

# Transjugular Intrahepatic Portosystemic Shunt (TIPS) versus Balloon-occluded Retrograde Transvenous Obliteration (BRTO) for the Management of Gastric Varices

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## ABSTRACT

Variceal bleeding is one of the major complications of portal hypertension. Gastric variceal bleeding is less common than esophageal variceal bleeding; however, it is associated with a high morbidity and mortality rate and its management is largely uncharted due to a relatively less-established literature. In the West (United States and Europe), the primary school of management is to decompress the portal circulation utilizing the transjugular intrahepatic portosystemic shunt (TIPS). In the East (Japan and South Korea), the primary school of management is to address the gastric varices (GVs) specifically by sclerosing them utilizing the balloon-occluded retrograde transvenous obliteration (BRTO) procedure. The concept (1970s), evolution, and development (1980s–1990s) of both procedures run parallel to one another; neither is newer than the other is. The difference is that one was adopted mostly by the East (BRTO), while the other has been adopted mostly by the West (TIPS). TIPS is effective in emergently controlling bleeding for GV's even though the commonly referenced studies about managing GV's with TIPS are studies with TIPS created by bare stents. However, the results have improved with the use of stent grafts for creating TIPS. Nevertheless, TIPS cannot be tolerated by patients with poor hepatic reserve. BRTO is equally effective in controlling bleeding GV's as well as significantly reducing the GV rebleed rate. But the resultant diversion of blood flow into the portal circulation, and in turn the liver, increases the risk of developing esophageal varices and ectopic varices with their potential to bleed. Unlike TIPS, the blood diversion that occurs after BRTO improves, if not preserves, hepatic function for 6–9 months post-BRTO. The authors discuss the detailed results and critique the literature, which has evaluated and remarked on both procedures. Future research prospects and speculation as to the ideal patients for each procedure are discussed.

**KEYWORDS:** History, BRTO, transvenous obliteration, varices, TIPS, rebleeding

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**Objectives:** Upon completion of this article, the reader should be able to identify the outcomes and limitations of both the transjugular intrahepatic portosystemic shunt (TIPS) and balloon-occluded retrograde transvenous obliteration (BRTO) procedures in managing gastric varices; state the advantages and disadvantages of both procedures and the significant limitation of the literature regarding the subject of minimal invasive management of gastric varices especially when utilizing stent grafts for TIPS in patients with gastric variceal bleeding.

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Minimally invasive procedural management of portal hypertension, whether endoscopic or image-guided, is at the forefront in the management of portal hypertension complications. Variceal bleeding is one of the major complications of portal hypertension. Esophageal variceal bleeding is more common and the role of minimally invasive procedures is well established and charted.<sup>1</sup> Gastric variceal bleeding is less common, however, and is associated with high morbidity and mortality rates (45–55% mortality); its management is largely uncharted due to a relatively less mature/less-established literature.<sup>1–4</sup> Furthermore, endoscopic management of gastric varices is usually less effective when compared with its role in the management of esophageal varices.<sup>4–8</sup>

From an interventional radiology (minimally invasive image-guided procedures) standpoint there is a controversy at the international level as to the ideal management of gastric varices.<sup>3,9–12</sup> In the West (United States and Europe), the primary school of management is to decompress the portal circulation utilizing the transjugular intrahepatic portosystemic shunt (TIPS). This is in line with the long history of decompressive surgeries (surgical portosystemic shunts) that were more popular prior to the advent of the TIPS procedure. In the East (Japan and South Korea), the primary school of management is to address the gastric varices specifically by sclerosing them utilizing the balloon-occluded retrograde transvenous obliteration (BRTO) procedure. Unfortunately, the spontaneous gastrorenal/gastrosplenorenal shunt (a natural portosystemic decompressive shunt) is occluded during the BRTO procedure;<sup>9,10,13</sup> thus there is aggravation of the portal hypertension,<sup>14–17</sup> which is contrary to the Western decompressive ideology/school of portal hypertension management. Herein lies the center of the controversy: to decompress or not to decompress; to manage portal hypertension globally, or to specifically address the complication at hand.

Here we discuss the controversy between TIPS and BRTO and display and critique the available outcome data of both procedures. Out of the limited data available, speculation of future research and clinical trends are also made.

## THE CONCEPT AND HISTORY OF THE TIPS AND BRTO PROCEDURES

One cannot discuss these two procedures (BRTO and TIPS) without addressing the clear East versus West geographic divide between them. To understand this dichotomy to impartially critique these procedures, one must understand the history and evolution of these two, very involved, but different procedures.

