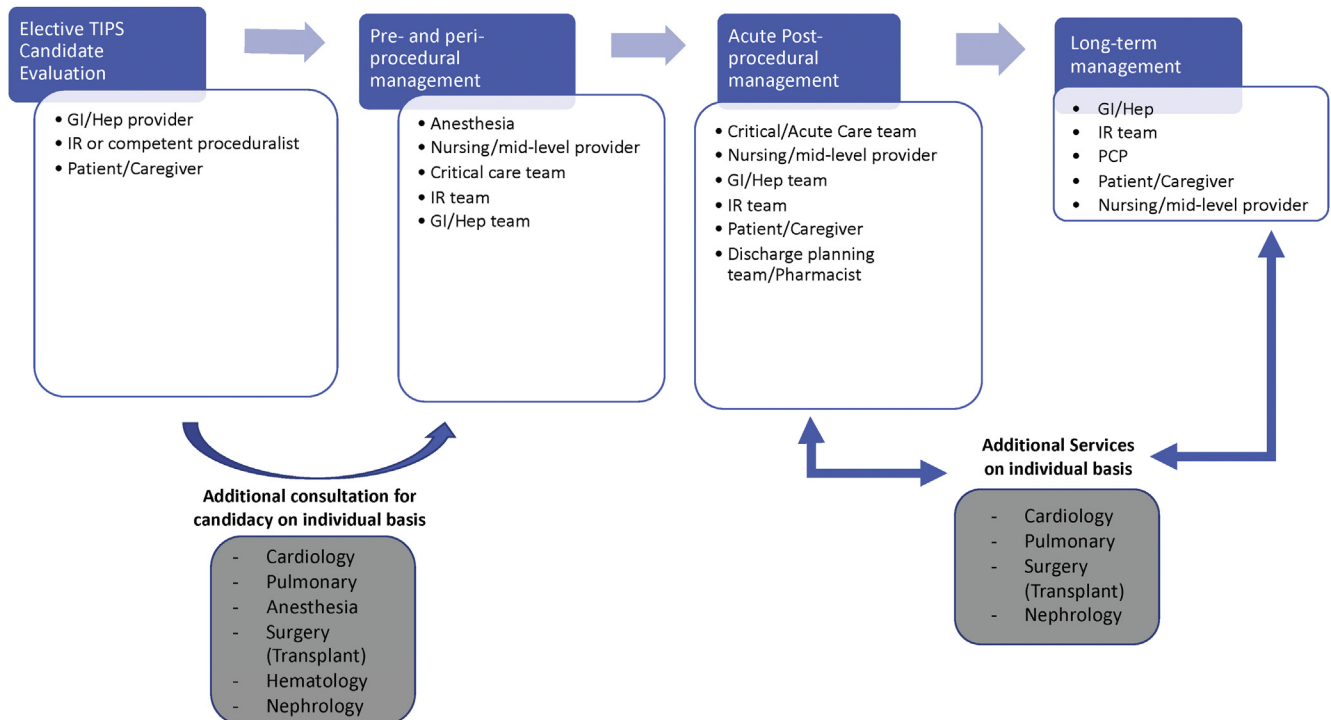
**Question 10. Should periprocedural antibiotics be used routinely in transjugular intrahepatic portosystemic shunt creation?** The use of periprocedural antibiotics will depend on patient (eg, prior biliary instrumentation) or

local risk factors.<sup>56,57</sup> There is insufficient evidence that the routine use of periprocedural antibiotics decreases infectious complications after TIPS creation.

**Question 11. Should transjugular intrahepatic portosystemic shunt creation be performed using general anesthesia or is deep or conscious sedation appropriate?** There is no evidence that the use of any specific type of anesthetic has an impact on procedural success, complication rate, or postprocedure outcomes. The use of general anesthesia, deep sedation, or conscious sedation will depend on patient risk factors and local practices.

**Question 12. Is the use of intravascular ultrasound recommended to assist with the portal vein puncture?** The use of intravascular ultrasound to facilitate access into the portal vein is associated with decreased needle passes through the liver, contrast use, procedure time, time to portal access, and radiation exposure.<sup>58,59</sup> However, no studies have shown that the use of intravascular ultrasound reduces complication rates or improves survival after TIPS creation.

**Question 13. What is the optimal location from which to measure the systemic venous pressure at the time of**



**Figure 1.** Team-based approach to TIPS care. A team-based approach to TIPS is of critical importance at all stages of TIPS planning and management. Initial consideration for decision on TIPS candidacy should involve the patient and corresponding caregiver as well as a gastroenterologist or hepatologist and a proceduralist with competency in TIPS. Complex cases should include consultation with additional specialties (eg, cardiology, pulmonology, transplant surgery, hematology, nephrology) as appropriate. Once a patient is determined to meet criteria for TIPS creation, longitudinal care includes a spectrum of multi-specialty (eg, anesthesia, critical care, IR, GI/hepatology, primary care provider), and multipractitioner providers (eg, nursing, physician, pharmacy, and midlevel providers). GI, gastroenterologist; Hep, hepatology; IR, interventional radiologist; PCP, primary care provider; TIPS, transjugular intrahepatic portosystemic shunt.

*transjugular intrahepatic portosystemic shunt creation?* Either the free hepatic or inferior vena cava (IVC) pressure should be used as the systemic venous pressure when measuring the portosystemic gradient (PSG) before and after TIPS creation. In patients with cirrhosis, the use of free hepatic venous pressure or IVC pressure as the systemic venous pressure, rather than the right atrial pressure (RAP), when calculating the hepatic venous pressure gradient is well validated.<sup>60,61</sup> Studies have shown the efficacy of these measurements when assessing clinical response after TIPS creation.<sup>62–64</sup> These studies also have shown a statistically significant difference between the hepatic venous or IVC pressure compared with the RAP owing to the effect of intra-abdominal pressure. This difference decreases the prognostic value of the PSG when the RAP is used and potentially could lead to underdilation or overdilation of the TIPS stent to achieve a target gradient.<sup>64</sup>

*Question 14. Are there specific technical factors that should be considered to ensure that transjugular intrahepatic portosystemic shunt creation does not adversely influence liver transplant candidacy?* LT candidacy should not be impacted by creation of TIPS. The presence of a patent TIPS in patients undergoing LT is unlikely to negatively impact surgical outcomes, although it may increase surgical complexity.<sup>65–68</sup> During LT, the

presence of TIPS may cause hyperdynamic circulation and increased portal flow,<sup>67,69</sup> but does not impact blood transfusion requirements, surgical time, or hospital length of stay.<sup>65–68</sup> Surgical factors are more favorable with TIPS compared with pretransplant surgical shunts.<sup>66</sup> TIPS malposition may affect up to 20% of transplants,<sup>66,68</sup> therefore, care should be taken to ensure that the TIPS device does not extend into the right atrium and leaves a segment of the portal vein for transplant anastomoses.

**Care of the post-transjugular intrahepatic portosystemic shunt patient.** *Question 15. What is the recommended duration of intensive postprocedure monitoring?* Most patients may be monitored safely overnight in an acute care unit after TIPS creation. Patients at high risk for TIPS-related decompensation based on patient factors (eg, cardiac dysfunction, overt HE) or immediate complications based on intraprocedural events (eg, transsplenic approach) may require a higher level of care.

*Question 16. What early testing is recommended after transjugular intrahepatic portosystemic shunt creation and at what interval?* Laboratory evaluation to assess for bleeding, hepatic dysfunction, and to allow calculation of MELD score before discharge after TIPS creation is considered standard of care (Supplementary Discussion section). Because early TIPS thrombosis is rare in the era of ePTFE-covered TIPS<sup>41,46</sup> and early Doppler

ultrasound of ePTFE-covered TIPS flow is obscured by the presence of microbubbles,<sup>70,71</sup> early post-TIPS Doppler ultrasound interrogation is unlikely to impact clinical decisions and is not recommended routinely. However, early imaging in select patients with a high risk of early thrombosis (eg, underlying thrombophilia) may be appropriate.

**Question 17.** *Should transjugular intrahepatic portosystemic shunt venography and intervention be based on ultrasound, clinical findings, or both?* The decision to perform TIPS venography and intervention should depend on the indication for TIPS creation due to low specificity (33%–95%) and high false-positive rates (50%) of Doppler ultrasound for detecting TIPS dysfunction.<sup>70,72</sup> In patients who have undergone TIPS for management of varices, TIPS stenosis will increase the PSG and risk for subsequent variceal hemorrhage.<sup>73</sup> Clinical (eg, ascites) or Doppler ultrasound findings suggesting stenosis in this cohort should prompt TIPS venography and manometry, in which stenosis can be confirmed and intervened upon or refuted.

In patients who undergo TIPS for ascites/HH and with an absence of clinically apparent ascites/HH, intervention based on Doppler ultrasound findings suggesting TIPS stenosis depends on other clinical factors. If ascites/HH is well controlled, confirmation of TIPS stenosis by venography and manometry may not necessarily prompt intervention.

In patients who undergo TIPS to reestablish portal vein patency, routine scheduled TIPS venography and manometry ± intervention is suggested within 1 to 2 months after portal vein recanalization and TIPS creation to assess for residual thrombus, perform additional portal vein recanalization, and embolize spontaneous competing portosystemic shunts as needed to help maintain portal vein patency ([Supplementary Discussion section](#)).<sup>74</sup>

**Question 18.** *What are the optimal techniques for altering transjugular intrahepatic portosystemic shunt flow when intervention is required?* When an indication to change the PSG is identified, stepwise dilation of a controlled expansion stent is the least invasive way to achieve this goal. When a TIPS has been dilated to its maximum potential diameter, the next step relies on individualized decision making. Interventions to further decrease the PSG include parallel TIPS creation and medical therapy. Multiple techniques have been described to increase the PSG by constraining the flow lumen of pre-existing TIPS. Comparative data between TIPS reduction techniques do not exist.

**Question 19.** *Who should see patients with transjugular intrahepatic portosystemic shunt in follow-up evaluation?* We recommend a multidisciplinary approach to post-TIPS management involving a gastroenterologist/hepatologist and a proceduralist given the need for ongoing liver care as well as monitoring for any post-procedural complications and the potential need for TIPS revision ([Figure 1](#)).<sup>15,16</sup>

### *Specific Considerations for Transjugular Intrahepatic Portosystemic Shunt by Indication*

The approach to TIPS creation should differ depending on clinical indication because the optimal balance between efficacy and morbidity may vary ([Table 2](#)).

**Transjugular intrahepatic portosystemic shunt in ascites or hepatic hydrothorax.** **Question 1.** *What is the optimal technical approach to transjugular intrahepatic portosystemic shunt creation among patients with cirrhosis and refractory ascites?* In the setting of elective TIPS for ascites, there is time to carefully titrate the amount of portal decompression obtained while monitoring for shunt morbidity, including HE. After weighing the advantages and disadvantages of various approaches ([Supplementary Table 2](#)), we favor the creation of a small-diameter TIPS (8 mm, based on the minimum 8-mm diameter with current generation on-label use of controlled expansion stent graft) followed by progressive dilation, if needed, based on clinical response at 6-week intervals. This approach minimizes the risks of overshunting and offers the greatest opportunity for procedural uniformity.

**Question 2.** *Is transjugular intrahepatic portosystemic shunt associated with better outcomes than serial large-volume paracentesis for the treatment of refractory ascites?* Compared with large-volume paracentesis (LVP), TIPS is associated with improved control of ascites, but an increased risk of HE ([Supplementary Table 3](#)).<sup>4,75–80</sup> The impact of TIPS on survival has been more controversial, with some,<sup>4,76,79,80</sup> but not all, RCTs showing improved transplant-free survival (TFS).<sup>77,78</sup> Several subsequent meta-analyses<sup>81–86</sup> have confirmed the superiority of TIPS compared with serial LVP in the prevention of recurrent ascites, but remained split in terms of TFS benefit, depending on methodology and whether one potentially outlier<sup>75</sup> article was included ([Supplementary Table 3](#) and [Supplementary Discussion section](#)).

**Question 3.** *Is there a threshold of liver dysfunction above which transjugular intrahepatic portosystemic shunt for refractory ascites should be contraindicated and how should it be defined?* Among patients with cirrhosis and RA, increased bilirubin, MELD score, and CTP class C cirrhosis are associated with increased post-TIPS complications including mortality.<sup>76,84–86</sup> However, strong evidence for a specific cut-off value for any of these parameters is lacking ([Supplementary Table 3](#) and [Supplementary Discussion section](#)).

**Question 4.** *What is the impact of age on candidacy for transjugular intrahepatic portosystemic shunt for refractory ascites?* Among patients with cirrhosis and RA, advanced age is associated with increased post-TIPS complications including HE and mortality. However, there are no studies that provide strong evidence of a specific cut-off value above which TIPS should be considered contraindicated ([Supplementary Table 3](#) and [Supplementary Discussion section](#)).

**Question 5.** *What is the role of transjugular intrahepatic portosystemic shunt in patients with ascites that is not refractory?* TIPS should be considered in selected

patients with at least 3 LVPs for tense ascites in a year despite optimal medical therapy.<sup>1</sup> Among RCTs comparing TIPS vs LVP, those which included patients not fulfilling strict criteria of RA showed improved TFS<sup>4,79</sup> or a trend for improved TFS.<sup>76</sup> Among trials including patients with RA with a strict definition, only 1 showed improvement in survival. The specific definitions of non-RA vary by trial (Supplementary Table 3).

**Question 6.** *What is the role of transjugular intrahepatic portosystemic shunt in hepatic hydrothorax?* For patients with HH on maximal medical therapy requiring frequent thoracentesis or those with significant clinical symptomatology (eg, hypoxia, resting dyspnea), TIPS should be considered.<sup>1</sup> TIPS creation for refractory HH leads to complete response in more than 50% of patients, with partial responses observed in approximately 20%, similar to response rates for RA.<sup>87-91</sup> Predictors of inferior outcomes of TIPS for recurrent HH are similar to those observed in TIPS placed for RA, including older age, severity of liver disease, and renal insufficiency.<sup>5,17,89</sup>

**Question 7.** *Is prior liver transplantation a contraindication to transjugular intrahepatic portosystemic shunt for refractory ascites? Is transjugular intrahepatic portosystemic shunt superior to surgical shunt, serial large-volume paracentesis, or splenic artery embolization in liver transplant recipients with refractory ascites?* There is insufficient evidence to support any recommendation regarding therapy (TIPS and other modalities) in LT recipients with RA (Supplementary Discussion section). The technical success for TIPS creation after LT is similar to that observed in patients pretransplant; however, the clinical efficacy is inferior to that observed in RA pre-LT.<sup>92-94</sup> Careful assessment for the underlying etiology of ascites should be undertaken before TIPS creation and the timing after LT should be considered.

**Question 8.** *What is the expected timeline for transjugular intrahepatic portosystemic shunt to be effective for reduction of ascites/hepatic hydrothorax?* In detailed pathophysiological studies, a negative sodium balance (under a very strict low-sodium diet) is achieved at approximately 4 weeks after TIPS.<sup>95</sup> With a less-restrictive diet, this level of natriuresis might not be achieved and patients may require the use of diuretics after TIPS. If using a staged approach to TIPS (progressive stent dilation from 8 to 9 to 10 mm diameter based on clinical response), the decision to increase TIPS diameter should not be made before 6 weeks.

**Transjugular intrahepatic portosystemic shunt in variceal bleeding.** **Question 1.** *When is transjugular intrahepatic portosystemic shunt indicated in acute variceal hemorrhage?* TIPS is recommended in patients with cirrhosis with uncontrolled acute variceal hemorrhage at endoscopy or who have successfully undergone endoscopic variceal ligation but who rebleed at any time during admission (after endoscopy).<sup>73</sup> In addition, select patients with CTP class C cirrhosis or CTP B with active bleeding at endoscopy are at highest risk for rebleeding and may benefit from early or pre-emptive TIPS within

72 hours of admission to improve survival (Supplementary Discussion section).<sup>2,3,96-101</sup>

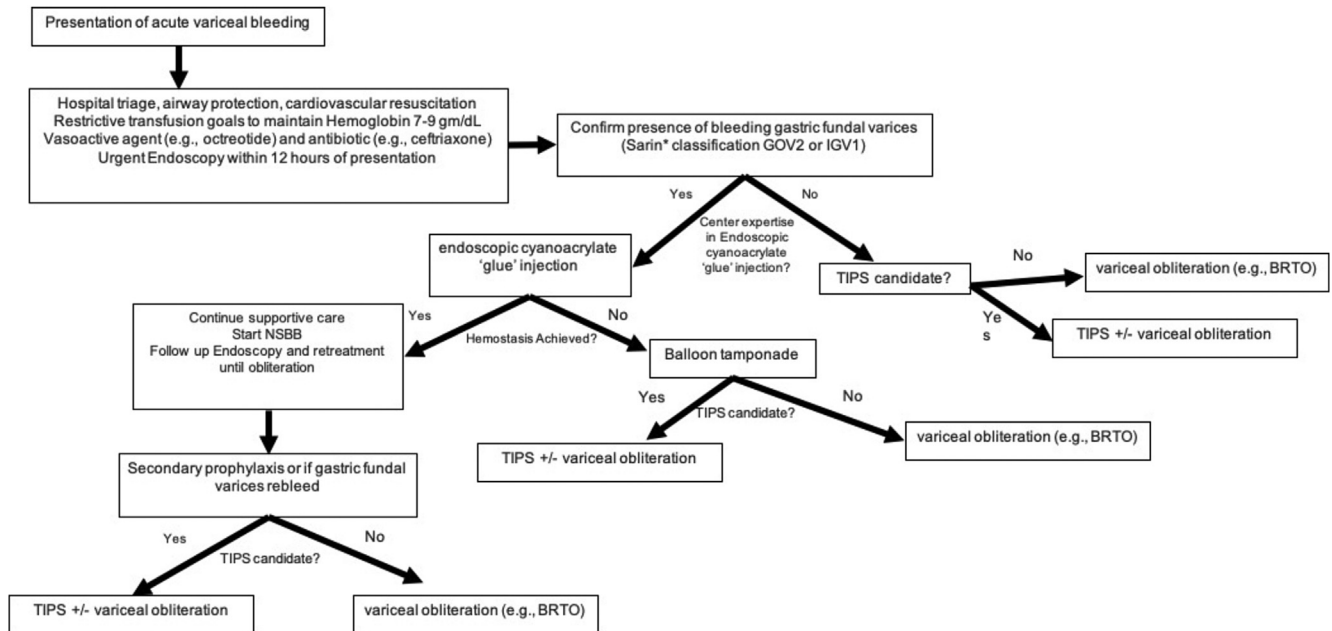
**Question 2.** *When should transjugular intrahepatic portosystemic shunt be used in the management of bleeding gastric fundal varices?* Variceal obliteration/embolization with or without TIPS should be considered for bleeding gastric fundal varices (GV) if unable to be managed endoscopically (Figure 2). TIPS combined with variceal obliteration may be associated with a decrease in rebleeding rates,<sup>102-104</sup> particularly when the pre-treatment PSG is less than 12 mm Hg. The most appropriate management for bleeding from GV will depend on the vascular anatomy of the portal venous system and center expertise (Supplementary Discussion section).<sup>94</sup>

**Question 3.** *What are the procedural considerations in transjugular intrahepatic portosystemic shunt creation for variceal hemorrhage?* The main procedural factors to consider are the target PSG, the optimal shunt diameter, and whether or not to perform concurrent variceal embolization. When placing a TIPS for variceal hemorrhage, the risk of rebleeding is decreased by obtaining an absolute PSG less than 12 mm Hg or a relative reduction in the PSG of at least 50% to 60% from the pre-TIPS gradient.<sup>10,63,105-107</sup> These thresholds are best studied in bleeding from esophageal varices because GV and other ectopic varices may bleed at a lower PSG.<sup>108</sup> Studies using shunt diameter as a predictor of rebleeding rates have shown mixed results.<sup>10,31,45</sup> Concurrent embolization at the time of TIPS creation decreases the risk of rebleeding in variceal hemorrhage.<sup>109-114</sup> There currently are insufficient data to show superiority of a specific embolic agent (Supplementary Discussion section).

