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Review Article

Transjugular intrahepatic portosystemic shunts versus balloon-occluded retrograde transvenous obliteration for the management of gastric varices: Treatment algorithm according to clinical manifestations

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ABSTRACT

Transjugular intrahepatic portosystemic shunts (TIPS) are widely used in the management of bleeding gastric varices (GV). More recently, several studies have demonstrated balloon-occluded retrograde transvenous obliteration (BRTO) as an effective treatment method for bleeding isolated GV, especially in patients with contraindications for a TIPS placement. Both TIPS and BRTO can effectively treat bleeding GV with low rebleeding rates. Careful patient selection for TIPS and BRTO procedures is required to best treat the patient's individual clinical situation.

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Keywords: Balloon occlusion; Embolization, therapeutic; Esophageal and gastric varices; Portosystemic shunt, transjugular intrahepatic

Introduction

Variceal bleeding is a serious complication of portal hypertension. Esophageal varices (EV) are routinely treated via endoscopic methods; however, the long term success of endoscopically treated gastric varices (GV) are limited in part due to high flow through the varix and also the location of the varices in the cardia/gastric fundus.^{1,2} In addition, due to its size, sclerosis of GV often requires a larger volume of sclerosant and creates a higher risk of non-target embolization predominately to the pulmonary system.^{3,4} Transjugular intrahepatic portosystemic shunts (TIPS) are also widely used in the management of GV; however, high-level evidence of its decompressive benefits for isolated GV are lacking and shunting portal blood flow can further compromise liver function and aggravate hepatic encephalopathy.^{5–7}

Several studies have demonstrated that balloon-occluded retrograde transvenous obliteration (BRTO) is effected in the treatment of bleeding isolated GV, which are often associated with spontaneous gastroduodenal shunts.^{8–11} Furthermore, this procedure is an effective way to treat GV in patients with contraindications for TIPS placement.^{8–11} Absolute contraindications for TIPS placement

are right heart failure, severe pulmonary hypertension, severe tricuspid regurgitation, uncontrolled systemic infection or sepsis, unrelieved biliary obstruction, and liver failure.^{6,7} Relative contraindication for TIPS placement are central hepatocellular carcinoma, obstruction of all hepatic veins, portal vein thrombosis, severe coagulopathy, hepatic encephalopathy and high MELD (model for end-stage liver disease) score.

Herein, we review the clinical outcomes of TIPS and BRTO procedures and propose a GV treatment algorithm to best treat the patient's individual clinical situation.

Clinical Outcomes of the TIPS Procedure for GV

Table 1 summarizes the clinical outcomes of TIPS procedures for the management of GV. There are limited data addressing TIPS for the treatment of GV, as most TIPS studies have included all EV with or without GV. There are eight studies evaluating the placement of a TIPS for bleeding GV.^{12–19} These eight studies evaluated a total of 201 patients (range for individual studies, 7–35 patients). Four of these studies have intra-institutional comparisons with BRTO outcomes.^{15,16,18,19} The first six studies report using

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Table 1 Clinical Outcomes of TIPS Procedure for the Management of Gastric Varices

Author (year)	Number of patients	Type of TIPS stent	Rebleeding rate (%)	Hepatic encephalopathy (%)
Chau et al (1998) ¹²	28	Bare stent	29	3
Barange et al (1999) ¹³	32	Bare stent	31	16
Rees et al (2000) ¹⁴	12	Bare stent	16	NA
Choi et al (2003) ¹⁵	13	Bare stent	14	43
Ninoi et al (2004) ¹⁶	27	Bare stent	20	19
Lo et al (2007) ¹⁷	35	Bare stent	11	26
Sabri et al (2014) ¹⁸	27	Covered stent	11	15
Sauk et al (2014) ¹⁹	27	Covered stent	7	22

TIPS, transjugular intrahepatic postsystemic shunts; NA, not available.