### The Concept and History of the BRTO Procedure

Transvenous obliteration is actually an older idea and was practiced in the mid-1970s in the pretransjugular intrahepatic portosystemic shunt (TIPS) era as an interventional radiology procedure for the management of bleeding esophageal and gastroesophageal varices from a percutaneous transhepatic approach.<sup>18–22</sup> These percutaneous transhepatic obliterations were mostly performed utilizing coils, Gelfoam, and/or sclerosants (such as absolute alcohol and 30–50% glucose solution).<sup>18–22</sup> These transhepatic procedures were usually performed without utilizing occlusive balloons that intend to modulate blood flow.<sup>18–22</sup> The initial transhepatic obliterative experience in the 1970s was short lived due to relatively poor clinical success<sup>18–22</sup> and ultimately the advent of the TIPS procedure in the early 1990s (see below).

The concept of balloon-occluded retrograde transvenous obliteration (BRTO) as we know it today is accessing the portosystemic gastrosplenic shunt via the left renal vein from a transjugular or transfemoral approach.<sup>9,10,13,23</sup> Most authors refer to Kanagawa et al (1991–1993) as the inventor of BRTO.<sup>13</sup> However, the first published document of an attempt at balloon-occluded sclerotherapy of the gastrosplenic shunt for the management of gastric varices was authored by Olson et al in 1984 out of Indiana University.<sup>23</sup> This is clearly 5 and 7 years prior to the commencement of the BRTO clinical practice (1991) and publication (1993), respectively, of Kanagawa et al.<sup>13</sup> Olson et al utilized a transfemoral balloon occlusion catheter and absolute alcohol for the successful sclerosis attempt.<sup>23</sup> Embolic coils were also placed in the outflow gastrosplenic shunt.<sup>23</sup> The term used for the procedure was “transrenal-vein reflux ethanol sclerosis” and not BRTO.<sup>23</sup>

Subsequently, Kanagawa et al revived the BRTO-concept and developed the BRTO-procedure in the early 1990s, coining the term, balloon-occluded retrograde transvenous obliteration (B-RTO).<sup>13</sup> They utilized ethanolamine oleate as an endovascular sclerosant which Western (European and American) interventional radiologists were not familiar with. Ethanolamine oleate is an established upper endoscopy variceal sclerosant. However, when used from an endovascular standpoint, there is a greater risk for hemolysis, hemoglobinuria, and potentially hemoglobin-induced renal tubular dysfunction.<sup>9,10</sup> The antidote of free hemoglobin is haptoglobin, which conjugates with it. Haptoglobin is available in Japan and is not available for human and commercial use in the United States. In fact, haptoglobin is routinely given, 2000 to (more commonly given) 4000 units, as an intravenous infusion with all ethanolamine oleate BRTO procedures in Japan.<sup>3,9-13,24-42</sup> Consequently, the Japanese developed, evolved, and clinically applied this procedure.<sup>3,9-13,24-42</sup> They took it to the clinical level and established it as a viable and successful procedure that it is today.<sup>3,9-13,24-42</sup>

There are two main hypotheses why BRTO has not been clinically practiced (until recently) in the United States. The first is the unfamiliarity of interventional radiologists in the United States with the BRTO-procedure as well as the well-described (in Japan and Korea) sclerosant: ethanolamine oleate. In addition, the lack of the antidote, haptoglobin (see above), potentially concerned many radiology interventionalists in using ethanolamine oleate. The second cause of the delayed utilization of BRTO in the United States is that the ideology or thought process of managing portal hypertension complications in the United States is decompression and reducing the portal pressure. It is not, as is the case with the BRTO procedure, mere management of a particular complication (in this case, potentially bleeding gastric varices) with the added risk of aggravating the portal hypertension and potentially having patients subsequently develop other complications of portal hypertension such as potentially bleeding esophageal varices and/or ascites. BRTO is known to cause aggravation of esophageal varices and may increase the risk of developing ascites (please see "Balloon-occluded Retrograde Transvenous Obliteration (BRTO): Technical Results and Outcomes" in this issue).<sup>3,9-13,24-42</sup> In addition, reinforcing the theory of decompression being favored over sclerosis, is the initial experience of transhepatic obliteration in Europe and the United States did not have a satisfactory technical, hemodynamic or clinical success.<sup>18-22</sup> The technical success of these early transhepatic procedures varied from 54% to 88% with a rebleed rate of successful cases of 29-86% and an overall intent-to-treat clinical success rate of 25-31% and an image based variceal recannulation of over 80%<sup>18-20</sup> (please compare with the BRTO results in

"Balloon-occluded Retrograde Transvenous Obliteration (BRTO): Technical Results and Outcomes" in this issue).