**Question 4.** *How should patients be monitored after transjugular intrahepatic portosystemic shunt creation for variceal hemorrhage?* Imaging surveillance with Doppler ultrasonography after TIPS for variceal hemorrhage is recommended because TIPS stenosis/occlusion can lead to recurrent variceal hemorrhage. The optimal frequency of surveillance is not known, but typically is performed 1 to 6 months after TIPS initially, and then every 6 to 12 months thereafter. If TIPS stenosis/occlusion is suspected based on imaging or recurrent symptomatic portal hypertension (eg, ascites, variceal bleeding), a TIPS venogram is indicated with consideration for TIPS revision. Nonselective  $\beta$  blockade can reduce the PSG even after TIPS,<sup>115</sup> and may be considered as an adjunctive treatment.

**Novel indications for transjugular intrahepatic portosystemic shunt.** **Question 1.** *Does preoperative transjugular intrahepatic portosystemic shunt creation in patients with portal hypertension improve perioperative outcomes after nontransplant abdominal surgery?* The use of prophylactic TIPS to prevent bleeding complications or improve survival after elective non-LT surgery is not recommended. Specific patient and surgical factors may warrant TIPS creation in individual cases (Supplementary Table 5).<sup>116,117</sup> The theoretical benefits of portal decompression before abdominal, non-LT





**Figure 2.** Proposed approach to gastric fundal variceal bleeding in cirrhosis. Management of gastric fundal variceal bleeding depends on the admitting center’s expertise as well as the patient’s portal vascular anatomy and severity of their liver disease. Initial management is similar to the approach for all patients presenting with acute gastrointestinal bleeding, particularly in the setting of known portal hypertension. Once gastric varices (GV) are confirmed as the bleeding source, use of endoscopic therapy with glue injection can be considered depending on the proceduralist’s expertise. If hemostasis is not achieved, TIPS evaluation ± variceal obliteration then should be considered. In addition, TIPS ± variceal obliteration should be considered for secondary prophylaxis or if there is GV rebleeding. BRTO, balloon-occluded retrograde transvenous obliteration; GOV, gastroesophageal varices; IGV, isolated gastric varices; NSBB, nonselective β-blocker; TIPS, transjugular intrahepatic portosystemic shunt. \*The Sarin classification is based on data from Sarin et al.<sup>208</sup>

surgery (eg, ascites control) must be weighed against the potential risks of TIPS in the preoperative setting (eg, overt HE, liver insufficiency).

**Question 2.** Does transjugular intrahepatic portosystemic shunt creation in patients with cirrhosis and portal vein obstruction facilitate listing for liver transplantation and/or improve outcomes after liver transplant? The specific degree of portal vein obstruction resulting in exclusion from LT candidacy varies by center. Although partially occlusive PVT can be extracted easily at surgery, this is not the case when complete obliteration of the lumen has occurred, particularly when surrounded by venous cavernoma. Increased case complexity and inferior outcomes are reported for LT in patients with extensive chronic PVT.<sup>118</sup> Successful recanalization of the main portal vein using a transhepatic and transsplenic approach followed by TIPS creation to re-establish a patent main portal vein has been reported in a single-center case series without a control population.<sup>74</sup>

**Question 3.** Does transjugular intrahepatic portosystemic shunt creation prevent or reduce portal hypertensive complications in patients with noncirrhotic portal hypertension resulting from extrahepatic portal vein obstruction? Acute or chronic extrahepatic PVT are associated with significant morbidity and may require urgent decompression. In general, TIPS creation is technically feasible and effective in reducing portal hypertension in patients with PVT, especially in patients with

extensive PVT and bowel ischemia (Supplementary Table 5).<sup>119,120</sup> There is a lack of studies comparing revascularization with or without TIPS creation with anticoagulation alone in patients with PVT (Supplementary Discussion section).

**Question 4.** Does transjugular intrahepatic portosystemic shunt creation in patients with idiopathic noncirrhotic portal hypertension and without extrahepatic portal vein obstruction prevent or reduce portal hypertensive complications? Limited series evaluating outcomes after TIPS creation in patients with idiopathic noncirrhotic portal hypertension, including 1 case-control series with a comparator group of patients with cirrhotic portal hypertension, have shown similar technical outcomes and control of portal hypertensive complications compared with patients with cirrhotic portal hypertension. It is unclear whether patients with idiopathic noncirrhotic portal hypertension have lower rates of overt hepatic encephalopathy and mortality compared with patients with cirrhotic portal hypertension (Supplementary Table 5).<sup>121–123</sup>

**Question 5.** Does transjugular intrahepatic portosystemic shunt creation improve outcomes in patients with Budd–Chiari syndrome? In patients with Budd–Chiari syndrome (BCS) who remain symptomatic or without improving liver function despite medical therapy and who are not candidates for percutaneous revascularization of the hepatic venous outflow tract, creation of a percutaneous portosystemic shunt, either TIPS or direct

intrahepatic portosystemic shunt, should be strongly considered.<sup>124</sup> TIPS creation is technically successful in 84% to 100% of BCS cases,<sup>125-130</sup> controls portal hypertensive complications, and is associated with good survival (72% overall and TFS).<sup>125-129,131,132</sup> Importantly, venoplasty with or without stenting should not preclude subsequent creation of a percutaneous portosystemic shunt in patients who remain symptomatic after initial revascularization ([Supplementary Discussion section](#)). Finally, in patients with BCS, re-intervention may be needed to maintain or restore TIPS patency because primary patency rates with ePTFE-covered TIPS for BCS varies widely (5-year primary patency, 45%-91%).<sup>133,134</sup>

### Cardiopulmonary, Renal, and Neurologic Considerations in Transjugular Intrahepatic Portosystemic Shunt

**Cardiopulmonary considerations in transjugular intrahepatic portosystemic shunt.** Cardiac decompensation after TIPS varies from 1% in 1 week<sup>135</sup> to 20% in 1 year.<sup>136</sup> The underlying pathophysiology is multifactorial, involving pre-TIPS subclinical cardiac dysfunction (eg, cirrhotic cardiomyopathy) and post-TIPS worsening in hyperdynamic circulation given increased preload and cardiac output with concomitantly decreased systemic vascular resistance.<sup>137</sup> Recommendations for cardiopulmonary considerations in TIPS are summarized in [Table 3](#).

*Question 1. What cardiopulmonary testing is indicated before elective transjugular intrahepatic portosystemic shunt?* Cardiac risk assessment before TIPS is essential and should incorporate contemporary echocardiographic measurements for left ventricular (LV) and right ventricular (RV) function, with particular attention to the recently updated criteria for cirrhotic cardiomyopathy ([Supplementary Table 6](#)).<sup>138,139</sup> An electrocardiogram is warranted for evaluation of arrhythmia if tachycardia or bradycardia is noted on the preprocedure assessment.

*Question 2. Does cirrhotic cardiomyopathy or diastolic dysfunction confer a risk for post-transjugular intrahepatic portosystemic shunt heart failure?* In patients undergoing TIPS creation, evaluating the presence and severity of systolic and/or diastolic dysfunction is an important part of risk stratification for adverse cardiac outcomes. There are limited data regarding TIPS outcomes in patients with LV ejection fraction less than 50%. Impaired global longitudinal strain, reflective of subclinical systolic dysfunction, is associated with poor post-TIPS survival.<sup>140</sup> Older studies have shown conflicting results about the impact of diastolic dysfunction on TIPS outcomes.<sup>141,142</sup> However, the new diastolic dysfunction criteria<sup>138</sup> have been found to be predictive of increased mortality and cardiac events after TIPS.<sup>136</sup>

*Question 3. Can transjugular intrahepatic portosystemic shunt be performed safely in patients with moderate or severe portopulmonary hypertension (ie, mean pulmonary artery pressure >35 mm Hg, pulmonary vascular*

*resistance >3 wood units)?* TIPS creation, if pulmonary hypertension is present, has the potential to precipitate right-sided HF and/or be ineffective at decreasing portal pressure.<sup>143,144</sup> There are no published data regarding TIPS in patients with portopulmonary hypertension (POPH). TIPS acutely increases RAP by 3 to 5 mm Hg in those without POPH.<sup>145-148</sup> One study specifically showed that RAP before and after TIPS of greater than 14.5 mm Hg and greater than 21.5 mm Hg, respectively, was associated with increased post-TIPS mortality, although whether these patients had POPH specifically is unknown.<sup>145</sup> Thus, significant caution should be exercised when considering TIPS in patients with moderate/severe POPH on treatment or increased RAP.

*Question 4. Can severe tricuspid regurgitation be prohibitive of transjugular intrahepatic portosystemic shunt creation?* Tricuspid regurgitation (TR) usually reflects volume overload and/or pressure overload from conditions resulting in pulmonary hypertension in patients with a normal tricuspid valve. Careful assessment of TR etiology is necessary to determine if TIPS risk is prohibitive. When volume overload is suspected, volume optimization is warranted before reassessment. In some cases, chronic volume overload results in RV dysfunction and tricuspid annular dilatation, leading to persistent moderate to severe functional TR, which can be prohibitive of TIPS.

*Question 5. Can a transjugular intrahepatic portosystemic shunt treat hepatopulmonary syndrome?* Given the risks associated with TIPS creation, current evidence does not support routine use of TIPS for treatment of hepatopulmonary syndrome alone ([Supplementary Discussion section](#)).<sup>149-151</sup>

*Question 6. Does stent size affect risk for post-transjugular intrahepatic portosystemic shunt heart failure in high-cardiac-risk patients?* A recent study showed that an 8-mm stent was associated with better survival than a 10-mm stent; however, cardiac deaths were not specified.<sup>152</sup> Generally, larger stent size leads to higher cardiac venous return, resulting in potentially higher decompensation risk. Thus, in patients with systolic and/or diastolic dysfunction or mild POPH who are undergoing TIPS, the desired PSG must be balanced with the potential risk for worsening cardiac dysfunction.

*Question 7. Is there a need for post-transjugular intrahepatic portosystemic shunt echocardiographic surveillance?* There are prompt incremental changes after TIPS involving cardiac output, cardiac index, RAP, as well as LV and RV end-diastolic and end-systolic volumes.<sup>137,153-155</sup> These changes peak at 3 months after TIPS, and tend to resolve within 6 to 12 months after TIPS in some, but not all, patients.<sup>153,156,157</sup> Surveillance in high-risk patients (eg, prior HF, increased RAP, LV dysfunction) may be beneficial to guide pre-emptive interventions (eg, initiation of HF guideline-directed anti-remodeling therapy).

**Renal considerations in transjugular intrahepatic portosystemic shunts.** The true incidence of acute kidney injury (AKI) or acute kidney disease (AKD) after TIPS

and the potential benefit in persons with chronic kidney disease (CKD) is unknown given a wide spectrum of indication and urgency for TIPS, the heterogeneity in measurement of kidney function (eg, measured vs estimated glomerular filtration rate [GFR], serum creatinine [sCr]), definitions of AKI or CKD, and patient selection. We suggest considering the primary indication, individualized risk factors, and physiologic goals of the intervention when considering TIPS creation in patients with kidney dysfunction (Table 3).

**Question 1. What is the best marker to assess kidney function before or after a transjugular intrahepatic portosystemic shunt?** Kidney function should be assessed before TIPS either through measurement of sCr or GFR (estimated or measured).<sup>75,158-162</sup> A change in GFR may best capture changes in kidney function. The limitations of sCr in cirrhosis have been well documented (Supplementary Discussion section).<sup>163</sup>

**Question 2. Is there an absolute cut-off value for kidney function for which a transjugular intrahepatic portosystemic shunt is contraindicated?** Kidney function (measured by sCr) is included in several predictive models of outcomes after TIPS.<sup>17-22,164,165</sup> Increased sCr is a risk factor for post-TIPS HE.<sup>166</sup> However, there is insufficient evidence to recommend an absolute sCr, CKD stage, or presence/absence of renal replacement therapy in which TIPS creation is contraindicated.

**Question 3. What can be done to prevent kidney complications after a transjugular intrahepatic portosystemic shunt?** Data regarding kidney protection strategies surrounding TIPS are lacking (Supplementary Discussion section). Maintenance of intravascular volume with albumin infusion in the setting of LVP if performed with TIPS creation may help prevent kidney dysfunction secondary to circulatory impairment.<sup>1,167-169</sup> Judicious use of iodinated contrast agents may minimize the risk of contrast nephropathy. The development of AKI and progression to AKD and CKD may not be recognized immediately after TIPS. The recognition-action-result framework for secondary prevention and follow-up evaluation based on AKI/AKD severity as outlined by the Acute Disease Quality Initiative may identify those at highest risk for progression and allow for early mitigation.<sup>170</sup>

**Question 4. What is the role of a transjugular intrahepatic portosystemic shunt for hepatorenal syndrome?** Data on TIPS in patients with HRS is limited.<sup>171</sup> The quality of available studies is low owing to small sample size and significant heterogeneity (Supplementary Discussion section). Larger randomized trials applying the most recent definition of HRS-AKI are needed before TIPS can be recommended for this indication.

**Hepatic encephalopathy and transjugular intrahepatic portosystemic shunt.** **Question 1. What is the risk of overt hepatic encephalopathy after a transjugular intrahepatic portosystemic shunt and what patient factors contribute to its development?** The incidence of overt HE is

estimated between 25% and 50% (Supplementary Discussion section).<sup>3,4,97,98,172-174</sup> Notably, most studies excluded patients with a history of recurrent overt HE. Patient factors for the development of post-TIPS overt HE includes prior HE, advanced liver dysfunction (CTP class C, MELD score >18),<sup>4,97,98,175,176</sup> older age,<sup>166</sup> increased creatinine level,<sup>166</sup> hyponatremia, and sarcopenia.<sup>177,178</sup>

**Question 2. What social factors should be considered a contraindication to elective transjugular intrahepatic portosystemic shunt as it relates to overt hepatic encephalopathy?** Patients and family members should be counseled about the manifestations of overt HE.<sup>179,180</sup> In patients who have poor social support, and therefore may be at greater risk of harm owing to post-TIPS HE, we favor non-TIPS management options. This does not apply to urgent TIPS for variceal bleeding, for which survival and prevention of rebleeding remains the priority.

**Question 3. What is the role for formal evaluation for covert or minimal hepatic encephalopathy before an elective transjugular intrahepatic portosystemic shunt?** The diagnosis of covert HE has been associated with a greater risk of post-TIPS HE,<sup>173,181,182</sup> and impaired health-related quality of life (Supplementary Discussion section).<sup>183-185</sup> In patients being considered for elective TIPS, a diagnosis of covert HE should guide discussion of the pros and cons of TIPS creation with patients, family members, and clinical teams.

