Transjugular Intrahepatic Portosystemic Shunts in Patients with Hepatic Malignancy

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ABSTRACT

Since its first clinical application in 1988, the transjugular intrahepatic portosystemic shunt (TIPS) has emerged as a safe and effective means of managing patients with morbid portal hypertension. Despite the considerable body of literature on TIPS, portal decompression in patients with malignancy has not been sufficiently examined. These patients typically experience sequelae of portal hypertension that requires palliation. The purpose of this article is to review the reported experience with TIPS in patients with malignancy.

KEYWORDS: Hepatic neoplasm, interventional procedure, portosystemic shunt, portal hypertension

Objectives: Upon completion of this article, the reader should (1) understand the anatomic and physiological aspects of hepatic perfusion in normal and diseased states, (2) realize the impact of surgical or percutaneous portosystemic shunt procedures on blood flow to the liver, and (3) identify those patients at high risk for these procedures on the basis of their hepatic perfusion profiles.

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Transjugular intrahepatic portosystemic shunt (TIPS) placement has emerged over the past 15 years as an effective, minimally invasive method of treating portal hypertension and its associated complications. Although the most studied and accepted indication for TIPS placement is refractory variceal hemorrhage,¹⁻³ other indications include refractory ascites,⁴ hepatic hydrothorax,^{5,6} and Budd-Chiari syndrome.^{7,8} According to the Society of Interventional Radiology's quality improvement guidelines,⁹ shunting should yield a technical and hemodynamic success rate of greater than 95% and a procedure-related major complication rate of less than 5%.

The absolute contraindications for TIPS include right heart failure, severe hepatic failure, uncontrolled hepatic encephalopathy, and uncontrolled systemic infection. Relative contraindications include polycystic liver disease and extensive primary or secondary hepatic malignancy.⁹ Excluding TIPS depends on the degree of hepatic involvement and the perceived increased risk of technical complications. Documentation on using percutaneous portosystemic shunting for patients with hepatic¹⁰⁻¹² or extrahepatic^{12,13} malignancy is limited. This article reviews the published experience with TIPS placement in patients with hepatic malignancy.

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Malignant tumors and concomitant portal hypertension pose a high level of clinical and technical complexity with regard to the decision for and the execution of portosystemic shunt insertion. Hepatic malignancy as a relative contraindication to TIPS insertion depends on the degree of hepatic involvement and the perceived increase in the risk of technical complications, most notably hemorrhage and tumor embolization. During the first decade of experience using TIPS, only a few case reports and larger patient series^{14,15} that included patients with hepatic malignancy were published, and none of those reports described the location of tumors with respect to intrahepatic shunts. In fact, several authors over this period used the presence of hepatic malignancy as an exclusion criterion.^{16,17}

Prognosis is believed to be a central factor for excluding patients with diffuse or extensive focal malignancy from undergoing TIPS. In a recent series ($n = 38$) from The University of Texas M.D. Anderson Cancer Center, we reported our experience with TIPS in patients with both intrahepatic ($n = 19$) and extrahepatic malignancies, in which a subset of patients ($n = 9$) had shunts placed through the tumor.¹² Our population included patients with considerable tumor burden and limited life expectancy, and TIPS was used to palliate complications of portal hypertension. In making the decision to proceed with TIPS, the risks and benefits of the procedure were seriously weighed.

As already mentioned, TIPS has been in clinical use for ~15 years, and when it is performed by experienced operators, the risk of fatal technical procedure-related complications is as low as 1.4%.¹⁸ However, the perceived increased risk of hemorrhage or vascular seeding is an issue that has not been satisfactorily investigated in patients with hepatic malignancy when shunts traverse tumor. In the series from the M.D. Anderson Cancer Center, no procedure-related hemorrhage or overt vascular tumor seeding was encountered despite the fact that shunts traversed the malignancy in nine of the 19 patients with hepatic malignancies. Uncovered stents were used to create all shunts in this series.¹² Jiang et al also recently reported their experience with TIPS in 14 patients with portal vein tumor thrombus using uncovered stents. No procedure-related hemorrhage was encountered, and one shunt traversed the malignancy with no evidence of metastasis from vascular seeding 3 months after the procedure.¹⁹