### The Concept and History of the TIPS Procedure

The concept of the transjugular intrahepatic shunt (TIPS) is, as the name implies, creating an intrahepatic connection between the portal vein and the hepatic outflow vein.<sup>43-50</sup> The first published experimental study in animals (canines) was by Burgener et al in 1979.<sup>43</sup> They performed the connection with balloon angioplasty of the tract without stent placement.<sup>43</sup> Dr. Burgener was a Swiss radiologist who practiced at the University of Rochester (Rochester, NY) and published more of these experimental animal studies in the 1980s.<sup>43-46</sup> The first published experimental TIPS animal study utilizing stents (Gianturco stents) was by Rosch et al from the Dotter Institute (Portland, OR) in 1987.<sup>47</sup> The actual practice of creating a TIPS in humans started in Europe and the United States ca. 1989-1990,<sup>48-51</sup> with early reports of TIPS in humans published from 1991 to 1992.<sup>48-50</sup> The first sizeable reports of TIPS (number of patients >40) in humans with commercially available stents (Wallstents and Strecker stents) was in 1993-1994.<sup>52,53</sup>

The transjugular intrahepatic portosystemic shunt (TIPS) was hindered by three main problems: patency, hepatic encephalopathy, and the toll it has on hepatic function. Longevity (patency) of the TIPS was a primary problem and disease recurrence was strongly related to lack of TIPS patency (TIPS dysfunction: stenosis or occlusion).<sup>54-57</sup> Experimentation on animal models in the 1990s demonstrated that most TIPS stenoses and possibly occlusions were due to biliary-TIPS fistulas.<sup>58,59</sup> The biliary leaks induced pseudointimal hyperplasia and the bile was also thrombogenic.<sup>58,59</sup> To counter this, the solution was creation of the shunt utilizing covered stents.<sup>58,59</sup> Experimentation with silicone-covered and expanded polytetraethylene- (e-PTFE-) covered stents showed superiority of the e-PTFE covered TIPS-stents.<sup>58-60</sup> From 2000 to 2003, early human reports on e-PTFE covered stent placements were published. Most reports were an amalgamation of de novo TIPS creation and TIPS revisions utilizing e-PTFE stent-grafts.<sup>60-63</sup> As of 2003, reports of de novo TIPS creation with numbers of human patients started to be reported from Europe.<sup>64-73</sup> These reports confirmed the clear superiority of e-PTFE stent grafts compared with bare stents<sup>64-73</sup> to the extent that the history of TIPS would be divided into the pre- and poststent-graft era.<sup>74</sup> However, there remains the two other problems with TIPS: the increased incidence of encephalopathy, and the toll that TIPS has on liver function.<sup>75-78</sup> Furthermore, there is relatively new data accumulating from the United States and Europe regarding candidacy of

patients for the TIPS procedure; where patients with poor hepatic reserve (MELD >17–19) have been shown to do poorly with the TIPS procedure.<sup>75–78</sup>

When discussing with Japanese interventional radiologists why the TIPS procedure is not commonly performed in Japan, they refer to the increased incidence of encephalopathy and post-TIPS hepatic dysfunction. In addition, they anecdotally refer to the fact that liver cirrhosis in Japanese patients presents with shrunken and hard livers which makes TIPS technically challenging (personal communication with Takashi Kitanosono, Showa University, Japan and Kenji Takizawa, St. Marianna University, Kawazaki, Japan, March 9, 2009).

### Summary of the History and Evolution of TIPS and BRTO

The concept, evolution, and development of both procedures run parallel to one another; neither is more novel than the other is. The concept of both procedures dates back to the 1970s with early experimentation in the 1980s. They both began to be performed on humans in the 1990s and matured to be effective and established procedures in the last decade. The difference is that one has been adopted mostly by the East (BRTO) and the other has been adopted mostly by the West (TIPS). They both were conceived from a certain managerial ideology and through their clinical success, they further engraved that ideology.