**Question 4. What transjugular intrahepatic portosystemic shunt stent diameter should be considered with regard to limiting post-transjugular intrahepatic portosystemic shunt hepatic encephalopathy?** Smaller shunts (eg, 8 mm vs 10 mm) may decrease overt HE, but also may be less effective for portal decompression (Supplementary Discussion section).<sup>10,31,186-188</sup>

**Question 5a. Is there a role for collateral embolization at the time of a transjugular intrahepatic portosystemic shunt to prevent hepatic encephalopathy?** In patients undergoing elective TIPS for ascites/HH, embolization of spontaneous portosystemic shunts (SPSS) greater than 6 mm may be considered to reduce the risk of post-TIPS HE. Large SPSS have been associated with an increased risk of overt HE and mortality in patients with cirrhosis (Supplementary Discussion section).<sup>189-192</sup>

**Question 5b. Is there a role for transjugular intrahepatic portosystemic shunt with shunt embolization in the management of refractory hepatic encephalopathy related to presumed portosystemic shunting?** In select patients with large (>6 mm) SPSS and refractory HE, we recommend that shunt embolization be considered. In those who develop portal hypertensive-associated complications after shunt embolization, a small-caliber TIPS creation could be considered. The prevalence of SPSS approaches 70% among patients with cirrhosis and with persistent overt HE.<sup>193</sup> Evidence on retrograde transvenous obliteration or embolization of SPSS for treatment of overt HE is limited to small series but with success rates of 59% to 100% free of overt HE.<sup>194-199</sup>

**Table 4.** Future Research Directions Related to TIPS

Area	Knowledge gap/future research
Standard setting in TIPS	<p>Prospective data are needed to establish threshold INR and platelet levels for safe TIPS creation as well as to investigate the role of fibrinogen and thromboelastography in the assessment of procedural bleeding risk.</p> <p>Prospective data could validate societal recommendations regarding the use of periprocedural antibiotics. Currently, these recommendations are based on expert consensus rather than studies showing improved outcomes or decreased infectious complications.</p> <p>Prospective data are needed to assess whether the use of intravascular ultrasound to assist with portal vein puncture leads to decreased complications or improved survival.</p> <p>Is there a MELD threshold for TIPS? Future studies require a large size, diverse geographic regions/multicenter studies, increased representation of populations with ascites, higher MELD scores, and standardized procedural techniques.</p> <p>Prospective data are needed to determine and assess quality indicators throughout the course of TIPS planning and for long-term management of post-TIPS patients.</p>
Ascites/hepatic hydrothorax	<p>Prospective data to understand the best approach to elective TIPS creation for refractory ascites, which balances safety and efficacy; in particular, more data are needed to understand whether a staged approach is safest, and whether the best target during the procedure should be stent diameter, decreases in HVPG, or changes in portal flow.</p> <p>Better refinement of parameters of liver function, such as MELD or total bilirubin, that should be used in risk stratification or as a contraindication to elective TIPS creation is needed.</p> <p>The role of TIPS creation in patients with ascites that is not refractory requires further study in prospective randomized controlled trials.</p> <p>Prospective data are needed to determine whether there is a clinical benefit to universal post-TIPS surveillance Doppler ultrasound to monitor for TIPS stenosis in patients who undergo TIPS for refractory ascites.</p> <p>A better understanding of the role of TIPS creation in transplant recipients with ascites is needed, including refinement of candidate selection criteria and comparison with other therapeutic strategies.</p>
Variceal bleeding	<p>Prospective data are needed to further refine criteria for pre-emptive TIPS, particularly studies that include a range of CTP class and stratify by etiology of cirrhosis.</p> <p>The timing of rescue TIPS creation and futility (or not) of the procedure in advanced CTP class C cirrhosis (score, 14–15) remains to be established.</p> <p>The timing of TIPS creation in patients with PVT diagnosed at the time of variceal hemorrhage needs to be established.</p> <p>Prospective data are needed on endoscopic therapy vs covered TIPS with/without variceal obliteration vs variceal obliteration alone to prevent GV rebleeding.</p> <p>Prospective data are needed to establish whether use of a small-diameter covered TIPS stent with and without variceal obliteration to control bleeding is efficacious to reduce HE.</p> <p>Prospective data are needed to determine predictors of GV rebleeding and HE after TIPS both with and without variceal obliteration.</p> <p>Data are needed to support standardization of surveillance protocols after GV treatment.</p> <p>Prospective data are needed to identify the target PSG after intervention to prevent GV rebleeding.</p> <p>Data are needed to determine the optimal frequency of surveillance for TIPS stenosis/occlusion.</p> <p>Prospective data are needed to determine whether long-term use of nonselective <math>\beta</math>-blockers after TIPS reduces risk for recurrent variceal hemorrhage.</p>
Novel indications for TIPS	<p>Multicenter studies, ideally controlled, evaluating portal hypertensive complications and post-liver transplant outcomes in patients with portal vein obstruction pre-LT who undergo portal vein reconstruction and TIPS creation before LT.</p> <p>Multicenter controlled studies evaluating safety and efficacy of medical and invasive interventions (including TIPS) in patients with symptomatic noncirrhotic portal hypertension resulting from extrahepatic portal vein obstruction.</p> <p><b>Budd–Chiari syndrome</b></p> <p>In the minority of patients in whom anticoagulation alone improves liver function and results in resolution of portal hypertensive complications, does a risk for progressive liver failure persist? If so, can this be avoided by earlier percutaneous intervention?</p> <p>Over what timeframe and based on what specific criteria should progression between stepwise management progress?</p> <p>What factors predict failure of anticoagulation alone, such that a patient presenting with BCS would proceed to venoplasty/stenting or TIPS (based on anatomy) immediately?</p> <p>In which patients should transjugular portosystemic shunting be avoided and urgent liver transplantation be the primary nonmedical therapy used?</p> <p><b>Long-term PV access</b></p> <p>Safety and efficacy of creating TIPS as an easily accessible intermediate or long-term route for portal infusion therapy (ie, portal chemoperfusion)</p>

Table 4. Continued

Area	Knowledge gap/future research
Cardiopulmonary considerations	<p>Utility of new cardiac imaging modalities (eg, MRI and PET) in pre-TIPS cardiac risk assessment and post-TIPS cardiac surveillance</p> <p>Post-TIPS changes in cirrhotic cardiomyopathy, its components, and severity</p> <p>Evolution of right heart function and pulmonary vascular hemodynamics after TIPS in patients with mild portopulmonary hypertension</p> <p>Role of cardiac biomarkers in post-TIPS surveillance</p> <p>Impact of post-TIPS echocardiographic surveillance on cardiac decompensation and survival</p> <p>Effect of TIPS on cardiac function after the first year post-TIPS</p> <p>The interplay between stent size and cardiac function post-TIPS</p> <p>Impact of valvular heart disease on TIPS outcomes</p>
Renal considerations	<p>What drivers of MELD or MELD-Na dictate outcomes? For the same MELD/MELD-Na score, does a creatinine-predominant MELD or MELD-Na have different outcomes compared with other drivers of MELD/MELD-Na score?</p> <p>What is the role of novel biomarkers in prediction of kidney outcomes after liver transplantation?</p> <p>What is the role of TIPS in patients with CKD, and those with sarcopenia?</p> <p>What is the role of periprocedure vasoconstrictor use to prevent kidney dysfunction?</p>
Hepatic encephalopathy and TIPS	<p>Objective metrics beyond patient characteristics and laboratory values are needed to better predict post-TIPS HE</p> <p>Future studies investigating the effect of medically controlled covert HE on post-TIPS OHE are necessary</p> <p>Future prospective RCTs are needed to investigate the role for medical prophylaxis to prevent post-TIPS OHE</p> <p>The indication of TIPS for embolization of large portosystemic shunts in the management of uncontrolled OHE requires further study</p>

CKD, chronic kidney disease; CTP, Child-Turcotte-Pugh; GV, gastric varices; HE, hepatic encephalopathy; HVP, hepatic venous pressure gradient; INR, international normalized ratio; LT, liver transplantation; MELD, model for end-stage liver disease; MELD-Na, model for end stage liver disease with serum sodium; MRI, magnetic resonance imaging; OHE, occult hepatic encephalopathy; PET, positron emission tomography; PSG, portosystemic gradient; PV, portal vein; PVT, portal vein thrombosis; RCT, randomized controlled trial; TIPS, transjugular portosystemic shunt

*Question 6a. What is the role for medical prophylaxis to prevent hepatic encephalopathy after a transjugular intrahepatic portosystemic shunt?* RCTs using uncovered TIPS stents showed no difference in the incidence of overt HE in a head-to-head comparison of lactulose, rifaximin, and placebo.<sup>193</sup> A recent RCT with a larger sample size, however, showed a significantly reduced incidence of first episode of HE after TIPS (44.2% vs 59.1%;  $P = .05$ ) in patients without a history of overt HE receiving rifaximin vs placebo as prophylaxis before TIPS.<sup>200</sup>

*Question 6b. What is the recommended medical therapy to treat overt hepatic encephalopathy after a transjugular intrahepatic portosystemic shunt?* Lactulose is recommended for treatment of the first episode of overt HE followed by the addition of rifaximin if there is a subsequent episode of overt HE.<sup>180</sup>

*Question 6c. What is the role for transjugular intrahepatic portosystemic shunt stent reduction/occlusion for treatment of persistent or refractory hepatic encephalopathy?* Severe refractory overt HE that requires shunt reduction occurs in approximately 8% of TIPS recipients.<sup>166</sup> There is no consensus definition of refractory overt HE; however, shunt reduction should be considered when there is persistent HE refractory to medical therapy or at least 3 or more episodes of unprovoked HE requiring hospitalization in the past 3 months.<sup>201</sup> Shunt reduction is effective at reducing

post-TIPS HE; however, recurrence of portal hypertensive complications are likely.<sup>166,202–207</sup>

## Conclusions and Future Directions

Tremendous progress has been made in the application of TIPS creation for the management of portal hypertension. With such a rapid evolution of knowledge, practice-based recommendations also must evolve. These North American consensus recommendations reflect multidisciplinary discussions required around TIPS creation, including consideration of alternatives and best practices to minimize short- and long-term complications and maximize benefit. There are multiple knowledge gaps and areas in need of future research regarding the clinical effectiveness and efficacy of TIPS across indications for use (Table 4). Of particular relevance is the notion of personalized TIPS, in which the benefits and risks of TIPS are tailored to the specific needs of the patient. With the advent of new controlled expansion stents, personalized TIPS is the future of precision medicine for the management of portal hypertension. As the field continues to develop and the research questions identified during this process are answered, the recommendations presented herein will evolve in the context of new data.

## Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at [www.cghjournal.org](http://www.cghjournal.org), and at <https://doi.org/10.1016/j.cgh.2021.07.018>.

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#### Conflicts of interest

These authors disclose the following: Justin R. Boike and Bartley G. Thornburg have received personal fees from W.L. Gore and Associates during the course of this consensus statement; Brett E. Fortune has received consulting fees from W.L. Gore and Associates before this consensus conference; Elizabeth C. Verna has received grants from Salix Pharmaceuticals and serves on the Advisory Board for Gilead Sciences; Jasmohan S. Bajaj has received institutional grants from Bausch Health and serves on the advisory board for Norgine unrelated to this consensus statement; Khashayar Farsad consults for Cook Medical; David C. Mulligan serves as at-large representative on the Governing Board of the American Association for the Study of Liver Diseases and is President of the United Network of Organ Sharing and Organ Procurement and Transplant Network unrelated to this consensus statement; Joseph J. Shatzel has received consulting fees from Aronora, Inc, unrelated to this consensus statement; and Lisa B. VanWagner receives investigator-initiated grant support paid to the institution from W.L. Gore and Associates, serves as an expert witness, receives in-kind research support from AMRA Medical, participates as a member of the Global Liver Institute, serves as a member of the Practice Guidelines committee for the American Association for the Study of Liver Diseases, serves as Chair of the Executive Committee of the American Society for Liver Transplantation Liver and Intestine Community of Practice, is a member of the American Heart Association Epidemiology and Prevention Statistics Committee, serves as topic coordinator for the International Liver Transplantation Society Cardiovascular Disease Interest Group, is a member of the Board of Directors and Medical Advisory Committee for the American Liver Foundation Greater Lakes Region Division, and serves as an Associate Editor for the journals *Clinical Liver Disease* and *Liver Transplantation*. The remaining authors disclose no conflicts.

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## Supplementary Methods

### Scope and Purpose

A consensus-building process was conducted consistent with the standards described in the Appraisal of Guidelines for Research and Evaluation II.<sup>1</sup> The consensus meeting used a modified Delphi approach to achieve consensus.<sup>2</sup> This is a formal group method in which an expert panel discusses and iteratively rates candidate recommendations. In the first round, the experts rated the proposed recommendations individually without meeting as a single group. After a face-to-face meeting in which the preliminary ratings were discussed, a second round of voting was held to re-rate statements through equally weighted voting.

The authors of the consensus statement are members of the Advancing Liver Therapeutic Approaches group. The group is independent of any other organization and, at the time of the conference, was run by a Steering Committee that convened the diverse expert panel of clinicians and researchers from North America to discuss issues relating to the use of TIPS in the management of portal hypertension at the Advancing Liver Therapeutic Approaches consensus conference on October 23, 2020. The broad objective of the conference was to produce expert-based statements and a summary of current knowledge pertaining to the use of TIPS in the clinical management of portal hypertension in adults, and identify evidence gaps to establish research priorities. Conference participants were divided into 7 work groups that were tasked with formulating strategies related to 3 overall domains related to TIPS, as follows: (1) candidate selection, (2) procedural best practices, and (3) post-TIPS management across the following 7 key topic areas: general considerations for TIPS, TIPS in the management of ascites/HH, TIPS in the management of variceal bleeding, novel indications for TIPS, cardiopulmonary considerations of TIPS including management of hepatopulmonary syndrome, renal considerations of TIPS including management of HRS, and HE and TIPS. Each work group determined the scope of their assigned topic by developing a list of targeted questions, which were used to direct the literature review.

### Methods of Review

**Stakeholder involvement.** These practice-based recommendations were developed by 30 physicians and researchers with extensive experience in clinical care and research activities related to the diagnosis or management of complications of portal hypertension and the use of TIPS. The target users are gastroenterologists involved in referring adult patients for consultation for TIPS and subspecialty physicians who provide longitudinal care for adult patients undergoing TIPS creation.

**Rigor of development.** PubMed, EMBASE, and Cochrane were queried for English language reports published between January 1, 1990, and July 1, 2020, using keywords along with terms specific to each working group. Terms were chosen through input from working group leaders and by consultation with a medical librarian. For most groups, results were limited to controlled trials, prospective and retrospective studies, reviews and meta-analyses, and technical reports. However, for some working groups in which the number of studies was limited, case reports were included. This resulted in a total of 2116 articles; 1413 were excluded by working group leaders, and 81 were added based on review of reference lists by the experts for a final total of 784 articles that were reviewed. Because of the broad scope of the PubMed database and the type of articles selected for this review, it should be noted that EMBASE and Cochrane did not supply additional articles beyond what the PubMed search strategy provided.

**PubMed search strings.** *General transjugular intrahepatic portosystemic shunt string.* The TIPS search string was as follows: (TIPS[Title] OR TIPSS[Title] OR "Portasystemic Shunt, Transjugular Intrahepatic"[Majr] OR "transjugular intrahepatic portosystemic stent-shunt"[Title/Abstract] OR "transjugular intrahepatic portosystemic shunt"[Title/Abstract] OR "transjugular intrahepatic portasystemic shunt"[Title/Abstract] OR "transjugular intrahepatic porto-systemic shunt"[Title/Abstract] OR "transjugular intrahepatic portal-systemic shunt"[Title/Abstract] OR "transjugular intrahepatic shunt"[Title/Abstract]) AND ("1990/01/01"[Date - Publication] : "2020/07/01"[Date - Publication]) AND (English[Language]).

*Transjugular intrahepatic portosystemic shunt in ascites.* The TIPS in ascites search string was as follows: (ascites[mesh] OR ascites[tw] OR ascites[tiab] OR hydrothorax[mesh] OR hydrothorax[tiab] OR "hepatic hydrothorax"[tw]).

*Transjugular intrahepatic portosystemic shunt in variceal bleeding.* The TIPS in variceal bleeding search string was as follows: ("Esophageal and Gastric Varices"[Mesh]) AND (hemorrhage[Mesh] OR bleeding[TW] OR bleed[TW]).

*Novel indications in transjugular intrahepatic portosystemic shunt.* The novel indications for TIPS search string was as follows: "abdominal surgery"[TW] OR (Abdomen [Majr] AND surgery[TW]) OR ("chronic liver disease"[TW] AND ("portal vein obstruction"[TW] OR ("Portal vein"[Mesh] AND obstruction[TW]))) OR "portal vein recanalization"[TW] OR "Budd-Chiari"[TW] OR "Budd Chiari"[TW] OR "VOD"[TW] OR "veno-occlusive"[TW] OR "venocclusive"[TW] OR "veno occlusive"[TW].

*Cardiopulmonary implications of transjugular intrahepatic portosystemic shunt.* The cardiopulmonary implications for TIPS search string was as follows: (Heart [Majr] OR cardiac[TW] OR cardiopulmonary[TW] OR "cardiac function"[TW] OR "cardiac implications"[TW] OR "heart failure"[TW] OR "cardiac failure"[TW] OR "heart failure"[Majr] OR MACE[TW] OR "preserved

ejection fraction" [TW] OR "reduced ejection fraction" [TW] OR "systolic dysfunction"[TIAB] OR "diastolic dysfunction"[TW] OR "myocardial strain"[TW] OR "global longitudinal strain"[TW] OR "pulmonary hypertension"[TW] OR "Hypertension, Pulmonary"[Mesh] OR "portopulmonary hypertension"[TW] OR "heart catheterization"[TW] OR "coronary catheterization"[TW] OR "swanz-ganz catheter"[TW] OR "Electrocardiography"[Mesh] OR "pulmonary function test"[TW] OR "myocardial energy expenditure"[TW] OR "exercise testing"[TW] OR "Hypoxia"[Mesh] OR "atrial fibrillation"[MeSH] OR "atrial flutter"[MeSH] OR "Arrhythmias, Cardiac"[Mesh] OR "prolonged QT"[TW] OR "Aortic Valve Stenosis"[Mesh] OR "aortic stenosis"[TW] OR "Aortic Valve Insufficiency"[Mesh] OR "aortic regurgitation"[TW] OR "Mitral Valve Stenosis"[Mesh] OR "mitral stenosis"[TW] OR "Mitral Valve Insufficiency"[Mesh] OR "mitral regurgitation"[TW] OR "Tricuspid Valve Insufficiency"[Mesh] OR "tricuspid regurgitation"[TW] OR "coronary artery disease"[Majr] OR "systemic hemodynamics"[TW] OR "systemic haemodynamics"[TW] OR "Natriuretic Peptide, Brain"[Mesh] OR "hyperdynamic circulation"[TW] OR "Echocardiography"[Mesh] OR "cardiac magnetic resonance imaging"[TW] OR "highly sensitive troponin"[TW]).

