The History and Future of Transjugular Intrahepatic Portosystemic Shunt: Food for Thought

Wael E. Saad, MD, FSIR¹

¹Department of Radiology, University of Michigan Medical Center, Ann Arbor, Michigan

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Address for correspondence: Wael E. Saad, MD, FSIR, Department of Radiology, University of Michigan Medical Center, 1500 E. Medical Drive, SPC 5868, Cardiovascular Center, #5588, Ann Arbor, MI 48109-5868 (e-mail: wsaad@umich.edu).

Abstract

The origins of transjugular intrahepatic portosystemic shunt (TIPS) date back to the 1960s with inadvertent portal access during the early years of transjugular cholangiography. TIPS is now the most frequently performed portal hypertension decompressive procedure performed by interventional radiologists, and has become the primary portosystemic shunt (surgical or percutaneous) performed in the United States. One of the least discussed major advantages of TIPS in the transplant era is that it is intrahepatic and thus is removed in situ during a liver transplant, while extrahepatic shunts (surgical or percutaneous) have to be ligated or revised during the liver transplantation. However, since the widespread clinical utilization of TIPS in the 1990s, it has been plagued with two major problems, namely, patency and hepatic encephalopathy. With the advent of commercially available expanded polytetrafluoroethylene (e-PTFE) covered stents a decade ago, 12- to 24-month TIPS patency has improved significantly (by ~20–30%). However, hepatic encephalopathy (although not proven to have increased due to e-PTFE covered stents grafts) remains a significant morbidity problem. The article discusses the history of TIPS, critiques the retrospective encephalopathy data in the literature, and discusses futuristic TIPS-design ideas about the management of post-TIPS hepatic encephalopathy.

Keywords

- TIPS
- history
- portosystemic shunt
- portal hypertension
- development
- interventional radiology

Objectives: Upon completion of this article, the reader will be able to recall the evolution of TIPS, and the remaining technical and clinical difficulties that provide opportunities for further development.

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The origins of transjugular intrahepatic portosystemic shunt (TIPS) date back to the 1960s with inadvertent portal access during the early years of transjugular cholangiography. This was subsequently followed by animal experiments with tract dilation and then later stent placement. TIPS was clinically introduced and widely practiced on humans in the 1990s; it is now the most common portal hypertension decompressive procedure performed by interventional radiologists and has become the primary portosystemic shunt (surgical or percutaneous) performed in the United States. One of the least discussed major advantages of TIPS in the transplant era is that it is intrahepatic and thus is removed in situ during liver transplantation, while extrahepatic shunts (surgical or percutaneous) have to be ligated or revised during the transplant procedure.¹

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However, TIPS has traditionally been plagued with two major problems: patency and hepatic encephalopathy. With the advent of commercially available expanded polytetrafluoroethylene (e-PTFE) covered stents a decade ago, 12- to 24-month TIPS patency has improved significantly (by ~20–30%). However, hepatic encephalopathy (although not proven to have increased due to e-PTFE covered stents grafts) remains a morbidity problem.

History

As a technique, TIPS dates to the 1960s (►Table 1). In 1969, Rösch et al reported portal venography via a transjugular approach and discussed the potential of a “radiologic portocaval shunt.”² This was subsequently followed by animal experiments, initially with tract dilation utilizing dilators and then balloons (►Table 1). However, dilation of animal (mostly canine) model livers without portal hypertension and without scaffolding (stents) to help reduce re-occlusion of the parenchymal tract leads to very short patency rates (within weeks they re-occluded).³ In 1982, Colapinto et al performed the first human balloon-dilated transjugular portosystemic shunt.^{4,5} However, it was in 1988 that the first human clinical procedure of a TIPS utilizing a metallic stent was documented (Palmaz stent) by Goetz Richter (Freiburg, Germany).⁶

Subsequently, in the early to mid-1990s there was widespread clinical use of TIPS utilizing bare-metal stents. Self-expanding stents predominated as the primary stent utilized during TIPS (particularly the Wallstent, Boston Scientific, Natick, Massachusetts, United States).^{7,8} In the second half

of the 1990s, animal experimentation on covered stents using silicone coating and e-PTFE showed favorable patency results for e-PTFE covered stents.^{9–11} Again, investigators at the Dotter Institute described a partly covered self-expanding stent, which the author believes has remarkable resemblance to the currently commercially available Viatorr stent (Gore and Associates, Flagstaff, Arizona, United States).¹⁰ In the early 2000s, early human e-PTFE covered stent grafts for TIPS creation showed favorable and safe results with improved TIPS patency.^{12–16} Finally, a decade ago (2003–2004) the Viatorr stent became commercially available in the United States and widespread utilization of this e-PTFE covered stent grafts for TIPS occurred (►Table 1). ►Table 1 places all of the above TIPS historic milestones on a timeline.