### OUTCOMES OF THE TIPS AND BRTO PROCEDURES FOCUSED ON THE MANAGEMENT OF GASTRIC VARICES

There is actually limited data in the literature that is specific to TIPS for gastric varices (six studies).<sup>26,79–83</sup> Most, even more recent studies, amalgamate all varices (vast majority esophageal, gastric, or gastroesophageal) and one cannot glean the outcomes specific to patients with gastric varices in these amalgamated studies. On the other hand, BRTO is a procedure that is specific to gastric variceal management and there is more data showing efficacy of the procedure (over 40 studies).<sup>3,9–13,24–42</sup> From this standpoint alone, the TIPS procedure stands at a disadvantage.

### Outcome of TIPS for Patients with Gastric Varices

There are six TIPS studies that address patients with portal hypertension complicated by gastric varices.<sup>26,79–83</sup> These six studies evaluate 147 patients (range for individual studies: 12–35 patients).<sup>26,79–83</sup> Two of these studies have intrainstitutional comparisons with BRTO outcomes.<sup>26,79</sup>

Two studies were published before the year 2000 and had 60 patients with actively bleeding gastric varices who had undergone TIPS created by bare stents.<sup>80,81</sup> The success of TIPS in controlling the active variceal bleeding was 94% (90–96%).<sup>80,81</sup> However, the 6–7 month and 12 month rebleeding rate was 26–29% and 31%, respectively.<sup>80,81</sup> The post-TIPS hepatic encephalopathy rate was 16%.<sup>81</sup>

The four studies published in the last decade evaluated 87 patients with gastric varices who underwent a TIPS procedure.<sup>26,79,82,83</sup> However, all the TIPS were still created with bare stents.<sup>26,79,82,83</sup> The 12- to 24- month post-TIPS rebleed rate was 11–20%.<sup>26,79,82,83</sup> The improved rebleeding rate when comparing the pre- and post-year 2000 studies may be due to better techniques and improved clinical and imaging (Doppler ultrasound) surveillance and follow-up. The main problem with all six of these studies is that the transjugular intrahepatic portosystemic shunts were created with bare stents and not stent grafts.<sup>26,79–83</sup> The use of stent grafts would probably make a significant difference considering that TIPS patency has improved from 30–69% (bare stents) to 76–92% (stent grafts) with the advent of the commercially available Viatorr stent graft (Gore & Assoc., Flagstaff, AZ).<sup>64–74,84</sup> This is particularly true when considering that over 70% of gastric variceal rebleeding after TIPS have been associated with TIPS dysfunction (TIPS stenosis or thrombosis).<sup>82</sup> Furthermore, a common quote in BRTO studies when referring to the TIPS literature, is that the gastric variceal rebleed rate after TIPS is 50%, referencing Sanyal et al.<sup>85</sup> This is not a true statement. This is the gastric variceal resolution rate and not the rebleeding rate ( $N=6/12$ ).<sup>85</sup> Moreover, four of the six unresolved gastric varices (75%) had a pre-TIPS portosystemic gradient of <12 mm mercury<sup>85</sup> (see discussion below). Not surprising. Chao et al showed that gastric varices bleed at a lower hepatic–portal venous gradient (mean gradient 11.2 for gastric, 15.5 for esophageal).<sup>86</sup>

The two studies that had intrainstitutional comparison between BRTO and TIPS had 85 BRTO cases and 40 TIPS cases.<sup>26,79</sup> Unfortunately, the study by Choi et al had a small sample (BRTO: 8, TIPS: 13) that was too small for a statistical comparison.<sup>79</sup> The rebleeding and encephalopathy rate was 15% versus 0% and 31% versus 0% for TIPS versus BRTO, respectively.<sup>79</sup> The more significant study was by Ninoi et al and had a larger sample (BRTO: 77, TIPS: 27).<sup>26</sup> The one year rebleeding rate was 20% versus 2% for TIPS versus BRTO, respectively ( $p < .01$ ).<sup>26</sup> Furthermore, the 1, 3, and 5 year survival after BRTO was better than after TIPS ( $p = .01$ ): 96, 83, 76% versus 81, 64, 40%, respectively.<sup>26</sup> However, the improved survival for BRTO compared with TIPS was limited to patients who were classified preprocedurally as Child-Pugh A. There was no difference in survival for patients who were classified

as Child-Pugh B or C.<sup>26</sup> Overall, the percentage of patients in both studies that experienced hepatic encephalopathy after TIPS was 19–31%.<sup>26,79</sup> The noncomparative study by Barange et al also showed a post-TIPS (all TIPS created for gastric varices) hepatic encephalopathy rate of 16%.<sup>81</sup>