*Renal implications of transjugular intrahepatic portosystemic shunt.* The renal implications of TIPS search string was as follows: ("Renal Insufficiency, Chronic"[Mesh] OR "Renal Insufficiency"[Mesh] OR "Hepatorenal Syndrome"[Mesh] OR "Acute kidney injury"[Mesh]).

*Hepatic encephalopathy and transjugular intrahepatic portosystemic shunt.* The HE and TIPS search string was as follows: ("encephalopathy" [Keyword] OR "encephalopathy" [TIAB] OR "hepatic encephalopathy" [Mesh]).

Members of the work groups performed reviews of the available literature in an organized manner and developed a consensus of opinion to distill literature and articulate a research agenda to address important unanswered questions. The level of evidence for all consensus statements was graded using the Oxford Centre for Evidence-based Medicine Levels of Evidence.<sup>3</sup> Between August 2020 and October 2020, each topic was discussed iteratively by a work group of physicians (5–6 physicians per topic) with expertise in the identified topics. Literature was distributed electronically to each work group, assessed with respect to ability to address the proposed topic, evaluated for quality, and then discussed electronically and by teleconference (3–5 meetings per group). Over this series of teleconferences, initial consensus was achieved (100% agreement of working group participants) after ongoing discussions regarding the assigned topic.

**Delphi Survey Method Process and Administration.** Draft consensus recommendations from the individual work groups were compiled into a single survey for distribution to conference participants. Surveys were administered via Northwestern's Research Electronic Data Capture.<sup>4</sup>

Individuals were asked to rate their agreement with each statement based on a 9-point scale, with 1 being strongly disagree and 9 being strongly agree; a "not qualified to answer" option also was available. Participants also were given a free text space for each statement to provide comments and questions. Statements were considered to reach consensus if they achieved a mean of score of greater than 7 (agree) with at least 80% (N = 24) of participants responding to the statement. The decision to require at least 80% of participants ranking a proposed statement was determined by the conference organizers. The rationale for this requirement was that because of the multidisciplinary training of participants (eg, proceduralists and nonproceduralists), there were some items in which respondents did not believe they had the expertise in which to rate the statement (eg, procedural aspects rated by medical practitioners or vice versa). Thus, an 80% response threshold was set in an attempt to represent the target audience, which includes a range of practitioners in both procedural and nonprocedural specialties. All statements receiving a mean score of less than 7 were reviewed during the face-to-face meeting. The final product then was assessed and aggregated at the face-to-face meeting attended by all participants. Statements with clear non-consensus or overlap with other statements based on discussions during the face-to-face meeting were discarded or combined. All remaining statements were voted on formally in a second round of postmeeting voting using the same methodology as described earlier. All postmeeting statements reached consensus in the second round of voting. This article then was drafted based on the final recommendations.

**Clarity of presentation.** The recommendations provided are specific because they clearly identify the target population and provide the level of evidence on which the recommendation is based.

**Applicability.** Results from this conference provide advice and a practical approach for the clinical assessment and management of patients undergoing consideration for TIPS creation. Facilitators and barriers relate primarily to distribution of these recommendations to the broad range of clinicians involved in the care of patients with portal hypertension. Monitoring and auditing of recommendations will be addressed in future studies.

**Editorial independence.** The views of the funders have not influenced the content of the guidance. Competing interests of Advancing Liver Therapeutic Approaches team members have been recorded.

## Supplementary Discussion

### *General Considerations for Transjugular Intrahepatic Portosystemic Shunt*

**Pre-transjugular intrahepatic portosystemic shunt considerations.** *Question 3. Is there a model for end-stage liver disease threshold above which an elective*

*transjugular intrahepatic portosystemic shunt should not be considered?* A multidisciplinary approach, rather than an absolute MELD cut-off value, is recommended to assess TIPS candidacy. The MELD score is the strongest predictor of 90-day mortality after TIPS when compared with MELD-sodium and other scoring systems (eg, Chronic Liver Failure Consortium Acute on Chronic Liver Failure score, CTP score, Emory score, Bonn TIPS Early Mortality score, and Platelet-Albumin-Bilirubin score).<sup>5-10</sup> The MELD score performs better in patients with TIPS for variceal bleeding compared with patients with RA.<sup>11-13</sup> Other studies have examined additional risk factors for poor outcomes with mixed results, including older age and specific numeric MELD score cut-off values.<sup>12-18</sup> Overall, it is difficult to generate definitive conclusions about additional risk factors for death after TIPS from these data. Limitations of studies include sample size, variation in center practices, spectrum of MELD score or selective diagnosis (eg, ascites or variceal bleed), as well as heterogeneous procedural techniques (eg, covered vs uncovered stents, stent diameter and dilation choices, variable volume/type of contrast agents used).<sup>19-23</sup> Thus, determination of TIPS candidacy using the MELD score should take into consideration the relative risk and benefit of TIPS creation to the specific patient under consideration in the context of the clinical indication for performing TIPS, comorbidities, and alternative treatment options.

**Care of the post-transjugular intrahepatic portosystemic shunt patient.** *Question 16. What early laboratory testing and/or imaging is recommended after transjugular intrahepatic portosystemic shunt creation and at what interval?* In all patients undergoing TIPS creation, routine laboratory tests (complete blood count, comprehensive metabolic panel, and prothrombin time/international normalized ratio) should be obtained on the day after TIPS creation. Of note, liver chemistries often are increased the day after TIPS and typically return to preprocedure levels over the ensuing week. Hemoglobin/hematocrit measurement may be obtained on the same day as the TIPS creation, particularly when patient or procedural factors increase the procedure-related bleeding risk or when clinical findings suggest procedure-related bleeding has occurred.

*Question 17. Should transjugular intrahepatic portosystemic shunt venography and intervention be based on ultrasound, clinical findings, or both?* The decision to perform TIPS venography and intervention is dependent on the indication for TIPS creation. In patients who have undergone TIPS creation for the management of varices, either Doppler ultrasound findings suggesting TIPS dysfunction or persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry  $\pm$  intervention. Ultrasound findings suggesting TIPS dysfunction include alterations in intrahepatic portal vein direction of flow, abnormal flow velocities within the TIPS, and persistent (eg, >6 weeks after TIPS) or recurrent ascites. In patients who

have undergone TIPS creation for management of ascites and/or hepatic hydrothorax, persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry  $\pm$  intervention. Medical decision making should be individualized in patients with well-controlled ascites and/or hepatic hydrothorax and ultrasound findings suggesting TIPS dysfunction. In select patients, such as those who have undergone TIPS creation for the management of portal vein thrombosis, scheduled TIPS venography with intervention is suggested in the early (1-2 months) post-TIPS period.

Notably, TIPS stenosis can be a precursor to TIPS occlusion or thrombosis.<sup>24</sup> From a procedural standpoint, intervening upon TIPS stenosis is technically simpler than intervening upon TIPS thrombosis. Detecting TIPS stenosis with noninvasive ultrasound and performing TIPS angioplasty may be beneficial if the patient would otherwise progress to TIPS thrombosis before developing clinical symptoms from the recurrent portal hypertension. On the other hand, if invasive TIPS venography is performed based on ultrasound findings only and without regard to clinical status (eg, ascites/HH control), it is possible that TIPS angioplasty may increase the patient's risk of HE without providing clinical benefit.

### *Specific Considerations for Transjugular Intrahepatic Portosystemic Shunt by Indication*

**Transjugular intrahepatic portosystemic shunt in ascites or hepatic hydrothorax.** *Question 1. What is the optimal technical approach to TIPS creation among patients with cirrhosis and RA?* In the setting of elective TIPS for ascites, there is time to carefully titrate the amount of portal decompression obtained while monitoring for shunt morbidity, including HE. After weighing the advantages and disadvantages of various approaches (Supplementary Table 1), we favor the creation of a small diameter TIPS (8 mm, based on the minimum 8 mm diameter with current generation on-label use of controlled expansion stent graft) followed by progressive dilation, if needed, based on clinical response at 6-week intervals. This approach minimizes the risks of overshunting and offers the greatest opportunity for procedural uniformity.

*Question 2. Is a transjugular intrahepatic portosystemic shunt associated with a better outcomes (ascites control, mortality) than serial large-volume paracentesis for the treatment of refractory ascites?* RA, or diuretic-resistant ascites, is a severe manifestation of portal hypertension that impacts approximately 10% of patients with cirrhosis and ascites.<sup>25</sup> There have been 7 RCTs evaluating the impact of TIPS vs serial LVP (Supplementary Table 2).<sup>19,26-31</sup> These trials have been heterogeneous in their definition of RA, whether non-refractory but recurrent ascites was included, the technical approach, stent type (only 1 with ePTFE-covered stents<sup>19</sup>), and the definition of treatment response.

Overall, studies consistently have shown improved control of ascites with TIPS compared with LVP, but an increased risk of HE (Supplementary Table 2).<sup>19,26-31</sup> The impact of TIPS on survival has been more controversial. Of 7 trials, 4 showed improved TFS with TIPS vs LVP in univariable and/or multivariable analyses,<sup>19,27,30,31</sup> 2 with no differences in TFS between groups,<sup>28,29</sup> and the earliest trial showed decreased TFS at 2 years.<sup>26</sup> The most recent study, which notably used nonexpandable PTFE-covered stents and also had less strict criteria for RA, showed the most significant benefit.<sup>19</sup> There have been several subsequent meta-analyses<sup>32-37</sup> that confirmed the superiority of TIPS compared with serial LVP in the prevention of recurrent ascites, but remained split in terms of TFS benefit, again depending on methodology and whether 1 potentially outlier<sup>26</sup> report was included (Supplementary Table 2). The most recent meta-analyses, which used time-to-event analysis, both showed improved TFS.<sup>36</sup>

*Question 3. Is there a threshold of liver dysfunction above which a transjugular intrahepatic portosystemic shunt for refractory ascites should be contraindicated and how should it be defined?* Among patients with cirrhosis and RA, increased bilirubin levels, increased MELD score, and CTP class C cirrhosis are associated with increased post-TIPS complications including mortality.<sup>27,35-37</sup> However, there are no studies that provide strong evidence of a specific cut-off value for any of these parameters above which TIPS should be considered contraindicated. It is important to note that patients with CTP greater than 11, a MELD score greater than 15, and a total bilirubin level greater than 3 to 5 mg/dL generally were not included in prospective randomized trials (Supplementary Table 2).

*Question 4. What is the impact of age on candidacy for a transjugular intrahepatic portosystemic shunt for refractory ascites?* Among patients with cirrhosis and RA, advanced age is associated with increased post-TIPS complications including HE and mortality. However, it is important to note that there are no studies that provide strong evidence of a specific cut-off age above which TIPS should be considered contraindicated.

*Question 7. Is prior liver transplantation a contraindication to a transjugular intrahepatic portosystemic shunt for refractory ascites? Is a transjugular intrahepatic portosystemic shunt a better treatment than surgical shunt, serial large-volume paracentesis, or splenic artery embolization in liver transplant recipients with refractory ascites?* Unlike TIPS for ascites and hepatic hydrothorax in cirrhosis, there is insufficient evidence to support any recommendation regarding therapy (TIPS and other modalities) in LT recipients with refractory ascites. Predictors of clinical success in treating RA after LT with TIPS include recurrent graft fibrosis and the presence of a significant PSG.<sup>38</sup> When alternative sources are identified, including early caval or hepatic venous outflow obstruction, alternative surgical and interventional strategies should be considered. In patients without outflow obstruction, there also are limited data on the

use of splenic artery embolization and mesocaval surgical shunts, but no significant studies that compare these approaches.<sup>38-40</sup>

**Transjugular intrahepatic portosystemic shunt in variceal bleeding.** *Question 1. When is transjugular intrahepatic portosystemic shunt indicated in acute variceal hemorrhage?* Rescue TIPS is recommended in patients with cirrhosis who have been banded successfully but who rebleed at any time during admission (after endoscopy). Standard of care in patients admitted with suspected acute variceal hemorrhage consists of cautious volume resuscitation, ceftriaxone, and intravenous infusion of octreotide.<sup>41</sup> Endoscopy is performed within 12 hours and endoscopic variceal ligation is performed if the esophageal variceal source is confirmed.<sup>41</sup> Octreotide/ceftriaxone is continued for 5 days and TIPS is recommended if bleeding recurs during this period.<sup>41</sup> However, patients with advanced (mostly CTP class C) cirrhosis who rebleed and have rescue TIPS placed have a very high mortality rate.<sup>42-44</sup> This led to the concept of pre-emptive TIPS, by which patients at high risk of failing standard of care undergo TIPS creation as soon as endoscopic variceal ligation is performed successfully and within 72 hours of admission. Individual meta-analysis of 3 RCTs<sup>45-47</sup> and 5 observational studies<sup>48-52</sup> have identified patients with CTP class C (10-13 points) and CTP class B (8-9 points) with active bleeding at endoscopy as being at highest risk for rebleeding and most likely to benefit from pre-emptive TIPS. Patients not meeting these criteria should be considered for rescue TIPS in case of rebleeding during admission. Any patient (independent of CTP class) with uncontrolled acute variceal hemorrhage at endoscopy should be considered for salvage TIPS. Balloon tamponade or stent should be used as a bridge to TIPS in rescue/salvage TIPS.<sup>53</sup>

*Question 2. When should transjugular intrahepatic portosystemic shunt be used in the management of bleeding gastric fundal varices or prevention of rebleeding resulting from cirrhosis?* Based on limited current data, the panel developed a consensus approach to GV bleeding and timing of TIPS in cirrhosis (Figure 2). Although endoscopic injection of N-butyl-2-cyanoacrylate (glue), is efficacious in the acute setting to obtain initial hemostasis, use of endovascular variceal obliteration (eg, balloon-retrograde transvenous obliteration), or TIPS creation result in lower short- and long-term rebleeding rates.<sup>54,55</sup> However, TIPS in GV bleeding is not as effective compared with TIPS in esophageal variceal bleeding because GV hemorrhage can occur at a lower PSG.<sup>56</sup> Based on limited data, as compared with variceal obliteration (mostly balloon-retrograde transvenous obliteration), TIPS is associated with a higher rebleeding risk (20%-50%) and a significantly higher risk for HE (20%-40%) without differences in survival.<sup>57-64</sup> Nevertheless, balloon-retrograde transvenous obliteration requires the presence of a spontaneous portosystemic shunt (eg, gastrosplenic or splenorenal shunt) and may be associated



with increased ascites and bleeding from esophageal varices. TIPS combined with variceal obliteration appears to be associated with a potential decrease in rebleeding rates (0%–15%),<sup>65–67</sup> particularly when the pretreatment PSG is less than 12 mm Hg. In addition to the earlier-described considerations, the most appropriate management for bleeding from GV will depend on the vascular anatomy of the portal venous system in addition to center and surgeon expertise.<sup>68</sup>

**Question 3. What are the procedural considerations in transjugular intrahepatic portosystemic shunt creation for variceal hemorrhage?** Based on moderate-quality data, when placing a TIPS for variceal hemorrhage, we recommend a goal PSG of less than 12 mm Hg or a 50% to 60% decrease from initial PSG.<sup>69–73</sup> Studies using shunt diameter as a predictor of rebleeding rates have shown mixed results and therefore we do not recommend using shunt diameter as a procedural end point.<sup>20,74</sup> Notably, a prospective trial of the controlled expansion stent showed that serial dilation of the stent from 8 mm to 10 mm to obtain a goal PSG less than 12 mm Hg led to control of variceal bleeding while mitigating the risk of HE.<sup>70</sup>

In cases of TIPS creation for variceal hemorrhage, we recommend concurrent obliteration of varices based on moderate- to high-quality evidence.<sup>75–80</sup> An RCT that showed reduced rebleeding rates with concurrent embolization showed improved TIPS patency when embolization was performed.<sup>78</sup> Studies have shown efficacy of embolization coils and vascular plugs for variceal embolization.<sup>81,82</sup> Liquid embolic agents also have been shown to be effective in this setting.<sup>80,83</sup> There currently are insufficient data to show the superiority of one embolic agent and the use of each will depend on surgeon expertise.

**Novel indications for transjugular intrahepatic portosystemic shunt.** **Question 3. Does transjugular intrahepatic portosystemic shunt creation prevent or reduce portal hypertensive complications in patients with non-cirrhotic portal hypertension owing to extrahepatic portal vein obstruction?** Four uncontrolled retrospective cohort studies described the use of TIPS in this patient population (encompassing both acute and chronic thrombosis, with and without various forms of thrombolysis) (Supplementary Table 4).<sup>84–87</sup> In general, TIPS creation was found to be technically feasible and effective in reducing portal hypertension in patients with acute and chronic PVT, especially in patients with extensive PVT and bowel ischemia. The evidence level remains low owing to the lack of prospective studies and a paucity of studies comparing direct intervention with anticoagulation alone. One cohort (n = 330) described a high rate of venous recanalization with anticoagulation monotherapy, particularly with direct oral anticoagulants, suggesting this approach should be considered initially in patients who are not critically ill.<sup>88</sup> However, 23% of patients who developed chronic portal hypertensive symptoms (n = 104) went on to receive a TIPS.<sup>88</sup> Based on available data, in patients with noncirrhotic

portal hypertension and acute portal vein thrombosis, we recommend immediate anticoagulation. In those who fail or have a poor response to anticoagulation, we recommend that portal vein thrombectomy/thrombolysis using a transjugular approach with or without small-caliber TIPS creation should be considered. In patients with acute noncirrhotic portal vein thrombosis who are not critically ill, evidence is insufficient to recommend TIPS vs anticoagulation alone. We recommend that a trial of anticoagulation be considered initially given the reported rates of venous recanalization. In patients with chronic portal hypertension secondary to noncirrhotic extrahepatic portal vein obstruction that is not responsive to anticoagulation, TIPS may be considered for the same indications as cirrhotic portal hypertension.

**Question 5. Does transjugular intrahepatic portosystemic shunt creation improve outcomes in patients with Budd–Chiari syndrome?** Cohort studies of patients with BCS (hepatic venous outflow tract obstruction) have shown technically successful creation of TIPS in 84% to 100% of cases,<sup>89–94</sup> excellent control of portal hypertensive complications, and good survival (72% overall and TFS).<sup>89–93,95,96</sup> The majority of published literature in BCS and on the use of TIPS in this disease comes from referral centers experienced in the complex management of BCS. However, whether patient outcomes in BCS differ based on treatment center experience has not been reported in the literature.