The recent emergence of a U.S. Food and Drug Administration–approved polytetrafluoroethylene (PTFE)–covered stent specifically designed for TIPS²⁰ should reduce the risk of tumor seeding from tumors within the liver, especially when the shunts traverse the malignancy. A recent case report by Hur et al described the use of a homemade stent-graft for TIPS in a patient with hepatocellular carcinoma and main portal vein invasion.²¹ Covered stents will not, however, reduce

the risk of seeding that may occur during shunt creation and will not address the potential risk of early development of pulmonary metastasis from gastrointestinal malignancies that may spread via the portal venous system. One maneuver to reduce the chance of traversing the malignancy or portal vein tumor thrombus is to use the left hepatic approach¹² or direct transcaval approach^{22,23} as an alternative if these proposed tracts are tumor-free.

Preprocedure imaging (computed tomography [CT] and magnetic resonance imaging [MRI]) is an essential planning tool to obtain a global perspective of the liver with regards to location and extent of tumor. Three-phase, contrast-enhanced CT is the cross-sectional imaging modality of choice at our institution. When MRI is utilized, flow-sensitive, single-slice, gradient-echo images in multiple planes perpendicular to the axis of flow are used to assess the portal system. Cross-sectional imaging also allows for the overall assessment of hepatic and portal venous orientation and patency. When portal compromise is present, preliminary imaging is helpful for optimal shunt placement especially when the main portal vein, superior mesenteric vein, or splenic vein are involved. Pre-TIPS imaging also provides other helpful landmarks to assist with identifying the level of the portal vein such as bony landmarks or clips from prior surgical intervention. Imaging is also a key step as anatomic distortions can occur with large central hepatic tumors or when major hepatic resections have occurred.

When the right hepatic vein and the right portal vein are sufficiently open, we typically use a Ring Transjugular Intrahepatic Access Set (Cook Incorporated, Bloomington, IN) with a 16-gauge modified Ross needle to access the portal system. For the left hepatic approach we tend to use the 21-gauge transjugular access set (Angiodynamic, Glen Falls, NY). Access of the portal vein through the left lobe generally involves advancing the 21-gauge needle in a relatively straight caudal direction from the left hepatic vein.

In patients with complex anatomy, including hepatic and portal venous compromise, TIPS placement has been accomplished, but higher rates of technical failure have been encountered in these patients than in those with conventional patent venous anatomy.^{24,25} In a series of 20 patients with portal vein thrombosis, Walser et al reported failure in the six patients who had cavernous transformation caused by the inability to cross the portal occlusion ($n = 2$) and difficult hepatic anatomy ($n = 4$). Of the remaining 14 patients in their series, 12 underwent successful TIPS placement.²⁴ Radosevich et al described TIPS in five of 10 patients with chronic portal vein thrombosis. TIPS placement was unsuccessful in three patients with chronic portal occlusion in whom only the transjugular route was used but was successful when transhepatic recanalization was performed

before TIPS creation.²⁵ Matsui et al used a combination of percutaneous and surgical approaches to recanalize a chronically occluded portal vein prior to TIPS insertion.²⁶ Three groups of investigators have reported successful shunt placement in patients with chronic portal vein occlusion and cavernous transformation using solely the jugular route. Yamagami et al demonstrated the insertion of a TIPS from the hepatic vein to a periportal collateral vein in a patient with superior mesenteric vein occlusion and splenic vein ligation.²⁷ In the M.D. Anderson series, portal compromise was encountered in eight of the 19 patients with hepatic malignancy; the primary technical success rate was 95%, with a left hepatic approach utilized in four patients, two of whom had chronic portal occlusion with cavernous transformation.¹² In the series by Jiang et al, eight of 14 patients with hepatocellular carcinoma had complete occlusion of the main portal vein, and the other six patients had incomplete thrombosis. Five of the eight patients with complete occlusion had cavernous transformation. The technical success rate in this series was 71%; all four failures occurred in the patients with cavernous transformation of the portal vein.¹⁹