### Outcome of BRTO for Patients with Gastric Varices

Details of the technical results and outcomes are discussed in this issue in “Balloon-occluded Retrograde Transvenous Obliteration (BRTO): Technical Results and Outcomes.” Overall the technical success of patients with gastrosplenic shunts (noncandidates not included) for BRTO only ranges from 79–100%.<sup>3,11,12,25–32,35,39–41,87–90</sup> Two studies clearly identified primary treatment of gastric varices with BRTO, reserving Balloon-occluded antegrade transvenous obliteration (BATO) via a percutaneous transhepatic route as a rescue.<sup>3,26</sup> These two studies had a BRTO technical success without and with BATO rescue of 84–98% and 100%, respectively.<sup>3,26</sup> The effectiveness of BRTO in controlling bleeding gastric varices is 91–100% in two studies evaluating 20 patients ( $N=19/20$ , controlled: 95%).<sup>3,25</sup> Procedural and long-term complications, when mentioned, are displayed in Table 1.<sup>3,11,12,24,25,27–29,31,32,35,36,39,87–92</sup>

The aggravation of nongastric (esophageal or duodenal) appears to be a major problem in the long-run and is reflective of increasing portal hypertension following BRTO.<sup>3,11,12,24,25,27,31,36,87,89–92</sup> It varies widely probably depending on the degree of vigilance, documentation and thoroughness of follow-up endoscopy. However, in four main studies evaluating 160 patients who had undergone BRTO who had continuous endoscopic follow-up post-BRTO, the esophageal variceal aggravation rate (expressed as a Kaplan-Meier analysis) at 1, 2, and 3 years was 27–35%, 45–66%, and 45–91%, respectively.<sup>11,31,35,42</sup> In another two studies evaluating 117 patients with BRTO, the percentage of patients with aggravated esophageal varices was 30–68% and the patients that had bleeding esophageal varices was 17–24% of patients (36–57% of patients with aggravated esophageal varices went onto to bleeding).<sup>27,90</sup> Again, one can argue that the percentage of esophageal variceal bleeding may be significantly reduced by a higher vigilance of endoscopic follow-up and more aggressive endoscopic therapy (esophageal banding and/or sclerotherapy). Other complications reflective of increased portal hypertension following BRTO are the development of portal hypertensive gastropathy (occurs in 5–13%) and possibly ascites (occurs in 0–44%) and hydrothorax/pleural effusion (occurs in 0–8%).<sup>28,31,32,35,39,88</sup>

The rebleeding rate following BRTO depends on how it is presented. We believe that there is a pressing need to standardize reporting of BRTO

**Table 1 Procedural Complications of Balloon-occluded Transvenous Obliteration (BRTO) Utilizing Ethanolamine Oleate**

Complication Type	Incidence (%)
Procedural Complications	
Gross hematuria	15–100*
All pulmonary embolism	1.5–4.1
Symptomatic pulmonary embolism	1.4–2.5
Cardiac arrhythmia	1.5
Anaphylaxis	2.2–5.0
Rapid / fulminant hepatic failure	4.8–7.0
Death within 30 days from fulminant hepatic failure	0.0–4.1
Renal failure	4.8
Long-term Complications	
Encephalopathy	17.6 <sup>†</sup>
Portal hypertensive gastropathy	5.3–13.2
Post-BRTO gastropathy (not to extent of portal hypertensive gastropathy)	56.5
Aggravation of esophageal varices	14–68 <sup>‡</sup>
Bleeding from esophageal varices	17–24 <sup>‡</sup>
Duodenal varices	Up to 3.2
Bleeding duodenal varices	Up to 2.3
Ascites	0–43.5
Spontaneous bacterial peritonitis	Up to 8.2
Pleural effusion (hydrothorax)	5.3–7.9
Portal vein thrombosis	Up to 4.7
Renal vein thrombosis (no clinical consequences)	Up to 5.0

Based on data from references <sup>3,11,12,24,25,27–29,31,32,35,36,39,87–92</sup>

\*This is a common complication and is usually without clinical consequences. The wide range is probably due to how well it is documented for the retrospective audit which most of studies are categorized as.

<sup>†</sup>The rate of encephalopathy is subject to definition and how closely there was clinical follow-up and may vary widely. This is a feature of the entire portal hypertension interventional radiology literature and is not specific to the BRTO literature.