Prospective cohort series and retrospective case series have shown favorable long-term outcomes after percutaneous revascularization of short-segment hepatic venous outflow tract obstruction with venoplasty and/or stent placement, with technical success rates of 78.6% to 100%.<sup>92,97–102</sup> Technically successful creation of a percutaneous portosystemic shunt, either TIPS or a direct intrahepatic portosystemic shunt, after hepatic venous outflow tract revascularization has been shown in multiple series.<sup>91,103–107</sup> These data indicate that venoplasty with or without stenting does not preclude subsequent creation of TIPS or a direct intrahepatic portosystemic shunt in patients who remain symptomatic after initial revascularization.

The rare presentation of BCS with acute liver failure deserves special consideration. In-hospital mortality in acute liver failure caused by BCS is between 58% and 62%.<sup>108</sup> The BCS-TIPS prognostic index was designed to predict 1-year TFS after TIPS for BCS.<sup>109</sup> Among 124 patients with BCS in the original multicenter retrospective cohort study used to derive the BCS-TIPS prognostic index score, 9 (7.3%) met acute liver failure criteria. Of these, 4 had BCS-TIPS prognostic index scores greater than 7, all of whom died as a consequence of progressive liver failure (mean, 9 d; range, 2–15 d). The other 5 patients with BCS and acute liver failure had BCS-TIPS prognostic index scores of 7 or less, and all survived without LT until the end of the follow-up evaluation. The prognostic value of the BCS-TIPS prognostic index score

in acute liver failure has not been validated externally, however, these findings support multidisciplinary discussion of whether to pursue TIPS or whether to proceed directly to LT in BCS patients with acute liver failure and BCS-TIPS prognostic index scores greater than 7.

Finally, 1 common element in the management of BCS patients is the need for re-intervention to maintain or restore TIPS patency in a portion of patients undergoing TIPS. Reported primary patency rates with ePTFE-covered TIPS vary, ranging from 45% to 91% for 5-year primary patency.<sup>110,111</sup> Secondary patency rates range from 85% to 100% over follow-up periods of 20 to 82 months in most series, signifying that even with TIPS occlusion salvage often is possible, precluding the need for LT.<sup>96,97,99,110-113</sup>

**Cardiopulmonary considerations in transjugular intrahepatic portosystemic shunt.** *Question 1. What cardiopulmonary testing is indicated before elective transjugular intrahepatic portosystemic shunt?* In patients undergoing elective TIPS creation, we recommend comprehensive echocardiographic evaluation to detect subclinical cardiac dysfunction (eg, cirrhotic cardiomyopathy). Cirrhotic cardiomyopathy describes systolic and/or diastolic dysfunction in patients with cirrhosis without known heart disease.<sup>114</sup> Systolic function should be assessed not only by ejection fraction, but also with other echocardiographic markers of LV function, including myocardial strain imaging according to contemporary practice guidelines.<sup>114,115</sup> RV systolic pressure greater than 45 mm Hg conventionally is considered the threshold for considering right heart catheterization. Decreased tricuspid annular plane excursion (<1.6 cm) and RV strain indicate impaired RV function.<sup>115</sup> Baseline RV indices are particularly important to assess the possibility of post-TIPS increased preload causing cardiopulmonary decompensation. In patients undergoing TIPS creation who have a RV systolic pressure exceeding 45 mm Hg or tricuspid annular plane excursion less than 1.6 cm, we recommend referral to cardiology for consideration of right heart catheterization to evaluate for RV dysfunction and pulmonary hypertension before TIPS creation. An electrocardiogram is warranted for evaluation of arrhythmia if tachycardia or bradycardia is noted on preprocedure assessment. Historically, a prolonged QTc interval was a cirrhotic cardiomyopathy criterion but updated guidance has removed it given its variability and multifactorial etiology.<sup>114</sup>

*Question 5. Can transjugular intrahepatic portosystemic shunt treat hepatopulmonary syndrome?* A recent systematic review of 12 case reports found some transient improvement in oxygenation in 9 patients after TIPS, with most having persistent intrapulmonary shunting.<sup>116</sup> Two single-center retrospective studies of patients with hepatopulmonary syndrome undergoing TIPS (1 in 7 patients with hepatopulmonary syndrome and BCS<sup>117</sup> and another in 81 patients with moderate

hepatopulmonary syndrome<sup>118</sup>), found only modest transient improvement in oxygenation after portal decompression over a 3-month follow-up period. Thus, we do not recommend TIPS as a therapy for hepatopulmonary syndrome, but it may be considered in patients with hepatopulmonary syndrome who have an established indication for TIPS.

**Renal considerations in transjugular intrahepatic portosystemic shunt.** The true incidence of AKI after TIPS is unknown given a wide spectrum of indication and urgency for TIPS, the heterogeneity in measurement of kidney function (eg, measured vs estimated GFR, sCr), definitions of AKI (based on change in creatinine value vs absolute cut-off values), and patient selection. In single-center studies, the incidence of post-TIPS AKI was 16%, although this may be overestimated and may not account for pre-TIPS AKI or CKD.<sup>119-121</sup> The presence of AKI after TIPS creation is associated with increased odds (odds ratio, 4.3) of inpatient mortality.<sup>122</sup>

The creation of TIPS and resultant reduction in PSG is associated with improvement in kidney function, especially when measuring GFR.<sup>123-130</sup> Compared with serial paracentesis, the incidence of AKI and HRS may be lower in patients with TIPS.<sup>28,36</sup> A change in estimated GFR is evident over 3 to 4 months after TIPS creation with a potential benefit in patients with CKD (GFR, <60),<sup>123,126</sup> suggesting that TIPS interrupts the natural history of decline in kidney function related to decreased effective circulating volume. Despite these physiologic improvements, there is insufficient evidence regarding clinical outcomes when considering TIPS in patients with advanced kidney dysfunction (eg, sCr, >3 mg/dL) because these patients often were excluded from studies.<sup>19,27-30</sup> In addition, TIPS is not well studied in the dialysis population, with only case reports in the literature.<sup>131</sup> The panel suggests considering the primary indication, predictive models such as MELD score, individualized risk factors, and physiologic goals of the intervention when considering TIPS creation in patients with a degree of kidney dysfunction (Table 3).

*Question 1. What is the best marker to assess kidney function before or after transjugular intrahepatic portosystemic shunt?* Kidney function assessment in TIPS is varied, with some studies reporting changes in sCr, creatinine clearance, measured (using inulin clearance) or estimated GFR (Modification of Diet in Renal Disease, Chronic Kidney Disease Epidemiology Collaboration).<sup>26,123,125,126,132,133</sup> Serum creatinine usually is used as a predictor of post-TIPS kidney dysfunction and mortality, along with other risk factors, such as age, presence of HE, and poor control of ascites.<sup>134-137</sup> Although sCr is easy to measure and obtain, sCr may underestimate the degree of kidney dysfunction, especially among women, decompensated cirrhosis patients, or those with low muscle mass.<sup>138</sup> The role of estimating GFR using equations that include both sCr and cystatin has not been studied in patients with TIPS.<sup>139</sup> Measured GFR may be preferable but is impractical to obtain.

Although several biomarkers have been described, these have been inadequately examined in patients with cirrhosis undergoing TIPS.<sup>140,141</sup> GFR equations developed in patients with cirrhosis and biomarkers that capture structural and functional changes in kidney function may be preferable.<sup>140,142</sup> In patients undergoing TIPS, sCr predicted mortality better for men whereas cystatin C predicted mortality better in women. However, GFR was not assessed in this study.<sup>143</sup> Assessment of kidney function is poor in patients with cirrhosis who are frail, sarcopenic, and/or have underlying CKD (without hemodialysis dependence) and are undergoing TIPS. Other biologic determinants of health, including sex, race, and ethnicity, have not been well studied in TIPS populations as it relates to kidney function.

*Question 3. What can be done periprocedurally to reduce the incidence of kidney complications after a transjugular intrahepatic portosystemic shunt? What secondary or tertiary preventive measures can be considered to avoid acute kidney injury, acute kidney disease, or de novo or progressive chronic kidney disease after a transjugular intrahepatic portosystemic shunt?* Data regarding pertinent kidney protection strategies in the TIPS population are lacking, therefore the panel extrapolated data from related clinical scenarios to suggest relevant rational strategies. In patients undergoing TIPS creation for ascites, albumin infusion should be considered in all patients undergoing concurrent paracentesis, and especially for those in whom more than 5 L are removed, to prevent paracentesis-induced circulatory dysfunction and AKI.<sup>25,144–146</sup> The role of vasoconstrictors at the time of LVP or in addition to albumin use during TIPS creation is unclear.<sup>147–150</sup>

Judicious use of intravascular iodinated contrast agents may minimize the risk of contrast nephropathy after TIPS creation. In an observational study, post-TIPS AKI (defined as  $\geq 0.3$  mg/dL increase in sCr within 48 hours after TIPS) increased with 50-mL increases in contrast load and increased baseline sCr (pre-TIPS AKI or CKD) levels.<sup>120</sup> The true incidence of, and risks for, contrast-induced nephropathy in the era of low-osmolality contrast agents is unknown. Rates of AKI in patients undergoing computed tomography scans with low-osmolality iodinated contrast agents compared with those having computed tomography scans without contrast may be equivalent.<sup>151,152</sup> Given the limitations of studies (patient selection and study design), the influence of iodinated contrast on inducing nephropathy cannot be entirely ignored, particularly in those with more severe kidney impairment.<sup>153,154</sup> Oral acetylcysteine is not recommended.<sup>155</sup> The risk of contrast nephropathy is extrapolated from the contrast literature; risk factors include baseline CKD, increased serum glucose levels ( $>200$  mg/dL), and serum total bilirubin levels greater than 2.0 mg/dL.<sup>156,157</sup>

*Question 4. What is the role of transjugular intrahepatic portosystemic shunt for hepatorenal syndrome?* The quality of available studies on TIPS for management of HRS is low owing to small sample size and significant

heterogeneity. For example, in a small prospective study ( $n = 7$ ), kidney function improved in 6 of 7 patients, with a decrease in median sCr level (5 mg/dL to 1.8 mg/dL) within 30 days after TIPS. However, 90-day mortality was high (58%) and was driven mostly by liver failure and sepsis.<sup>124</sup> In a subsequent study with 14 patients with type 1 HRS (50% on renal replacement therapy) and 17 patients with type 2 HRS, improvement in kidney function was observed in 77% of patients and discontinuation of hemodialysis was possible in 57% of patients.<sup>130</sup> High survival rates were observed (90% in HRS-2, 55% in HRS-1 at 12 weeks), likely related to strict patient selection. Both studies were conducted in the pre-MELD era and, although these data may seem encouraging, they were heavily limited by a non-randomized design and a strong selection bias. TIPS creation prevented HRS-1 recurrence in responders to vasoconstrictive therapy ( $n = 5$ ), with normalization of sCr without HRS recurrence up to  $17 \pm 5$  months after TIPS.<sup>158</sup> In addition, TIPS creation may reduce the incidence of HRS in patients with diuretic RA.<sup>28</sup> Finally, a meta-analysis of 9 studies<sup>128</sup> showed significant improvement in kidney function, as measured by sCr, with a pooled response rate of 93% in HRS-1 and 83% overall.<sup>159</sup>

**Hepatic encephalopathy and transjugular intrahepatic portosystemic shunt.** *Question 1. When counseling patients, what is the overall risk of overt hepatic encephalopathy after a transjugular intrahepatic portosystemic shunt and what patient-specific factors contribute to the development of overt hepatic encephalopathy?* The incidence of overt HE in uncovered (non-PTFE) stents was 33% for variceal bleeding and 53% for ascites compared with 19% and 32%, respectively, in patients who received standard medical management.<sup>160,161</sup> In direct comparative studies of uncovered and covered stents, there was no difference in the incidence of overt HE. Hence, it is reasonable to apply the incidence data for overt HE from uncovered stents to contemporary covered stents.<sup>160–162</sup> The only RCT in covered TIPS stents vs LVP for ascites showed similar rates of 35% in new incidence of overt HE.<sup>19</sup> In several RCTs investigating pre-emptive TIPS for acute variceal hemorrhage, incidence rates of overt HE were similar in the pre-emptive TIPS groups compared with endoscopic therapy and ranged from 35% to 50%.<sup>46–48</sup> It should be noted that these studies had selective inclusion criteria and excluded patients with a history of recurrent overt HE.

In a meta-analysis, the strongest independent predictors of post-TIPS HE included pre-TIPS HE (odds ratio, 3.07; 95% CI, 1.75–5.40) and CTP class C cirrhosis (odds ratio, 4.0; 95% CI, 1.4–11.1).<sup>163</sup> In RCT multivariate analyses, MELD score pre-TIPS is not predictive of post-TIPS HE compared with incidence of HE in medical management control arms.<sup>19,47,48</sup> These RCTs, however, were limited based on narrow ranges of MELD scores (eg, MELD range, 10–20) among TIPS recipients. Limited

single-center studies have suggested a MELD score greater than 18 is associated with an increased incidence of post-TIPS overt HE.<sup>164</sup> Other risk factors for post-TIPS HE include older age (hazard ratio, 1.09; 95% CI, 1.05–1.13) and increased creatinine levels (hazard ratio, 1.52; 95% CI, 1.02–2.26).<sup>165</sup> More recent prospective data have shown that sarcopenia, as evident on lumbar or psoas computed tomography measurements, is associated strongly with the development of HE (hazard ratio, 31.3; 95% CI, 4.5–218).<sup>166,167</sup>

**Question 3.** *What is the role for formal evaluation for covert or minimal hepatic encephalopathy before an elective transjugular intrahepatic portosystemic shunt?* The diagnosis of covert HE has been associated with a greater risk of post-TIPS HE.<sup>161,168,169</sup> Covert HE is associated with poor daily function and impaired health-related quality of life and is associated with the development of overt HE even in patients who do not undergo TIPS.<sup>170–172</sup> However, there is no recommendation to treat patients with covert HE with medical interventions (eg, lactulose, rifaximin) before TIPS. Recommendations for testing to detect covert HE include psychometric hepatic encephalopathy score, EncephalApp Stroop, or Critical Flicker frequency testing.<sup>173</sup> Few studies have determined the role of oral glutamine challenge in prognostication for overt HE after TIPS.<sup>174–176</sup> Cognitive testing by and large worsens after TIPS, which can contribute to further worsening of health-related quality of life.<sup>161,177</sup> In patients being considered for elective TIPS, a diagnosis of covert HE should guide discussion of the pros and cons of TIPS creation with patients, family members, and clinical teams. Future studies investigating the effect of covert HE with and without treatment on the incidence of post-TIPS overt HE are necessary.

**Question 4.** *What transjugular intrahepatic portosystemic shunt stent diameter should be considered with regard to limiting post-transjugular intrahepatic portosystemic shunt hepatic encephalopathy?* Although potentially providing less portal decompression, smaller shunts have been proposed as a way to decrease overt HE. In a multicenter RCT of elective TIPS for ascites, 8-mm diameter TIPS led to a PSG less than 12 mm Hg in only 61% of patients, but the rate of occult hepatic encephalopathy was only 18%.<sup>178</sup> Several other studies have shown significantly less overt HE in 8-mm compared with 10-mm TIPS.<sup>20,179,180</sup> In a recent prospective single-arm trial of the controlled expansion stent dilated to 8 mm, the shunts did not self-expand beyond 8 mm and the rate of grades II to III HE was only 6%.<sup>70</sup> However, 17% of patients required dilation up to 10 mm to achieve adequate clinical response.<sup>70</sup>

**Question 5a.** *Is there a role for collateral embolization at the time of transjugular intrahepatic portosystemic shunt?* In patients undergoing elective TIPS for ascites and/or hepatic hydrothorax, embolization of SPSSs greater than 6 mm is recommended to reduce the risk of post-TIPS hepatic encephalopathy. Large SPSSs have been associated with an increased risk of overt HE and mortality in patients with cirrhosis.<sup>181,182</sup> Hence,

embolization of SPSSs could be beneficial to patients undergoing TIPS to prevent post-TIPS HE. In a retrospective cohort of 903 patients using covered TIPS stents, 51% of patients with an identified SPSS greater than 6 mm left in place at the time of TIPS developed overt HE compared with 39% among those with an embolized SPSS.<sup>183</sup> A smaller study comparing 33 TIPS patients with SPSS embolization and 33 TIPS patients without SPSS embolization showed no significant difference in post-TIPS HE rates.<sup>184</sup>

**Question 6a.** *What is the role for medical prophylaxis to prevent hepatic encephalopathy after a transjugular intrahepatic portosystemic shunt?* Early RCTs using uncovered TIPS stents showed no difference in the incidence of overt HE in a head-to-head comparison with lactulose, rifaximin, and placebo.<sup>185</sup> However, a recent RCT with a larger sample size showed a significantly reduced incidence of a first episode of HE after TIPS (44.2% vs 59.1%;  $P = .05$ ) in patients without a history of overt HE receiving rifaximin vs placebo as prophylaxis before TIPS.<sup>186</sup> The major limitation to the newer study is that lactulose was not allowed in the trial before TIPS, even among those with a history of overt HE (12% prevalence in both arms), although could be used for the treatment of overt HE if it developed. Thus, standard of care was not met in the pre-TIPS population with a history of HE who had an indication for lactulose, dampening enthusiasm for the study findings.