The reported rate of hepatic encephalopathy following TIPS ranges from 13 to 47%.²⁸ The rate of encephalopathy in the series by Jiang et al was 35% (stage I)¹⁹ and in the M.D. Anderson series was 44%.¹²

Several TIPS follow-up series conducted before the use of stent-grafts became routine demonstrated poor primary patency, with revisions for shunt stenosis and occlusion required in up to 67%¹⁶ within the first year of the procedure. Saxon et al reported an acute (< 30-day) shunt occlusion rate of 17% in a series of 116 patients.²⁹ Premature (< 30-day) shunt occlusion was also encountered in 3 (8%) of 38 patients in the M.D. Anderson series¹²; these three occurred in the nine patients whose shunts traversed the malignancy.³⁰ We are uncertain about the cause of these premature failures, and we can only speculate that the trauma to the tumor may release fragments of tumor or factors that promote coagulation. This is suggested by the fact that oncology patients have a relatively high risk for venous thrombotic complications. It is also possible that bile duct trauma during TIPS with subsequent leakage—one accepted cause of premature shunt occlusion³¹—could have caused the early failures. Our experience with premature shunt occlusion that occurred only in those patients whose shunt traversed the malignancy perhaps favors the relationship with trauma to the tumor rather than with bile leakage. It is doubtful that the tumor grew into the uncovered stent within such a short time. Using stent-grafts for TIPS that traverse the malignancy is an appropriate use of this technique not only to reduce acute shunt occlusions and improve long-term patency but also to reduce the potential for vascular spread of the tumor. PTFE-covered stents were not commercially available

for use in our early patients, but because preliminary clinical results from the use of PTFE stent-grafts for TIPS are promising, with a 1-year primary patency rate of 80%,^{20,32} these PTFE-covered stents would likely be the best option to use.

In the presence of a comorbidity, the desired potential benefit from TIPS must be a major consideration. In the M.D. Anderson series, the issue of limited life expectancy in terms of 30-day survival rate was higher (84%)¹² than the published rates for TIPS in patients in Child-Pugh class C (60 to 77%).^{15,33,34} No statistically significant difference in 30-day survival was found between patients with ascites- or hepatic hydrothorax-related indications and those with variceal- or portal gastropathy-related indications, but a significant survival difference was demonstrated between the two groups 90 days after TIPS placement (27 versus 84%, respectively; $P=0.0075$). The 90-day survival rate was not significantly different between the subgroup of patients with hepatic malignancy and that with extrahepatic malignancy ($P=0.1103$), but there was a significant difference ($P=0.0077$) in survival rate when comparing patients with primary hepatic malignancy (36%) and the remaining study patients with hepatic metastasis and extrahepatic malignancy (74%).¹² The 27% 90-day survival rate for our patients with ascites¹² was far below the reported range of 1-year transplant-free survival rates of 41 to 69% for patients with ascites who have undergone TIPS.^{4,35} Thus, we urge caution in the use of TIPS in patients with concomitant malignancy and hepatogenic ascites and in those with a hepatic primary malignancy, regardless of indication.

The model for end-stage liver disease (MELD) score, which was originally developed to assess the short-term prognosis of patients with cirrhosis after TIPS, has recently been adopted as a disease-severity index for patients with end-stage liver disease who are awaiting liver transplantation. Previous series that used the MELD score identified a score of 18 as a threshold for high-risk patients with a median survival duration of less than 90 days.^{17,36} Angermayr et al, however, found that a MELD score of greater than 18 was insufficient to rank patients into high- and low-risk groups; using a population of 475 TIPS patients, they determined that a MELD score of greater than 14 was a statistically better threshold value.³⁷ Like Angermayr et al, we found that a lower MELD score (≥ 12) was required to improve our ability to predict short-term prognosis in our unique patient population with substantial comorbidities.¹²

Despite the relatively high incidence of portal venous compromise in patients with hepatic malignancies, TIPS placement can be performed safely. Based on the report by Wallace et al¹² in patients with cancer, subgroups of patients with malignancy and ascites, primary hepatic malignancy, or MELD scores of ≥ 12 have the lowest 90-day survival rates.