<sup>‡</sup>The rate of variceal aggravation is subject to definition and how closely there was endoscopic follow-up and may vary widely. In addition (anecdotally), aggressive pre-BRT banding may reduce the incidence esophageal varices and/or bleeding from these varices even with close post-BRTO endoscopic follow-up.

research. Most studies display a gastric variceal rebleed rate of patients who had undergone a successful BRTO-procedure that ranges between zero and 20% (all studies except one with a gastric rebleed rate under 10%).<sup>3,11,12,25–32,35,41,87,88,90,92</sup> However, when factoring in an intent-to-treat basis (including technical failures) for the results, the gastric variceal rebleed rate is zero to 31.6%.<sup>3,11,12,25–32,35,41,87,88,90,92</sup> Many studies do not clearly state what, if any, is the global rebleed rate from: gastric, esophageal, duodenal varices as well as portal hypertensive gastropathy.<sup>3,11,12,26,28–32,35,41,87,88,92</sup> In three clearly reported studies evaluating 141 patients who had undergone a BRTO procedure, the gastric variceal rebleed rate of successful BRTO procedures, the intent-to-treat

gastric variceal rebleed rate, and the global (all types of varices) variceal rebleed rate was: 3.2–8.7%, 10–20%, and 19–31%, respectively.<sup>25,27,90</sup> Compare these results with the latest four studies evaluating 87 patients who underwent a TIPS procedure with a 12–24 month global rebleed rate of 11–20%.<sup>26,79,82,83</sup> Both sets of studies (BRTO vs TIPS) leave room for improvement. The BRTO studies probably can reduce rebleeding with aggressive endoscopic management and the TIPS studies probably can reduce rebleeding by utilizing stent grafts and a strict Doppler ultrasound follow-up.

Perhaps one of the greatest advantages of BRTO over TIPS is its preservation of hepatic function and its reduction in the risk of hepatic encephalopathy. In fact, one of the indications for BRTO is encephalopathy with the presence of a gastrosplenic or gastrosplenorenal shunt.<sup>3,12,24,33–35,40,88</sup> In five studies evaluating 35 patients with encephalopathy, there was resolution or significant reduction in encephalopathy in all (100% success) patients.<sup>3,12,33,35,88</sup> The Kaplan-Meier survival rate after BRTO is impressive. The 1-, 2-, 3-, and 5-year survival rates range from 83–98%, 76–79%, 66–85%, and 39–69%, respectively.<sup>3,27,31,35,40–42,90</sup> Obviously, the greatest determinate of survival is the patient's hepatic reserve (Child-Pugh score and/or MELD score).<sup>3,27,40,41</sup> However, hepatocellular carcinoma (HCC) is also a significant determinate of survival<sup>35,40,41</sup> to the extent that prior authors have considered an intrahepatic HCC of >5 cm as a contraindication for BRTO.<sup>35</sup>

## DISCUSSION

Above is a brief literature-based synopsis of the history and clinical effectiveness of both the balloon-occluded transvenous obliteration (BRTO) and the transjugular intrahepatic portosystemic shunt (TIPS) procedures specific to managing gastric varices. The following discussion is based on our opinion with speculations and proposals on how gastric varices can possibly be managed by interventional radiologists (BRTO and/or TIPS) in the United States. The literature for both procedures leaves a lot to be desired and thus leaves a lot of room for speculation. For TIPS, an evaluation of the upper gastrointestinal rebleed rate for TIPS created by stent grafts is required. For BRTO, a completely disclosed upper gastrointestinal rebleed rate (not just from gastric varices) with adequate follow-up is required. In addition, the effectiveness of the BRTO procedure should be evaluated for patients with a poor hepatic reserve (MELD >17–19). To date, there is no evaluation of the effect of BRTO on the MELD score (there is for the Child-Pugh score) let alone stratification of hepatic function and survival based on the MELD score. Furthermore, we agree with Jalan and Hayes that a

randomized controlled clinical trial comparing TIPS with BRTO is needed.<sup>93</sup>

We also agree with Jalan and Hayes and stress that the common reference to the 50% rebleed rate following TIPS is incorrect,<sup>93</sup> especially because it was based on bare-stent technology. This is the obliteration rate/lack of flow in the gastric varices ( $N=6/12$ ) following TIPS.<sup>85</sup> Even when evaluating the gastric varix obliteration rate (50% for TIPS and 75–100% for BRTO) is an uneven comparison. First, the two procedures are different. One procedure (BRTO) is a direct sclerotherapy of the varices and the other procedure (TIPS) is a shunt that competes with the blood flow within the varices. Second, and more importantly, rebleeding is what counts ultimately and is the true gauge of clinical success and not whether there is flow within the gastric varix. The latter is a technical/anatomical variable and not a clinical variable.