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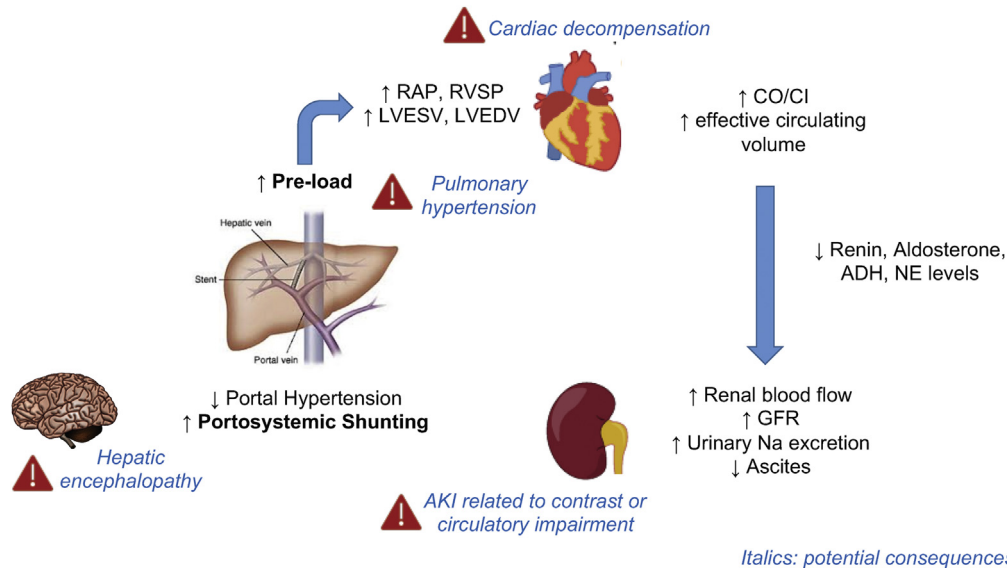
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**Supplementary Figure 1.** Mechanisms of TIPS for the treatment of portal hypertension and the effect of TIPS creation on portal, cardiac, and renal hemodynamics. According to the peripheral arterial vasodilation hypothesis, pooling of blood in the splanchnic/portal circulation leads to decreased effective circulating volume in cirrhosis.<sup>195</sup> As a means of compensation, there is increased kidney retention of sodium/water and renal vasoconstriction, which leads first to ascites formation, hyponatremia, and, later, increased sCr reflecting functional kidney injury.<sup>196,197</sup> TIPS creation for ascites and poor kidney perfusion leads to decompression of portal hypertension, restores end-organ perfusion, alleviates maladaptive vasoconstriction, and decreases retention of sodium/water.<sup>198</sup> Creation of TIPS is associated with a transient increase in cardiac index, central blood volume, with deactivation of RAAS, decreases in renin, aldosterone, and norepinephrine levels, with an increase in urinary sodium excretion and renal blood flow.<sup>26–28,124,132,136,199–210</sup> TIPS also is associated with increased portosystemic shunting, which can result in new or worsening hepatic encephalopathy.<sup>167</sup> ADH, antidiuretic hormone; AKI, acute kidney injury; CI, cardiac index; CO, cardiac output; GFR, glomerular filtration rate; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; NE, norepinephrine; RAP, right atrial pressure; RVSP, right ventricular systolic pressure; TIPS, transjugular intrahepatic portosystemic shunt.

**Supplementary Table 1.** Final Voting Results for the Full List of Candidate Guidance Statements Related to Use of TIPS in the Management of Portal Hypertension Stratified by Topic Area

Question	Statement	Mean	SD	Response, %
Pre-TIPS considerations				
Question 1. Who should be involved in the decision to place a TIPS and what other preprocedure consultations are recommended?	Before TIPS creation, we recommend that a gastroenterologist or hepatologist should be involved in the initial decision to place an emergent or nonemergent TIPS, with subsequent consultation by an interventional radiologist or other proceduralist with competency in TIPS. If center expertise is not available, we recommend referral to an expert center. Additional specialty consultations (eg, transplant surgery, cardiology, critical care, hematology, nephrology) may be considered on a case-by-case basis.	8.33	0.92	90.0
Question 2. What services should be readily available at centers where TIPS is performed and what referral pathways should be established for a higher level of care?	For all patients undergoing TIPS creation, we recommend that TIPS should occur at a center with available IR, gastroenterology/hepatology, cardiology, pulmonary surgery, hematology, nephrology, and critical care services to provide an adequate level of support for patient management before and after TIPS. In patients requiring a higher level of care, such as possible liver transplant candidates, or in whom the need for further IR expertise is indicated (eg, extensive portal vein thrombosis), we recommend referral to centers with adequate experience in these areas.	8.5	0.69	93.3
Question 3. Is there a MELD threshold above which elective TIPS should not be considered?	In patients with cirrhosis undergoing TIPS, a multidisciplinary approach, rather than an absolute MELD cut-off score, is recommended to assess TIPS candidacy.	8.73	0.53	86.7
Question 4. What imaging and/or preprocedural evaluation is required before TIPS creation?	Q4a. In patients undergoing elective TIPS, we recommend the following: <ul style="list-style-type: none"> <li>• Contrast-enhanced multiphasic cross-sectional imaging (CT/MRI) to assist with TIPS planning.</li> <li>• Comprehensive echocardiography to assess for abnormalities in cardiac structure, function, and right ventricular systolic pressure.</li> </ul> Q4b. In patients with cirrhosis undergoing emergent TIPS, best clinical judgement should be applied. We suggest at least a liver ultrasound with Doppler to evaluate the patency of the portal venous system and consideration of a limited (bedside) echocardiogram, evaluating left ventricular ejection fraction and right ventricular systolic pressure.	8.19	1.27	90.0
Question 5. What are absolute contraindications (medical and anatomic) to elective TIPS creation?	In patients undergoing elective TIPS, the absolute contraindications to TIPS creation are severe cardiac dysfunction (right- or left-sided), moderate-severe pulmonary hypertension (based on invasive measurements) despite medical optimization, severe valvular heart disease, uncontrolled systemic infection, unrelieved biliary obstruction, or tumors in the liver parenchyma that would preclude TIPS creation.	8.32	1.25	93.3
Question 6. Should all patients being considered for TIPS undergo evaluation for liver transplantation before TIPS creation?	In patients with cirrhosis undergoing elective or emergent TIPS, there is insufficient evidence to recommend universal preprocedure liver transplant evaluation.	8.19	1.27	90.0
TIPS procedural considerations				
Question 7: Who should perform TIPS creation?	We recommend that TIPS creation should be performed by a credentialed, board-certified interventional radiologist or a certified provider with equivalent training and procedural competency. <sup>a</sup>	8.35	1.13	90.0

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 8. What type of stent is recommended for TIPS creation?	For patients undergoing TIPS placement, we recommend the use of an ePTFE-lined stent graft (1b) with controlled expansion, which allows the surgeon to tailor the amount of portosystemic shunting based on the indication, target gradient, and patient comorbidities (2b).	8.56	1.26	83.3
Question 9. Should coagulopathy be corrected before TIPS placement?	Because of insufficient evidence, we do not recommend a specific target INR or platelet threshold when placing a TIPS in a patient with cirrhosis.	7.88	1.63	86.7
Question 10. Should periprocedural antibiotics be used routinely in TIPS creation?	There are no studies to show that the routine use of antibiotics during TIPS placement decreases infectious complications and their use should depend on patient and local risk factors.	8.04	1.11	86.7
Question 11. Should TIPS creation be performed using general anesthesia or is deep or conscious sedation appropriate?	The use of general anesthesia, deep sedation, or conscious sedation all may be appropriate for TIPS placement and their use will vary depending on patient risk factors and local practices.	8.15	1.26	86.7
Question 12. Is the use of intravascular ultrasound recommended to assist with portal vein puncture?	For patients undergoing TIPS creation, although there is insufficient evidence to recommend the universal use of intravascular ultrasound guidance, it may facilitate efficient portal access in certain situations. Its use will depend on equipment availability and surgeon preference.	7.8	1.55	83.3
Question 13. What is the optimal location from which to measure the systemic venous pressure at the time of TIPS creation (hepatic vein, IVC, right atrium)?	We recommend the use of the free hepatic vein or IVC pressure as the systemic pressure when measuring the portosystemic gradient before and after TIPS placement.	7.65	1.81	83.3
Question 14. Are there specific technical factors that should be considered to ensure that TIPS placement does not adversely influence liver transplant candidacy?	Q14a. In patients undergoing TIPS placement who are potentially eligible for liver transplant, we recommend positioning the stent as to not interfere with the portal and hepatic vein anastomoses, presuming that this does not detrimentally affect TIPS function or patency. This positioning includes leaving a segment of unstented main portal vein and not extending the TIPS stent into the right atrium.	8.35	1.06	83.3
	Q14b. Liver transplant candidacy should not be impacted by placement of TIPS.	8.19	1.27	90.0
Care of the post-TIPS patient				
Question 15. What is the recommended duration of intensive postprocedure monitoring?	After TIPS creation, we recommend that all patients undergo in-hospital overnight observation at a minimum. The level of care during post-TIPS observation should be dictated by the patient's condition, indication for TIPS, and intraprocedural technical complexity.	8.0	1.55	86.7
Question 16. What early laboratory testing and/or imaging is recommended after TIPS creation and at what interval?	Q16a. In all patients undergoing TIPS creation, routine laboratory tests (complete blood count, comprehensive metabolic panel, and PT/INR) should be obtained on the day after TIPS creation. Hemoglobin/hematocrit laboratory tests may be obtained on the same day of TIPS creation, depending on the institution and/or surgeon discretion.	7.77	1.21	86.7
	Q16b. Predischarge imaging is not indicated in most patients undergoing TIPS creation.	8.08	1.41	86.7

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 17. Should TIPS venography and intervention be based on ultrasound, clinical findings, or both?	Q17a. In patients who have undergone TIPS creation for management of varices, either Doppler ultrasound findings suggesting TIPS dysfunction or persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry $\pm$ intervention. Ultrasound findings suggesting TIPS dysfunction include alterations in intrahepatic portal vein direction of flow, abnormal flow velocities within the TIPS, and persistent (eg, >6 weeks after TIPS) or recurrent ascites.	8.33	0.82	80.0
	Q17b. In patients who have undergone TIPS creation for management of ascites and/or hepatic hydrothorax, persistence or recurrence of portal hypertensive complications should prompt TIPS venography and manometry $\pm$ intervention. Medical decision making should be individualized in patients with well-controlled ascites and/or hepatic hydrothorax and ultrasound findings suggesting TIPS dysfunction.	8.21	0.78	80.0
	Q17c. In select patients, scheduled TIPS venography with intervention is suggested in the early (1–2 mo) post-TIPS period. An example of such a scenario would be TIPS creation in a patient with portal vein thrombosis.	7.22	2.21	80.0
Question 18. What are the optimal techniques for increasing or decreasing TIPS flow when intervention is required?	Q18a. In patients in whom a further decrease in portal pressure is desired, we recommend stepwise dilatation of TIPS to its maximum diameter. If it is already at maximum diameter, other interventions to decrease portal pressure (eg, nonselective $\beta$ -blockers, parallel TIPS creation) should be evaluated.	8.04	1.19	80.0
	Q18b. In patients in whom an increase in portal pressure is desired, there is insufficient evidence to recommend a specific technique to reduce portosystemic shunting through a TIPS.	8.23	0.81	80.0
Question 19. Who should see patients with TIPS in follow-up evaluation?	In patients who have undergone TIPS creation, we recommend that a gastroenterologist or hepatologist and a competent proceduralist (eg, interventional radiologist) should follow-up the patient to ensure ongoing management of chronic liver disease, postprocedural complications, and to determine any need for potential device revision.	8.0	1.33	90.0
TIPS in ascites or HHT				
Question 1. What is the optimal technical approach to TIPS creation among patients with cirrhosis and refractory ascites?	Q1a. For patients with cirrhosis and diuretic refractory or resistant ascites undergoing elective TIPS, we recommend the use of an ePTFE-covered controlled expansion stent.	8.04	1.73	80.0
	Q1b. For patients with cirrhosis and diuretic refractory or resistant ascites undergoing elective TIPS, we recommend a staged approach to TIPS creation with an initial procedural stent dilation to 8 mm followed by clinical assessment, and then subsequent progressive stent dilation to 9 mm and then 10 mm at 6-week intervals if needed to optimize clinical response.	7.92	1.93	83.3
Question 2. Is TIPS associated with better outcomes (mortality, ascites control) than serial large-volume paracentesis for the treatment of refractory ascites?	Q2a. For carefully selected patients with cirrhosis and refractory ascites, TIPS is recommended over LVP to prevent recurrent ascites.	8.26	1.02	90.0
	Q2b. For carefully selected patients with cirrhosis and refractory ascites, TIPS is recommended over LVP to improve transplant-free survival.	8.11	1.15	90.0
Question 3. Is there a threshold of liver dysfunction above which TIPS for refractory ascites should be contraindicated and how should it be defined?	Among patients with cirrhosis and refractory ascites, increased bilirubin, increased MELD score, and CTP class C cirrhosis are associated with increased post-TIPS complications including mortality. There is insufficient evidence to recommend a cut-off value above which any of these measures should be considered a contraindication to TIPS.	7.30	1.92	90.0

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 4. What is the impact of age on candidacy for TIPS for refractory ascites?	Among patients with cirrhosis and refractory ascites, advanced age is associated significantly with post-TIPS complications including severe hepatic encephalopathy and death. There is insufficient evidence to recommend a cut-off age that should be considered a contraindication to TIPS.	7.44	1.5	90.0
Question 5. What is the role of TIPS in patients with ascites that is not refractory?	In patients not fulfilling a strict definition of refractory ascites but requiring at least 3 LVP for tense ascites in a year despite optimal medical therapy, we recommend that TIPS creation should be considered.	8	1.17	86.7
Question 6. What is the role of TIPS in HHT? Is patient selection similar for patients with ascites vs patients with HHT?	For patients with HHT requiring recurrent thoracentesis, we recommend that TIPS should be considered.	7.74	1.32	90.0
Question 7. Is prior liver transplantation a contraindication to TIPS for refractory ascites? Is TIPS a better treatment than surgical shunt, serial LVP or splenic artery embolization in liver transplant recipients with refractory ascites?	Unlike TIPS for ascites and HHT in cirrhosis, there is insufficient evidence to support any recommendation regarding therapy (TIPS and other modalities) in liver transplant recipients with refractory ascites.	7.23	1.73	86.7
Question 8. What is the expected timeline for TIPS to be effective for reduction of ascites/HHT?	In the setting of TIPS creation for ascites or hepatic hydrothorax, we recommend using a staged approach by starting with the TIPS stent with the smallest diameter with concomitant use of diuretics as tolerated. Reassessment for need to further dilate the TIPS stent should be performed every 6 weeks.	8.29	1.04	80.0
TIPS in variceal bleeding				
Question 1. When is TIPS indicated in acute variceal hemorrhage?	For acute variceal hemorrhage, we recommend TIPS creation in the following scenarios: <ul style="list-style-type: none"> <li>• Pre-emptive TIPS in patients who have been banded successfully but who meet high-risk criteria for rebleeding. High-risk criteria are CTP class C (10–13 points) or CTP class B &gt;7 points with active bleeding at endoscopy. TIPS should be performed within 72 hours of admission in patients without contraindications to TIPS.</li> <li>• Rescue TIPS in patients who have been banded successfully but who rebleed at any time during admission (after endoscopy).</li> <li>• Salvage TIPS should be performed emergently for patients in whom endoscopic band ligation cannot be performed because of profuse bleeding or bleeding persists at endoscopy despite endoscopic band ligation.</li> </ul>	7.46	1.07	86.7
Question 2. When should TIPS be used in the management of bleeding gastric fundal varices or prevention of rebleeding?	Q2a. We recommend that the initial management of bleeding gastric-fundal varices should be based on center expertise. Variceal obliteration/embolization with or without TIPS should be considered for bleeding gastric-fundal varices if unable to be managed endoscopically.	8.04	1	86.7
	Q2b. For rebleeding gastric-fundal varices after endoscopic therapy, we recommend variceal obliteration with or without TIPS creation.	7.8	1.85	83.3
Question 3. What are the procedural considerations in TIPS creation for variceal hemorrhage?	Q3a. When placing a TIPS for variceal hemorrhage, we recommend a goal PSG of <12 mm Hg or 50%–60% decrease from initial PSG. We do not recommend using shunt diameter as a procedural end point.	7.64	1.11	83.3
	Q3b. In cases of TIPS creation for variceal hemorrhage, we recommend concurrent obliteration of varices.	7.33	1.59	83.3



Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 4. How should patients be monitored after TIPS creation for variceal hemorrhage?	Q4a. In the setting of TIPS creation for variceal bleeding, we recommend surveillance with Doppler ultrasonography 3 months after TIPS creation and every 6 months thereafter to monitor for post-TIPS stenosis or occlusion.	8.4	0.87	83.3
	Q4b. If TIPS stenosis/occlusion is suspected or if patient rebleeds after TIPS creation, TIPS venogram with pressure measurements is indicated with consideration of TIPS revision.	8.04	1.29	90
Novel indications for TIPS				
Question 1. Does preoperative TIPS creation in patients with portal hypertension reduce surgical complications and/or improve perioperative outcomes after nontransplant abdominal surgery?	Q1a. In patients with portal hypertension requiring nontransplant surgery, there is insufficient evidence to recommend that preoperative TIPS prevents bleeding complications or the need for blood transfusion during or after invasive nontransplant surgical procedures.	7.88	1.28	83.3
	Q1b. In patients with cirrhosis without clinically significant ascites, there is insufficient evidence to recommend preoperative TIPS in abdominal surgery to prevent complications of ascites. In patients with cirrhosis with clinically significant ascites requiring abdominal surgery, a multidisciplinary team approach (hepatology and hepatobiliary surgery) is recommended to individualize the surgical/medical management.	7.92	1.26	83.3
	Q1c. There is no evidence that preoperative TIPS has an impact on postoperative mortality after invasive nontransplant surgical procedures.	7.08	1.81	86.7
Question 2. Does TIPS creation in patients with cirrhosis and portal vein obstruction facilitate listing for liver transplantation and/or improve outcomes after liver transplantation?	Q2a. In patients with cirrhosis and chronic, complete portal vein thrombosis, portal vein recanalization and TIPS creation could be considered to facilitate transplant eligibility.	8.08	1.13	86.7
	Q2b. Patients with cirrhosis and complete portal vein thrombosis otherwise being considered for liver transplantation or denied listing because of technical challenges associated with complete portal vein obstruction should be considered for portal vein reconstruction and TIPS. Referral to a center with specialized expertise may be necessary.	7.26	1.46	90.0
Question 3. Does TIPS creation prevent or reduce portal hypertensive complications in patients with noncirrhotic portal hypertension owing to extrahepatic portal vein obstruction?	Q3a. In patients with noncirrhotic portal hypertension and acute portal vein thrombosis, we recommend immediate anticoagulation. In those who fail or have a poor response to anticoagulation, we recommend that portal vein thrombectomy/thrombolysis using a transjugular approach with or without small-caliber TIPS creation should be considered.	7.85	0.97	86.7
	Q3b. In patients with acute noncirrhotic portal vein thrombosis who are not critically ill, evidence is insufficient to recommend TIPS vs anticoagulation alone. We recommend that a trial of anticoagulation be considered initially given the reported rates of venous recanalization.	7.56	1.15	90.0
	Q3c. In patients with chronic portal hypertension secondary to noncirrhotic extrahepatic portal vein obstruction that is not responsive to anticoagulation, TIPS may be considered for the same indications as cirrhotic portal hypertension.	7.35	1.35	86.7
Question 4. Does TIPS creation in patients with noncirrhotic portal hypertension and without extrahepatic portal vein obstruction prevent or reduce portal hypertensive complications?	In patients with chronic idiopathic portal hypertension/portosinusoidal vascular disease TIPS may be considered for the same indications as cirrhotic portal hypertension.	7.38	1.39	86.7