Figure 1 Portal venous phase images demonstrate the following: (A) a patent left hepatic vein (black arrow); (B) a central low-density mass (white arrowhead), with bile duct dilation in the right lobe of the liver despite the presence of an endoscopic stent (white arrow); (C) a central low-density mass (white arrowhead), with bile duct dilation in the right lobe of the liver despite the presence of an endoscopic stent (white arrow), and a patent main left portal vein (black arrow) reconstituted just cephalad to the portal bifurcation; (D) central and right portal vein occlusion was identified as evidenced by numerous periportal collaterals present (black arrowheads).

TIPS in patients with hepatic malignancies can be performed without higher rates of technical procedure-related complications compared with patients without cancer. Hepatic neoplasm alone should not be a contraindication to percutaneous shunting in the management of patients with severe portal hypertension.

CASE ILLUSTRATION

A 38-year-old man with cholangiocarcinoma involving the central portion of the liver presented for transjugular intrahepatic portosystemic shunt for management of portal gastropathy requiring frequent blood transfusions. His history included chemoradiation therapy for treatment of his hepatic malignancy and multiple episodes of cholangitis for which endoscopic stent placement and exchanges were performed on several occasions. Prior to TIPS three-phase contrast-enhanced CT of the liver was performed for planning purposes. Portal venous phase images (Fig. 1A to 1D) demonstrate a patent left hepatic vein (Fig. 1A; black arrow) and a central low-density mass (Fig. 1B, 1C; white arrowhead), with bile duct

Figure 2 Following right internal jugular vein access the left hepatic vein was selected and venography demonstrated a modest-size hepatic vein for TIPS.

Figure 3 A long 21-gauge transjugular access set (Angiodynamic, Glen Falls, NY) was then advanced in a caudal direction until a peripheral portal vein radicle was accessed.

Figure 4 Anterior-posterior (AP) subtraction.

Figure 5 Nonsubtraction cranially angulated-AP.

dilation in the right lobe of the liver despite the presence of an endoscopic stent (Fig. 1B, 1C; white arrow). Central and right portal vein occlusion was identified as evidenced by numerous periportal collaterals present (Fig. 1D; black arrowheads). A patent main left portal vein (Fig. 1C; black arrow) reconstituted just cephalad to the portal bifurcation. Considering the presence of a large central mass with right and main portal vein occlusion, the decision was made to perform a TIPS through the left lobe of the liver. Following right internal jugular vein access the left hepatic vein was selected and venography (Fig. 2) demonstrated a modest-size hepatic vein for TIPS. A long 21-gauge transjugular access set (Angiodynamic, Glen Falls, NY) was then advanced in a caudal direction until a peripheral portal vein radicle was accessed (Fig. 3). A peripheral entry site was favorable to provide the maximum possible intraportal distance for catheter manipulation to recanalize the portal vein. Anterior-posterior (AP) subtraction

Figure 6 (A,B) Images during portal vein recanalization with subsequent splenoportography.

Figure 7 (A,B) Confirming the presence and extent of portal occlusion with demonstration of numerous periportal collateral veins present consistent with cavernous transformation of the portal vein.

(Fig. 4) and nonsubtraction cranially angulated-AP (Fig. 5) left portal venography was performed with a diagnostic catheter positioned in the patent central portion of the left portal vein. Cranial angulation of the image intensifier provided a profile view of a tapered and occluded left portal vein (Fig. 5; black arrow). Fig. 6A and 6B shows images during portal vein recanalization with subsequent splenoportography confirming the presence and extent of portal occlusion with demonstration of numerous periportal collateral veins present, consistent with cavernous transformation of the portal vein (Fig. 7A and 7B). Identification of the

tapered occlusion in the portal vein was the key step for recanalization. Final TIPS venography (Fig. 8) after stent placement demonstrates good primary flow through the shunt. Collateral veins within the portal system were not longer visualized after shunt creation. The patient died 135 days after TIPS.

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Figure 8 Final TIPS venography after stent placement demonstrates good primary flow through the shunt.

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