A not uncommon discussion in the BRTO literature is the ability of the BRTO procedure to divert portal blood flow toward the liver and thus improving, if not preserving, hepatic function.<sup>11,27,32,35,36,90</sup> However, admittedly certain patients have preserved or improved hepatic function and others are unresponsive to the increased flow.<sup>32,90</sup> Furthermore, the patients that do have an improved hepatic function return to baseline within 6 to 9 months (The improvement of hepatic function is transient).<sup>32,35,36</sup> The theories to explain this include (1) gradual reduction in the hepatic vascular resistance, and/or (2) development of portosystemic shunts particularly the esophagoazygous route (esophageal varices) that auto-decompress the portal system.<sup>35</sup> The hypothesis behind why certain patients do not respond to the portal flow diversion is that certain patients have irreversible hepatic disease/damage that does not respond to increased portal blood flow.<sup>32</sup> However, all these studies neglect the fact that there is another major component of this blood flow diversion theory that has to be taken into account. This neglected factor is the potential variability in the amount of portal blood flow that is diverted. This is because not all gastrosplenic or gastrosplenorenal have the same throughput that can potentially be diverted after a BRTO procedure. How can this throughput be gauged? (flow meters, Doppler ultrasound, perfusion MR). What is the portal pressure before and after the BRTO and can that be stratified to responders versus nonresponders? We find this to be a very interesting area of research that can be pivotal in the BRTO versus TIPS versus BRTO combined with TIPS debate. Do very large gastrosplenic shunts with significant throughput, when blocked, divert large volumes of portal blood toward the liver causing a significant rise in the portal pressure particularly with severely diseased noncompliant livers? Do these high throughput gastrosplenic shunts then require a TIPS to compensate for their sudden occlusion by a BRTO

procedure in an attempt to prevent nongastric varices aggravation or ascites development? Can these TIPS be intentionally temporary just to last for 6 to 9 months (the period when the improved hepatic function returns to baseline). Is this the return of TIPS utilizing bare stents for this particular scenario? Conversely, when performing a TIPS and finding a portosystemic gradient of 12 mm Hg, does this signify a significant gastrosplenic shunt that will not respond to TIPS shunting. Even more so, is this gastrosplenic shunt so significant that it can act as a competing shunt with the TIPS and potentially lead to TIPS thrombosis with or without portal vein thrombosis? Remember, that 75% of unobliterated gastric varices had a pre-TIPS portosystemic gradient of less than 12 mm Hg.<sup>85</sup> Anecdotally, a significant gastrosplenic shunt is defined as a pre-TIPS portosystemic gradient of <12 mm Hg and/or hepatofugal (reversed) flow in the splenic vein with contrast escaping into the left renal vein despite a well placed and widely patent TIPS with a portosystemic gradient <10–12 mm Hg.

In addition, to the throughput theory where some gastrosplenic shunts have significant blood flow competing with the TIPS and decompressing the portal circulation rendering a pre-TIPS portosystemic gradient <12 mm Hg, there is another theory that may explain why TIPS may be less effective in decompressing gastric varices compared with esophageal varices. This theory is “the proximity theory” (our term). The portal feeder to the gastric varices is usually the posterior or short gastric vein(s), which are closer to the gastrosplenic shunt (on the left side of the portal circulation) than they are to the TIPS (intrahepatic and in the right side of the portal circulation). Compare this with the usual portal feeder to the esophageal varices (coronary vein/left gastric vein). The left gastric vein originates in the right side of the portal circulation. In fact the distance between a TIPS and the portal origin of posterior gastric vein (and even more so, the short gastric vein) is approximately twice the distance compared with the distance between a TIPS and the portal origin of the left gastric vein. This brings the discussion to another anatomic variable that ideally should be taken into account. Gastroesophageal varices can be fed primarily from the coronary vein; and thus the gastric varix component may resolve with a TIPS. Possibly, a large number of the gastric varices that do respond to TIPS are actually complex gastroesophageal varices with dominant left gastric veins and poorly supplied by the more distant posterior and short gastric veins. Therefore, from a fluid mechanics standpoint, when hemodynamically discussing steal/sump/diversion flow phenomena it is not only the throughput between the competing shunts (in this case TIPS vs gastrosplenic shunts), but their proximity to what they are “competing over” to decompress. The original surgical doctrine of surgically placed portosystemic shunts took note of this.<sup>94–96</sup> If there was a “left-sided portal problem”