Table 2 Clinical Outcomes of BRTO Procedure for the Management of Gastric Varices

Author (year)	Number of patients	Technical success (%)	Rebleeding rate (%)	Complete obliteration (%)
Kanagawa et al (1996) ²⁰	32	100	0	97
Sonomura et al (1998) ²¹	14	100	0	86
Kitamoto et al (2002) ²²	24	96	9	88
Ninoi et al (2004) ¹⁶	78	87	0	95
Arai et al (2005) ²³	11	100	9	91
Cho et al (2007) ²⁴	49	84	0	100
Hiraga et al (2007) ²⁵	34	97	3	91
Sabri et al (2014) ¹⁸	23	91	0	88
Sauk et al (2014) ¹⁹	25	100	12	87

BRTO, balloon-occluded retrograde transvenous obliteration.

bare stents for the creation of TIPS¹²⁻¹⁷ and more recent studies report using covered stents.^{18,19} Two studies were published before the year 2000 and had a total of 60 patients with actively bleeding GV that underwent TIPS with bare metal stents.^{12,13} The 6- to 7-month and 12-month rebleeding rates were 26% to 29% and 31%, respectively. Another four studies were published between 2000 and 2007, which evaluated a total of 87 patients with GV that underwent a TIPS procedure with bare metal stents.¹⁴⁻¹⁷ The post-TIPS rebleeding rates were between 11% and 20%, after a median follow-up of 33 to 75 weeks. It is important to note that the TIPS created with bare metal stents are known to have lower patency rates when compared to covered stents, and likely account for their higher rebleeding rates. The two most recent studies evaluated the outcome for the treatment of GV by creating a TIPS using covered stents.^{18,19} These studies showed lower rebleeding rates (7%–11%) compared with previous TIPS created with bare stents (11%–20%).¹⁴⁻¹⁷ The post-TIPS hepatic encephalopathy rates have been reported ranging from 3% to 43% without significant differences between patients treated with bare stents versus covered stents.

Clinical Outcomes of BRTO Procedures for GV

Table 2 summarizes the clinical outcomes of BRTO procedures for the management of GV. Overall, the technical success rates of BRTO for patients with gastrenal/splenorenal shunts and GV range from 89% to 100%.^{16,18-25} Procedural complications include gross hematuria with hemoglobinuria-induced renal failure (up to 4.8%), pulmonary embolism (1.5%–4.1%), anaphylaxis to etha-

nolamine oleate (up to 5%), cardiac arrhythmias (up to 1.5%), and rapidly declining hepatic function (5%–7%). The 30-day mortality rates range from zero to 4.1%, and the most common cause of death is progressive liver failure.^{8,11,16,20-25} Most of these complications were related with use of ethanolamine oleate. However, ethanolamine oleate is no longer available in many countries including Korea since several years ago. After that, sodium tetradecyl sulfate (STS) foam is widely used for BRTO procedure,^{18,19} and complication of BRTO has also changed. For example, STS foam does not make renal failure. But it could make air embolism. So, total amount of STS foam is limited to avoid air embolism. Another potential complication of BRTO using STS foam might be cerebral stroke related to portopulmonary venous anastomosis.²⁶

Other complications from increased portal hypertension after BRTO are the development of portal hypertensive gastropathy (5%–13%) and possibly ascites (0%–44%) and hydrothorax/pleural effusion (0%–8%).^{8,11,16,20-25}

One of the most important reported complications associated with BRTO is the aggravation of EV. Reported rates of worsening EV vary up to 63%, with 11% to 24% subsequent variceal bleeding rate.^{8,11,16,20-25} The wide range of reported rates is thought to be related to the variation in patient population, causes and severities of liver disease, as well as the durations of follow-up.

New techniques of BRTO using vascular plug or coils have introduced although it would be premature to be the confirmative techniques for the treatment of gastric varix yet.²⁷⁻²⁹ Because sclerosing agent and techniques have been changed, complication would be also different from complications from previous BRTO procedures.

Fig. 1. Gastric varices treatment algorithm according to clinical manifestations. TIPS, transjugular intrahepatic portosystemic shunts; BROTO, balloon-occluded retrograde transvenous obliteration; MELD, model for end-stage liver disease; PV, portal vein; GR shunt, gastroduodenal shunt; HCC, hepatocellular carcinoma.

Fig. 2. A 64-year-old male with alcoholic cirrhosis, portal vein thrombosis and cavernous malformation of the gastric variceal bleeding. (A) Initial venogram following access through the right internal jugular vein and catheterization of the gastroduodenal shunt shows filling of the collateral left inferior phrenic vein (dashed arrows) along with the gastric varices (GV) (arrow). (B) Left inferior phrenic vein is embolized using a microcatheter and micro-Nester coils. (C) Spot image post-embolization of the GV shows inflated balloon catheter along with pooling of the dense embolization material within the GV (arrowhead). (D) Follow-up upper gastrointestinal endoscopy 6 months after the procedure shows grade II lower esophageal varices (EV) (arrows), without evidence of bleeding. These EV are successfully banded. (E) Follow-up computed tomography scan of the abdomen 12 months post-procedure shows persistent portal vein thrombosis (arrow) with cavernous malformation of the portal vein (dashed arrow). (F) Note persistent dense embolization material within the previous GV (arrow). Patient remains symptoms free on the follow-up for more than 3 years.