Current Practice and the Stent-Graft Era

Although the initial clinical indication for TIPS was management of variceal bleeding with the procedural end point of reducing the portosystemic gradient to less than 12 mm Hg, patients with concomitant variceal bleeding and ascites were noted to have resolution of ascites. Gradually, medical and endoscopic management of variceal bleeding improved and the effectiveness of TIPS to treat ascites developed; the current indication for TIPS in most universities in the United States is for ascites, with 80 to 90% of all TIPS being performed electively.^{17–20} Ascites resolves after TIPS creation in approximately 70% of patients.²¹

Since its initial use in humans, TIPS has had two major problems: patency and hepatic encephalopathy. With the

Table 1 TIPS history and milestones

Timeline	Milestone
1960s	Inadvertent portal access during transjugular cholangiography
1969	Rosch discussed the potential of a “radiologic portocaval shunt”
1982	Colapinto creates the first human balloon dilated TIPS
1988	Richeter creates the first human Palmaz stent TIPS
Early to mid-1990s	Widespread clinical use with self-expanding bare stents
Mid- to late-1990s	Animal experimentation using silicone and e-PTFE coated stents to improve TIPS patency
2001	Procedure endpoint defined as a reduction in PSG to less than 12 mm Hg
Early 2000s	<ul style="list-style-type: none"> • Early human e-PTFE covered stent-graft experience • Defining TIPS candidacy by prognostic parameters (e.g., MELD)
2003–2004	Widespread human use of commercially available e-PTFE covered stent-grafts
2005	AASLD places practice guidelines on the “role of TIPS in the management of portal hypertension”
2009	AASLD adds Budd–Chiari as an additional indication for TIPS and considers e-PTFE covered stent grafts as standard of practice
2013–2014	Present day: <ul style="list-style-type: none"> • > 80–90% of TIPS elective • Technical success rate > 97% • Fatality of procedure < 1–2% • 1-year patency rate > 80% • >2,300 citations on PubMed

Abbreviations: AASLD, American Association for the Study of Liver Disease; e-PTFE, expanded polytetrafluoroethylene; MELD, Model for End-Stage Liver Disease; PSG, portosystemic gradient; TIPS, transjugular intrahepatic portosystemic shunt.

advent of e-PTFE covered stent grafts, the 12-month and 24-month patency rates approach 80 to 90% and 70 to 80%, respectively.²² This has drastically improved the historic patency of TIPS of 30 to 70% at 6 to 12 months utilizing bare metal stents; however, the problem with hepatic encephalopathy still remains (see below).²²

The last decade has also witnessed a considerable clinic advancement that is as important as the use of e-PTFE stent grafts. In the last decade, many studies evaluated patient candidacy of TIPS by evaluating clinical outcome and survival based on physiologic and hepatologic metrics and scoring systems.^{23–26} These studies helped define TIPS candidacy and improved survival and thus long-term follow-up. It is now understood that TIPS placed in patients who are Child–Pugh class A and have a Model for End-Stage Liver Disease (MELD) score of less than 18 has better clinical outcomes and patient survival. In addition, a MELD score of greater than 18, but driven primarily by a higher creatinine and not by a high serum bilirubin, may also provide better outcomes.^{23–26} Moreover, patients with a high creatinine due to hepatorenal syndrome may improve their renal function after TIPS and, as a result, have a subsequent reduction in their MELD score.^{23–26}

Post-TIPS Hepatic Encephalopathy

Hepatic encephalopathy after TIPS is now the single most important outcome that affects patient morbidity. TIPS is known to increase the risk of hepatic encephalopathy due to altered hepatic function and portosystemic shunting.²⁷ After TIPS, patients have an incidence of hepatic encephalopathy of 30 to 40%. In theory, as patient survival improves, the risk of sustaining a single episode of hepatic encephalopathy will concomitantly increase. Moreover, the longer a patient survives, the more likely there will be progression of cirrhosis and deterioration of liver disease, which will also increase the risk of hepatic encephalopathy. Many of the TIPS publications are retrospective and rely on incomplete data that are mostly subjective in identifying hepatic encephalopathy. In the published retrospective studies, the better and more thorough the follow-up, the more likely the patient will have documentation of hepatic encephalopathy. In addition, hepatic encephalopathy is subject to overall patient health and the patients' compliance with dietary restrictions as well as ammonia-reducing medication and purgatives, in addition to social support and habituation of the patient. Based on the above discussion points and scenarios, it is the author's opinion that retrospective evaluation of hepatic encephalopathy is significantly subjective and thus is greatly flawed. More objective criteria for retrospective studies are to limit the reporting of post-TIPS hepatic encephalopathy to "major hepatic encephalopathy," for example, encephalopathy requiring hospitalization, needing TIPS reduction or liver transplantation, or leading to coma or death.

Futuristic Designs for TIPS

Since hepatic encephalopathy is the most important adverse outcome after TIPS, it is the author's opinion that

futuristic TIPS designs should focus on reducing hepatic encephalopathy. Since the incidence of hepatic encephalopathy may vary with dietary variations, overall patient health, and patient compliance in taking medication, the ideal next step in TIPS design is to have a variable diameter TIPS that can change the degree of portosystemic shunting remotely to accommodate for varying requirement. For example, if hepatic encephalopathy occurs, the TIPS can be remotely and temporarily narrowed to decrease portosystemic shunting. To the contrary, increasing the degree of portosystemic shunting may be required in the setting of variceal bleeding. Similar technology that is currently in use is "artificial sphincter" technology that has been used for urinary incompetence and bariatric surgery. However, this would require the TIPS stent to be tethered to a port/reservoir, and thus it would not be completely remotely controlled. Moreover, this would be a cumbersome procedure and possibly be more prone to procedure-related infections. Another technology on the horizon, but has not yet become readily available to medicine/biomedical engineering is electromagnetic doorways or apertures. This technology may be the advancement that will enable interventional radiologists to realize a remotely controlled variable diameter TIPS.

Conclusion

TIPS has come a long way from an inadvertent portal vein access to what it is today with improved patency, thanks to advancements in technology and innovations in interventional radiology. TIPS has been plagued with two main problems since its inception: patency and hepatic encephalopathy. Patency has significantly improved with the advent of e-PTFE covered stent-grafts; however, encephalopathy remains a major problem. Perhaps, another technological advancement will lead to a TIPS with variable diameters that will accommodate varying portosystemic shunting and reduce the incidence of post-TIPS encephalopathy.

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