(spleen of splenic vein), the best shunt would be a left-sided shunt (distal splenorenal shunt, for example) and if it was a right-sided or liver problem a central or right-sided shunt is more appropriate.<sup>94–96</sup> The distal splenorenal shunt (in essence a surgically made left-side/shunt somewhat equivalent to a spontaneous gastrosplenic or gastrospleno renal shunt) is known to “compartmentalize” the portal circulation maintaining hepatopetal flow in the main portal vein due to a maintained high pressure along the mesoportal axis, while reducing the portal pressure for the left, posterior, and short gastric veins.<sup>94–96</sup> The Warren-Salem distal splenorenal shunt was designed to maintain the hepatic function while decompressing the origins of gastroesophageal varices.<sup>94–96</sup> It was proven to be ineffective for right-sided portal circulation (hepatic/sinusoidal) problems such as ascites.<sup>94–96</sup> In the case of a TIPS it is the opposite. It is a right-sided shunt placed to decompress a left-sided portal circulation problem, i.e., gastric varices and their, not uncommonly associated, gastrosplenic shunt.

Another common remark in the BRTO literature is that the BRTO procedure is “easier” than the TIPS procedure.<sup>93</sup> We, who perform both these procedures routinely, disagree. They are largely non-comparable. They both are involved procedures requiring a different skill set and anatomic knowledge of different parts of the portal circulation; however, both can be quite challenging. We agree that BRTO is definitely less invasive.

When discussing the logistics and the utilization of hospital resources, each procedure’s utilization of resources may differ from one institution to another and it is difficult to make a general remark about logistics. The first stage of the BRTO procedure usually does not require anesthesia and usually takes less than 1–2 hours in experienced hands.<sup>24–27,31–35</sup> Subsequently, the balloon is retained for 6 to 24 hours (usually 6–12 hours) and the patient is to return for a fluoroscopic-guided balloon deflation and removal.<sup>24–42</sup> On the other hand, the TIPS procedure is a one-stage procedure and is also completed within 1–2 hours in experienced hands. However, some institutions do require the TIPS procedure to be done under general anesthesia. This raises the hospital resource requirements and increases the overall utilization of the angiography suite.

Until all of the above matters are clarified, one can only speculate as to what is the better option in particular patients with portal hypertensive complications. TIPS is probably the better option for a patient with gastric varices and refractory ascites because it manages portal hypertension globally. BRTO can definitely be resorted to when patients are not TIPS candidates. This population is not necessarily small. This includes patients who are encephalopathic at baseline, have a poor hepatic reserve (MELD >17–19), have had a failed TIPS

procedure, have active gastric variceal bleeding with intractable coagulopathy, have had prior lobar chemoembolizations or patients with HCC who can be candidates for subsequent chemoembolization. The latter should be evaluated as a global hepatobiliary and oncology consult: BRTO with subsequent chemoembolization versus TIPS and other alternative systemic treatments or percutaneous tumor ablation. Anecdotally, a patient with HCC that is not a chemoembolization candidate (bilirubin >3.0 mg/deciliter) is usually not going to be a TIPS candidate to begin with (more likely has a high MELD score). A patient with hepatic encephalopathy, ascites, and gastric varices probably has a poor hepatic reserve and a poor outcome regardless of what would be done, if anything at all.

## CONCLUSION

Both the TIPS and the BRTO procedures are valuable procedures in the armamentarium of interventional radiologists. They require a different skill-set and they have proven to be effective in managing gastric varices. A lot of research work is required to determine the effectiveness of one procedure over the other especially in particular clinical scenarios. Ideally, in the future, patients with gastric varices would be stratified according to (1) the severity of portal hypertension and the size of the gastrosplenic shunt throughput in unison, (2) other complications of liver cirrhosis and/or portal hypertension (HCC, ascites, encephalopathy), and (3) hepatic reserve to undergo the ideal procedure (BRTO vs TIPS vs both). Until this research is performed adequately, the ideal BRTO versus TIPS candidate is speculative. Having said that, BRTO most likely is a procedure that preserves the hepatic function; thus, patients with poor hepatic reserve along with other non-TIPS candidates should be triaged to undergo a BRTO procedure if it is feasible (if a gastro-renal shunt exists).

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