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 5. Does TIPS creation improve outcomes in patients with Budd–Chiari syndrome?	Q5a. Patients with Budd–Chiari syndrome should be evaluated and managed at centers with experience and expertise in hematologic evaluation, clinical management, and percutaneous intervention in this patient population. Ideally, the center also will have expertise in liver transplantation, should this be warranted at initial evaluation or during subsequent follow-up evaluation. If these resources are not available at the presenting institution, strong consideration of transfer to such an institution should be given while medical management is initiated.	8.04	1.32	90.0
	Q5b. In patients with Budd–Chiari syndrome who remain symptomatic or without improving liver function after initiation of appropriate medical therapy and who are not candidates for percutaneous revascularization of the hepatic venous outflow tract (short segment obstruction), creation of a percutaneous portosystemic shunt, either TIPS or direct intrahepatic portosystemic shunt, should be strongly considered.	8.04	1.02	90.0
	Q5c. In patients with Budd–Chiari syndrome undergoing TIPS, we recommend close clinical monitoring and imaging follow-up evaluation.	7.52	1.42	90.0
Cardiopulmonary considerations in TIPS				
Question 1. What cardiopulmonary testing is indicated before elective TIPS?	Q1a. In patients undergoing elective TIPS creation, we recommend comprehensive echocardiographic evaluation incorporating, in addition to the assessment of LVEF, measurement of left ventricular global longitudinal strain, when feasible, and the contemporary surrogates of left ventricular diastolic function.	7.7	1.29	90.0
	Q1b. In patients undergoing elective TIPS creation, we recommend assessment of right ventricular function using TAPSE and RVSP. Right ventricular strain has not become standard of care in most centers but should be measured if available.	7.12	1.61	86.7
	Q1c. In patients undergoing TIPS creation who have a RVSP exceeding 45 mm Hg or TAPSE less than 1.6 cm, we recommend referral to cardiology for consideration of right heart catheterization to evaluate for RV dysfunction and pulmonary hypertension before TIPS creation.	7.32	1.68	93.3
	Q1d. In patients undergoing TIPS creation who have tachycardia or bradycardia on physical examination, we recommend pre-TIPS electrocardiographic assessment to evaluate for arrhythmia.	7.46	1.98	90.0
Question 2. Does cirrhotic cardiomyopathy or diastolic dysfunction confer a risk for post-TIPS heart failure?	Q2a. In patients undergoing elective TIPS creation, we recommend considering the presence of systolic and/or diastolic dysfunction, which may suggest cirrhotic cardiomyopathy in the absence of other cardiac history, a significant risk factor for post-TIPS heart failure.	7.92	1.15	80.0
	Q2b. In patients undergoing evaluation for elective TIPS, we recommend avoiding TIPS if LVEF is less than 50% or if there is grade III diastolic dysfunction, given the risk of post-TIPS cardiac decompensation.	7.21	1.71	93.3
Question 3. Can TIPS be performed safely in patients with moderate or severe POPH?	Q3a. In patients with moderate or severe POPH on treatment (ie, mean pulmonary artery pressure >35 mm Hg, PVR >3 wood units), we recommend significant caution when considering TIPS insertion because it may precipitate right-sided heart failure.	7.64	1.31	93.3
	Q3b. In patients undergoing elective TIPS who do not have evidence of POPH on screening, we recommend measuring the right atrial pressure at the time of planned TIPS insertion and if >14 mm Hg, we recommend considering right heart catheterization before TIPS creation to exclude POPH based on the clinical situation.	7.46	1.28	80.0
Question 4. Can tricuspid regurgitation severity be prohibitive of TIPS creation?	In patients being considered for elective TIPS who have moderate or severe tricuspid regurgitation despite optimization of volume overload, we recommend evaluation for the underlying cardiopulmonary etiology, which can prohibit proceeding with TIPS.	7.56	1.08	83.3

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 5. Can TIPS treat HPS?	We do not recommend TIPS as a therapy for HPS, but it may be considered in patients with HPS who have an established indication for TIPS.	7.7	1.3	90.0
Question 6. Does stent size affect risk for post-TIPS HF in high-cardiac-risk patients?	In patients with systolic and/or diastolic dysfunction or mild POPH who are undergoing TIPS, we recommend balancing the desired portosystemic gradient with potential worsening of cardiac function by initially deploying the endoprosthesis to 8-mm diameter. If the desired gradient is achieved, no additional dilatation of the shunt should be pursued.	7.36	1.68	83.3
Question 7. Is there a need for post-TIPS echocardiographic surveillance?	In patients with systolic and/or diastolic dysfunction, pulmonary hypertension, or moderate to severe valvular disease, we recommend echocardiographic surveillance at 3 months after TIPS or earlier, if indicated. Surveillance beyond 3 months can be considered if there is echocardiographic worsening at 3 months (compared with baseline) or if there is clinical indication.	7.0	1.89	93.3
<b>Renal considerations in TIPS</b>				
Question 1. What is the best marker to assess kidney function before or after TIPS?	Q1a. In patients with cirrhosis undergoing TIPS, kidney function should be assessed before the procedure either through measurement of serum creatinine or GFR (estimated or measured). A change in GFR may better capture changes in kidney function, although there is insufficient evidence to recommend one equation over another.	7.37	1.52	90.0
	Q1b. The optimal method to assess kidney function in cirrhosis patients with sarcopenia or chronic kidney disease is not known.	7.44	1.4	90.0
Question 2. Is there an absolute cut-off value for kidney function for which TIPS is contraindicated?	There is insufficient evidence to recommend an absolute serum creatinine, CKD stage, or presence/absence of renal replacement therapy where TIPS creation is contraindicated.	7.19	1.55	90.0
Question 3. What can be done periprocedurally to reduce the incidence of kidney complications after TIPS? What secondary or tertiary preventive measures can be considered to avoid AKI, acute kidney disease, or de novo or progressive CKD after TIPS?	Q3a. In patients undergoing TIPS creation for ascites, albumin infusion should be considered in all patients undergoing concurrent paracentesis, and especially for those in whom >5 L are removed, to prevent paracentesis-induced circulatory dysfunction and AKI.	7.96	1.7	90.0
	Q3b. LVP with albumin infusion may be performed either within 24 hours before, or concomitantly during TIPS creation.	7.42	1.79	86.7
	Q3c. Adequate hydration and judicious use of iodinated contrast are rational strategies to help reduce the risk of contrast-related injury.	7.96	1.06	90.0
	Q3d. In patients with AKI/CKD before TIPS or in those who develop AKI after TIPS creation, kidney function should be closely followed up within 1 week of discharge after TIPS creation.	7.85	1.12	86.7
Question 4. What is the role of TIPS for HRS?	Q4a. There is insufficient evidence to recommend for or against the use of TIPS for treatment of HRS; however, presence of HRS is not an absolute contraindication for TIPS creation in the presence of other indications (eg, refractory ascites, variceal bleeding).	7.56	1.31	90.0
	Q4b. Mortality in patients with HRS undergoing TIPS appears to be driven by liver function (ie, serum bilirubin, INR), therefore, careful patient selection is recommended.	7.56	1.05	90.0
<b>Hepatic encephalopathy and TIPS</b>				
Question 1. When counseling patients, what is the overall risk of overt hepatic encephalopathy after TIPS and what patient-specific factors contribute to the development of overt HE?	We recommend counseling patients that TIPS is associated with a risk of overt HE in approximately 25%–50% of recipients (1b). Patient-specific risk factors for the development of post-TIPS overt HE include prior history of overt HE, advanced age, advanced liver dysfunction (CTP class C), hyponatremia, renal dysfunction, and sarcopenia (2a).	7.96	1.09	90.0

Supplementary Table 1. Continued

Question	Statement	Mean	SD	Response, %
Question 2. What social factors should be considered a contraindication to elective TIPS as it relates to overt HE?	We recommend avoiding elective TIPS in patients with cognitive impairment and limited family or social support.	7.59	1.25	90.0
Question 3. What is the role for formal evaluation for covert or minimal HE before elective TIPS?	In patients being considered for elective TIPS, testing for covert or minimal HE could be considered for prognostication and discussion with the patient.	7.58	1.36	83.3
Question 4. What TIPS stent diameter should be considered with regard to limiting post-TIPS HE?	In patients undergoing elective TIPS for ascites, we recommend starting with a smaller-diameter, controlled-expansion stent to potentially reduce rates of HE.	7.24	1.33	83.3
Question 5a. Is there a role for collateral embolization at the time of TIPS?	In patients undergoing elective TIPS for ascites and/or hepatic hydrothorax, embolization of SPSS >6 mm may be considered to reduce the risk of post-TIPS hepatic encephalopathy.	7.52	1.27	80.0
Question 5b. Is there a role for TIPS with shunt embolization in the management of refractory HE related to presumed clinically significant portosystemic shunting?	In select patients with large (>6 mm) SPSS and refractory HE, we recommend that shunt embolization be considered. For select patients who develop portal hypertensive-associated complications (ascites, varices) after shunt embolization, we recommend that small-caliber TIPS creation could be considered.	7.56	1.08	83.3
Question 6a. What is the role for medical prophylaxis to prevent HE after TIPS?	In patients without a history of overt HE undergoing TIPS, we do not recommend medical prophylaxis to prevent HE after TIPS.	7.15	1.56	90.0
Question 6b. What is the recommended medical therapy to treat overt HE after TIPS?	We recommend medical management of post-TIPS overt HE based on current guidelines with the use of lactulose and rifaximin.	8.0	1.07	90.0
Question 6c. What is the role for TIPS stent reduction/occlusion as the treatment of persistent or refractory HE?	We recommend consideration of TIPS stent diameter reduction in patients with persistent or refractory HE after TIPS.	8.08	0.93	86.7

AKI, acute kidney injury; CKD, chronic kidney disease; CTP, Child-Turcotte-Pugh; ePTFE, expanded polytetrafluoroethylene; GFR, glomerular filtration rate; HE, hepatic encephalopathy; HF, heart failure; HHT, hepatic hydrothorax; HPS, hepatopulmonary syndrome; HRS, hepatorenal syndrome; INR, international normalized ratio; IVC, inferior vena cava; LVEF, left ventricular ejection fraction; LVP, large volume paracentesis; MELD, Model for End-Stage Liver Disease; POPH, portopulmonary hypertension; PSG, portosystemic gradient; PVR, pulmonary vascular resistance; RVSP, right ventricular systolic pressure; SPSS spontaneous portosystemic shunt; TAPSE, tricuspid annular plane systolic excursion; TIPS, transjugular intrahepatic portosystemic shunt.

**Supplementary Table 2.** Technical Approaches to Elective TIPS Creation for Ascites

Approach/target	Advantages	Disadvantages
Initial dilation to 8 mm without consideration of PSG	The most uniform and reproducible technique across surgeons and institutions. Uniform initial use of an 8-mm stent is likely to minimize complications of encephalopathy and liver failure	Does not take into consideration individual patient hemodynamics and thus may be less effective in treating ascites May delay successful treatment of ascites in some patients
Base the stent diameter on a target PSG; dilate progressively from 8 mm to 9 mm to 10 mm until the PSG reaches a specified value	TIPS surgeons are comfortable using PSG as a target value for creating TIPS There is some support in the literature for using a target value of <12 mm HG or <10 mm Hg as thresholds for clinical success	PSG measurements vary based on the definitions surgeons use, the conditions under which TIPS is performed, and the precision and quality of the measurement
Base the stent diameter on a target percentage reduction in PSG	Percentage reduction is more targeted to individual patient hemodynamics than an absolute final PSG Minimizes the concern about PSG measurement definitions and accuracy because the value is “normalized” and is obtained the same way for the pre- and post-measurements	Requires a percentage calculation during the procedure that is not intuitive and not commonly performed in real time Little data for the percentage of PSG reduction in TIPS for ascites (more commonly applied to TIPS for bleeding).

PSG, portosystemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

**Supplementary Table 3.** Prospective Randomized Controlled Trials and Meta-Analyses Comparing TIPS vs LVP for Refractory Ascites

Study	N	Patient population	Technical details	Ascites outcomes	Mortality outcome	Comments
Prospective randomized controlled trials						
Lebrec et al, <sup>26</sup> 1996	25 (12 TIPS, 13 LVP) CTP B, 17 CTP C, 8	Refractory ascites	Uncovered stents Expanded to a diameter of 10 mm 2-3 stents placed per patient	4 months: CTP B, improved in 5 of 9 TIPS vs 0 of 8 LVP; CTP C, improved in 0% in both groups	2-year survival 29% with TIPS vs 56% in LVP ( $P < .05$ ) In CTP B, no difference in mortality	Increased HE in TIPS
Rössle et al, <sup>27</sup> 2000	60 (29 TIPS, 31 LVP)	Refractory ascites or recurrent ascites	Uncovered stents	3 months: 61% vs 18% no ascites ( $P = .006$ )	TFS at 1 year 69% TIPS vs 52% LVP ( $P = NS$ ) In multivariable analysis, TIPS associated with TFS (adjusting for age <60 y, sex, bilirubin level <3, and Na level >125)	HE similar between groups
Ginès et al, <sup>28</sup> 2002	70 (35 TIPS, 35 LVP)	Refractory ascites	Uncovered stents Strategy: to reduce PPG <12	Ascites recurrences 49% TIPS and 83% LVP ( $P = .003$ )	TFS at 1 year 41% TIPS vs 35% (NS)	HE no significant difference except severe
Sanyal et al, <sup>29</sup> 2003	109 (52 TIPS, 57 LVP)	Refractory ascites	Uncovered stents	TIPS superior to LVP in preventing recurrent ascites ( $P < .001$ )	No difference in deaths (identical in 2 groups) Median TFS times were longer in TIPS (19.6 vs 12.4 mo) but log rank of TFS overall was not significant	Nonsignificantly higher rate of moderate to severe HE
Salerno et al, <sup>30</sup> 2004	66 (33 TIPS, 33 LVP)	Refractory or recidivant ascites	Uncovered stents Strategy: to reduce PPG <12	TIPS (39%) superior to LVP (97%) in preventing recurrent ascites ( $P = .0012$ )	1 year TFS 77% TIPS vs 52% LVP ( $P =$ .021), TIPS predictive of survival in MVA controlling for MELD	Higher rates of HE
Narahara et al, <sup>31</sup> 2011	60 (30 TIPS, 30 LVP)	Refractory ascites	Uncovered stents Strategy: to reduce PPG <12 Initially dilated to 6 or 8 mm, then further dilated if PPG >12	TIPS superior to LVP in control of ascites ( $P$ < .005)	1-year survival 80% TIPS vs 49% LVP ( $P$ < .005)	TIPS associated with increased HE
Bureau et al, <sup>19</sup> 2017	62 (29 TIPS, 33 LVP)	Recurrence tense ascites	Viatorr (W.L. Gore & Associates, Flagstaff, AZ) 10- mm covered stent	Decreased LVPs needed in follow-up evaluation	1 year TFS 93% TIPS and 52% LVP ( $P =$ .003)	No difference on overt HE

Supplementary Table 3. Continued

Study	N	Patient population	Technical details	Ascites outcomes	Mortality outcome	Comments
		Trials included		Recurrent ascites	Mortality	
Meta-analyses						
Deltenre et al, <sup>32</sup> 2005	330	Lebrec et al, <sup>26</sup> Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al <sup>30</sup>	Uncovered	4 months: 66% vs 23.8%; $P < .001$ 12 months: 54.8% vs 18.9%; $P < .001$	1 year: 61.7% vs 56.5% (NS) 2 years: 50% vs 42.8%	Increased HE
D'Amico et al, <sup>33</sup> 2005	330	Lebrec et al, <sup>26</sup> Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al <sup>30</sup>	Uncovered	Pooled odds ratio, 0.14 95% CI (0.07–0.27)	Pooled odds ratio, 0.74 95% CI (0.40–1.37)	Meta-regression to exclude outlier trial (Lebrec et al <sup>26</sup> )
Albillos et al, <sup>34</sup> 2005	330	Lebrec et al, <sup>26</sup> Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al <sup>30</sup>	Uncovered	Pooled RR, 0.56 (0.47–0.66)	Pooled RR, 0.93 (0.67–1.28)	Random effects model
Saab et al, <sup>37</sup> 2006	330	Lebrec et al, <sup>26</sup> Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al <sup>30</sup>	Uncovered	3-month odds ratio, 0.07 (0.03–0.18; $P < .01$ ) 12-month odds ratio, 0.14 (0.06–0.28; $P < .01$ )	30-day odds ratio, 1.00 (0.10–10.06, $P = 1.0$ ) 24-month odds ratio, 1.29, (0.65 to 2.56, $P = .5$ )	Cochrane
Salerno et al, <sup>35</sup> 2007	305	Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al <sup>30</sup>	Uncovered	Tense ascites 42% vs 89% ( $P < .001$ )	Actuarial probability of TFS significantly better in TIPS ( $P = .035$ ) TIPS associated with better TFS in MVA including age, Total bilirubin, sodium	Did not include Lebrec et al <sup>26</sup> study Time to event analysis included Requires IAC criteria for refractory ascites
Bai et al, <sup>36</sup> 2014	390	Lebrec et al, <sup>26</sup> Rössle et al, <sup>27</sup> Ginès et al, <sup>28</sup> Sanyal et al, <sup>29</sup> Salerno et al, <sup>30</sup> Narahara et al <sup>31</sup>	Uncovered	Odds ratio, 0.15 ( $P < .001$ )	TFS HR 0.61 ( $P < .001$ )	Additional study included Time to event analysis included Lebrec et al <sup>26</sup> study not included in main TFS estimation

CTP, Child-Turcotte-Pugh; HE, hepatic encephalopathy; IAC, International Ascites Club; LVP, large-volume paracentesis; MELD, model for end-stage liver disease; MVA, multivariable; PPG, portal pressure gradient; RR, relative risk; TFS, transplant-free survival; TIPS, transjugular intrahepatic portosystemic shunt.

**Supplementary Table 4.** Patients With Nonrefractory Recurrent Ascites Included in Randomized Controlled Trials

Trial	Definition used
Rossle et al, <sup>27</sup> 2000	Tense ascites that recurred on at least 3 occasions within a 12-month period despite standard treatment
Salerno et al, <sup>30</sup> 2004	Recurrent ascites was defined as recurrence of at least 3 episodes of tense ascites within a 12-month period despite prescription of a low-sodium diet and adequate diuretic doses
Bureau et al, <sup>19</sup> 2017	Recurrent tense ascites (requiring $\geq 2$ LVPs in the previous 3 weeks), but excluding patients who had required $>6$ LVPs within the previous 3 months

LVP, large-volume paracentesis.



**Supplementary Table 5.** Summary of Selected Studies on TIPS for Novel Indications

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
TIPS before nonliver transplant surgery							
Vinet et al, <sup>187</sup> 2006	Retrospective case series with historical controls	35		Elective abdominal surgeries <ul style="list-style-type: none"> <li>• Colectomy, n = 10</li> <li>• Antrectomy, n = 5</li> <li>• Other, n = 3</li> </ul>		No difference in survival, bleeding, HE, or surgical outcomes	CTP, 8 in TIPS group vs 6 in non-TIPS Selection bias an issue Small sample size
Tabchouri et al, <sup>188</sup> 2019	Retrospective case series with concomitant controls	124		Elective abdominal surgeries; good selection of surgeries including colon resection and cholecystectomy		No difference in severe postoperative complications or mortality at 90 days Less ascites postoperatively in TIPS group TIPS patients actually required numerically more blood during the surgery and postoperatively	Propensity score analysis helped balance groups, but selection bias still an issue
TIPS in noncirrhotic portal hypertension resulting from extrahepatic portal vein obstruction							
Fanelli et al, <sup>189</sup> 2011	Retrospective case series	13	Mean, 17.4 mo	Portal cavernoma <ul style="list-style-type: none"> <li>• Recurrent variceal bleeding (n = 8)</li> <li>• Intestinal ischemia (n = 2)</li> <li>• High-risk varices with need for anticoagulation (n = 2)</li> <li>• Refractory ascites (n = 1)</li> </ul>	Transjugular portal vein recanalization and ePTFE TIPS placement ± manual aspiration thrombectomy PSG: 22.9 ± 6 to >8 ± 2.7 mm Hg	TIPS technical success 83.3% (10 of 12) Primary patency through follow-up evaluation, 70% Secondary patency through follow-up evaluation, 90% Survival 70% through follow-up evaluation (deaths: acute sepsis, 6 mo; ischemic stroke, 24 mo; neoplasm, 6 mo)	1 patient with shunt failure within 24 hours requiring emergent surgical shunt 2 patients with late TIPS dysfunction managed with TIPS revision 2 patients with isolated single episodes of HE during follow-up evaluation

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
Qi et al, <sup>190</sup> 2012	Retrospective case series	20	Median, 19.9 mo	Portal cavernoma with variceal rebleeding or refractory ascites, with absence of cirrhosis and malignancy	Transjugular (n = 1), transjugular/transhepatic (n = 4), or transjugular/transplenic (n = 2) portal vein recanalization and bare metal stent TIPS PSG: 26.3 ± 1.1 to >12.4 ± 1.1 mm Hg	TIPS technical success, 35% (7 of 20) Primary patency through follow-up evaluation, 71% Secondary patency through follow-up evaluation, 86% Variceal rebleeding (P = .057) • 14% TIPS success • 69% TIPS failure  Mortality (P = .587) • 29% TIPS failure • 15% TIPS success	No episodes of post-TIPS HE
Klinger et al, <sup>85</sup> 2017	Retrospective case series	17	Median, 28.6 mo	Acute PVT with imminent intestinal infarction (n = 10)	Combination of transjugular thrombectomy, local fibrinolysis, and, depending on thrombus resolution, TIPS	Recanalization, 94.1% 1- and 2-year patency, 88.2%	Major complications (n = 3) resolved spontaneously in all but 1 patient (heparin-induced thrombocytopenia type 2 with intestinal infarction) Symptoms improved in all patients Segmental bowel resection performed in 11.8% (n = 2)
Klinger et al, <sup>86</sup> 2018	Retrospective case series	17 (n = 15 with cavernous transformation)		Chronic PVT • Variceal bleeding (n = 13) • RA (n = 2) • Portal biliopathy with recurrent cholangitis (n = 1) • Abdominal pain (n = 1)	Combination of transjugular balloon angioplasty, mechanical thrombectomy, and, depending on extent of residual thrombosis, TIPS and additional stenting of portal venous system	Recanalization, 76.5% Secondary patency: 1-year, 69.5%; 2-year, 69.5%	Complications (n = 3): • Intraperitoneal bleeding (n = 1) • Liver hematoma (n = 1) • Nosocomial pneumonia (n = 1)

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
Rosenqvist et al, <sup>84</sup> 2016	Retrospective case series	10	Median, 17 mo (range, 1.5–72 mo)	Acute and chronic PVT <ul style="list-style-type: none"> <li>• Bowel ischemia (n = 4)</li> <li>• Variceal bleeding (n = 6)</li> </ul>	Local thrombolysis combined with TIPS used in 6 of 10	Recanalization, 70% 2-year patency, 70% 1 death, remaining 9 patients asymptomatic at last follow-up evaluation	
Marot et al, <sup>87</sup> 2018	Retrospective case series	15	Means, 42 ± 28 mo	Chronic PVT <ul style="list-style-type: none"> <li>• GI bleeding (n = 6)</li> <li>• Portal biliopathy (n = 2)</li> <li>• Reduce portal pressure before surgery (n = 4)</li> <li>• Other (n = 3)</li> </ul>		Recanalization, 87% 1- and 2-year patency, 77% (87% vs 60% in patients who received anticoagulation or not, respectively; <i>P</i> = .3)	PVR is feasible in most patients with noncirrhotic, nontumoral portal vein occlusion when there is no extension of the occlusion to distal branches
TIPS, n							
TIPS for INCPH Bissonnette et al, <sup>191</sup> 2016	Retrospective multicenter case series	41	Means, 27 ± 28 mo	Biopsy-confirmed INCPH <ul style="list-style-type: none"> <li>• Refractory variceal bleeding (n = 25)</li> <li>• Refractory ascites (n = 16)</li> </ul>	Standard TIPS technique with ePTFE TIPS in 80%, bare metal stent TIPS in 20% PSG: 19 ± 6 mm Hg to >7 ± 3 mm Hg	Primary patency through follow-up evaluation, 73% Secondary patency through follow-up evaluation, 100% Variceal rebleeding, 28% Ascites (n = 9 alive at last follow-up evaluation) 67% no residual ascites 33% low-dose diuretic controlled	Early mortality 5 of 41 (1 peritoneal bleeding, 1 heart failure, 2 liver disease, 1 renal failure) Post-TIPS overt HE 34% (14 of 41) Serum creatinine ( <i>P</i> = .005), ascites as indication ( <i>P</i> = .04), and significant comorbidities ( <i>P</i> = .01) associated with death

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
Regnault et al, <sup>192</sup> 2018	Retrospective single-center series	25	Means, 39 ± 37 mo	Biopsy-confirmed noncirrhotic portal HTN; if cavernoma, liver histology showed pathology excluding simple extension of extrahepatic PV obstruction Varices rebleeding prevention (n = 14) Refractory ascites (n = 5) Varices and ascites (n = 5) Before cholecystectomy (n = 1)	TIPS prosthesis: • ePTFE (Viatorr; W.L. Gore & Associates, Flagstaff, AZ) n = 22 • Bare metal stent n = 3  PSG: 14.7 ± 3.8 to >5.0 ± 2.3 mm Hg	Patency: 2 early stent thrombosis Patency through follow-up evaluation (n = 20) Primary, 80% Secondary, 100% N = 4 recurrence of presenting symptoms (3 ascites, 1 hemorrhage) between 1 and 5 mo after TIPS	Mortality 24% (n = 6) over follow-up period n = 1 TIPS-related (stent malposition, liver failure) n = 2 portal HTN-related (1 bleeding, 1 ascites with complications) Overt HE 40% (n = 10) through follow-up evaluation Five of 10 respond medical tx Three of 10 TIPS reduction Two of 10 deaths from complications of hepatic coma
Lv et al, <sup>193</sup> 2019	Retrospective case-control series	76 (INCPH TIPS group)	Median, 36.4 mo (INCPH group) and 34.3 mo (cirrhosis group)	Biopsy-confirmed INCPH and variceal bleeding • Emergency TIPS n = 10 • Elective TIPS n = 66	Prosthesis: ePTFE TIPS 78% PSG: 25.5 ± 4.7 mm Hg to >8.8 ± 3.5 mm Hg	5-year outcomes c/w matched cirrhotic patients Shunt dysfunction: INPCH, 35%; CPH, 36% (P = .627) Rebleeding: INCPH, 33%; CPH, 32% (P = .358) Overt HE: INCPH, 16%; CPH, 33% (HR, 0.35; P = .007) Mortality: INCPH, 11%; CPH, 36% (HR, 0.37; P = .022)	Single-center case-control series showing TIPS in INCPH has similar efficacy for variceal hemorrhage and similar rates of TIPS dysfunction compared with matched patients with CPH undergoing TIPS However, patients with INCPH undergoing TIPS for variceal bleeding had less HE and overall less mortality over 5 years compared with CPH group

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
TIPS for BCS Plessier et al, <sup>92</sup> 2006	Prospective single-center cohort	21	Median, 35 mo (cohort, n = 51)	Data for full cohort (n = 51) Acute, 6% Chronic, 69% Acute-on-chronic, 25% Ascites, 71% Asymptomatic, 6%	BMS 48% ePTFE stent graft 52%	TIPS primary patency 62% through follow-up evaluation (30% bare metal stent, 91% ePTFE stent graft) TIPS complete clinical response 95%	Clearest criteria for progression through stepwise management algorithm among cohort of BCS patients
Garcia-Pagán, <sup>109</sup> 2008	Retrospective single-center case series	124	Mean, 36.7 mo	Ascites, 98%	BMS, 49% ePTFE stent graft, 39% Both, 12%	Primary patency 59% over follow-up period OS, 87% through follow-up period TFS: 1-year, 88% 5-year, 78% 10-year, 69%	Large high-quality multicenter retrospective study BCS-TIPS score developed from cohort as predictor of 1-year OS after TIPS in BCS
Seijo et al, <sup>95</sup> 2013	Prospective multicenter cohort	62	Median, 50 mo (cohort, n = 157)	Data for full cohort: ascites, 82%	BMS vs ePTFE stent graft not reported	TIPS OS: 1-year, 88% 3-year, 83% 5-year, 72% TIPS TFS: 1-year, 85% 3-year, 78% 5-year, 72%	Large, multicenter, prospective cohort study providing highest level of evidence available in BCS
Eldorri et al, <sup>96</sup> 2011	Prospective single-center cohort	13	Mean, 20 mo (cohort, n = 25)	Data for full cohort: Fulminant, 4% Acute, 12% Chronic, 84% Ascites, 96%	BMS 100%	TIPS primary patency: 1-year, 62% End of follow-up evaluation, 62% TIPS secondary patency: 1-year, 92% End of follow-up evaluation, 85% TIPS OS: 1-year, 100% End of follow-up evaluation, 100%	Small prospective cohort study, TIPS all performed with bare metal stents with expected loss of primary patency, excellent survival

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
Hayek et al, <sup>110</sup> 2017	Retrospective single-center case series	54	Mean, 56 mo	Subacute, 2% Chronic, 76% Acute-on-chronic, 22% Ascites, 93%	ePTFE stent graft 100%	TIPS primary patency: 1-year, 64% 5-year, 45% 10-year, 45% TIPS secondary patency: Final follow-up evaluation, 96% OS: 1-year, 96% 2-year, 88% 5-year, 83% 10-year, 76%	Large retrospective series with clearly defined management algorithm, follow- up protocol, and outcome definition
Shalimar et al, <sup>93</sup> 2016	Retrospective single-center case series	80	Median, 600 d	Acute, 8% Subacute, 28% Chronic, 65% Ascites, 86%	BMS + ePTFE stent graft 100%	Primary patency: 1-year, 91% 3-year, 86% 5-year, 86% OS: 1-year, 94% 3-year, 89% 5-year, 84%	Large modern series using alternative ePTFE construct (BMS + stent graft) with very high primary patency rates and OS Data did not validate BCS-TIPS PI score as predictor of 1-year survival after TIPS in BCS, although patient population with overall low BCS- TIPS PI scores at baseline
Tripathi et al, <sup>102</sup> 2017	Retrospective single-center case series	67	Mean, 82 mo	Ascites 80%	BMS, 30% ePTFE stent graft, 70%	Primary patency: 5-year BMS, 27% 5-year ePTFE stent graft, 70% Secondary patency, 99% OS: 1-year, 92% 5-year, 80% 10-year, 72%	Large retrospective series with exceptionally long mean follow-up period Patency ePTFE stent graft > BMS

Supplementary Table 5. Continued

Study	Study design	N	Follow-up time	Indication(s) for TIPS	Technical details	Outcomes	Comments
Qi et al, <sup>105</sup> 2014	Retrospective single-center case series	51	Mean, 732 d	Ascites 94%	BMS, 65% ePTFE stent graft, 35%	Primary patency: 1-year, 62% 2-year, 44% 5-year, 24% OS: 1-year, 84% 3-year, 77% 5-year, 56%	Large series from China confirming technical feasibility of TIPS/ direct intrahepatic portosystemic shunt after prior hepatic venous outflow tract obstruction BCS-TIPS PI score was found to predict OS in this series
Rathod et al, <sup>101</sup> 2017	Retrospective single-center case series	106	Median, 42 mo	Acute, 7% Subacute, 35% Chronic, 58% Ascites, 79%	ePTFE stent graft 100%	TIPS patency through follow-up period: Primary, 87% Secondary, 100%	Large retrospective series showing high patency rates over intermediate term with ePTFE stent graft
Sakr et al, <sup>194</sup> 2017	Retrospective single-center cohort study	106	1 year	Acute/subacute, 30% Chronic, 79%	BMS vs ePTFE stent graft not specified	TIPS primary patency: 1-year, 80% OS TIPS: 1-year, 90%	Large retrospective series with good patency and high OS rates at 1 year BCS-TIPS PI score was found to predict OS in this series

BCS, Budd–Chiari syndrome; BMS, bare metal stent; CTP, Child–Turcotte–Pugh; c/w, consistent with; ePTFE, expanded polytetrafluoroethylene; GI, gastroenterologist; HE, hepatic encephalopathy; HR, hazard ratio; HTN, hypertension; INCPH, idiopathic noncirrhotic portal hypertension; OS, overall survival; PI, prognostic index; PV, portal vein; PVR, portal vein recanalization; PVT, portal vein thrombosis; RA, refractory ascites; TFS, transplant free survival; TIPS, transjugular intrahepatic portosystemic shunt; tx, treatment.

**Supplementary Table 6.** Components of a Comprehensive Echocardiographic Evaluation pre-TIPS

Left ventricular function assessment	Right ventricular function assessment
Systolic function <ul style="list-style-type: none"> <li>o Ejection fraction (normal: &gt;50%)</li> <li>o Global longitudinal strain (normal: absolute value <math>\geq</math>18%)</li> </ul> Diastolic function <sup>a</sup> <ul style="list-style-type: none"> <li>o Early diastolic transmitral flow to early diastolic mitral annular tissue velocity (E/e') ratio (normal: <math>\leq</math>14 cm/s)</li> <li>o Septal e' velocity (normal: <math>\geq</math>7 cm/s)</li> <li>o Left atrial volume index (normal: <math>\leq</math>34 mL/m<sup>2</sup>)</li> <li>o Tricuspid regurgitation velocity (normal: <math>\leq</math>2.8 m/s)</li> </ul>	Right ventricular systolic pressure (normal: age-dependent, up to 45 mm Hg) Tricuspid annular plane systolic excursion (normal: >1.6 cm)

<sup>a</sup>Two or more abnormalities are needed to make the diagnosis of diastolic dysfunction. The degree of diastolic dysfunction is to be determined by the cardiologist depending on additional measures such as early to late diastolic transmitral flow velocity (E/A) ratio (at rest or during Valsalva), left atrial strain, and left ventricular strain. Guidance is adapted from the American Society for Echocardiography guidelines and the Cirrhotic Cardiomyopathy Consortium practice guidance.<sup>114,115</sup>