In most studies, gastric variceal rebleeding rates of patients who had undergone a successful BRTO procedure range from zero to 12% after a median follow-up of 33 to 75 weeks, and rates for complete obliteration of GV range from 86% to 97%.^{8,11,16,18,19,20-25}

Comparative Studies of TIPS and BRTO Procedures for GV

Limited intra-institutional studies have compared the outcomes of TIPS and BRTO in management of GV.^{15,16,18,19} In a study by Choi et al,¹⁵ 21 patients with active gastric variceal bleeding due to cirrhosis were treated with either TIPS ($n = 13$) or BRTO ($n = 8$), and no statistically significant difference in hemostasis and rebleeding was noted after a mean follow-up of 14 months. A larger study by Ninoi et al¹⁶ evaluated 104 patients, 27 of which were treated with TIPS, and 77 patients with transcatheter sclerotherapy, treated through a retrograde or antegrade approach. Cumulative gastric variceal bleeding rate at one year was significantly better in the BRTO group (TIPS = 20% vs BRTO = 2%, $P < 0.01$). Furthermore, survival rates at 1, 3, and 5 years after a BRTO was performed were significantly better than that after a TIPS. However, the improved survival was only statistically significant for patients preoperatively categorized as Child-Pugh class A,

but not Child-Pugh class B or C.¹⁶ Bare stents were used in these two studies, which, as discussed before, are known to have lower patency when compared to covered stents, and likely account for the higher rebleeding rates. More recently, Sabri et al¹⁸ demonstrated equivalent short term rebleeding rates for isolated GV managed by TIPS with covered stents (11%) and BRTO (0%) in 50 patients ($P = 0.25$). Another recent study by Sauk et al¹⁹ demonstrated no significant difference in rebleeding rates from isolated GV managed by TIPS with covered stents (7%) and by BRTO (12%) in 52 patients ($P = 0.46$). In this study, two of 27 patients who received TIPS presented with rebleeding from an oozing gastric varix, one of whom required a TIPS revision. Among the BRTO group, two of 25 patients presented with repeat gastric variceal bleeding within two days following the procedure, which were subsequently treated with a TIPS placement.

GV Treatment Algorithms according to Clinical Manifestations

We propose an algorithmic and staged approach for the treatment of GV according to the patients' clinical situation (Fig. 1).

As discussed from the review of the literature, for the treatment of isolated GV, both TIPS and BRTO can effectively treat GV

Fig. 3. A 53-year-old man with underlying hepatitis C cirrhosis, ascites and large multifocal hepatocellular carcinoma (HCC) status post 2 × TACE (transcatheter arterial chemoembolization) with recurrent isolated gastric varices (GV). (A) Upper gastrointestinal endoscopy shows large GV around the gastric fundus with active oozing (arrow). (B) Axial venous phase computed tomography (CT) scan through the liver shows large necrotic HCC within the right lobe of the liver. (C) Coronal venous phase CT scan image through the liver shows a large necrotic HCC in S7 and S8 of the liver. Also note large enhancing GV around the gastric fundus (arrow) with gastro-renal shunt (dashed arrow). (D) Balloon occluded venogram of the gastro-renal shunt shows contrast filling of the GV (arrowhead) along with a draining inferior phrenic collateral vein (dashed arrow). (E) Repeat balloon occluded venogram following coil embolization of the inferior phrenic vein (arrow) shows filling of the more GV (arrowhead). This is followed by injection of sodium tetradecyl sulfate (Sotradecol; AngioDynamics, Queensbury, NY, USA) mixed with Lipiodol into the GV. (F) Abdominal radiograph on the next day following shows pooling of the dense Lipiodol (Ethiodol; Savage Laboratories, Melville, NY, USA) in the left upper quadrant around the gastric fundus.

with low rebleeding rates. If there is EV in addition to GV, a TIPS procedure or BRTO after endoscopic ligation of the EV can be performed.

For patients with GV and intractable ascites or hydrothorax, TIPS is a better option because it will also decompress the portal system and treat the ascites or hydrothorax. However, if a patient's MELD score is high, a BRTO procedure would be a better option because it will preserve hepatic function as opposed to the TIPS, while exacerbating the ascites or hydrothorax. A recent retrospective study, by Saad and colleagues,^{30,31} concluded that the presence of a patent TIPS prior to BRTO or the creation of TIPS at the time of BRTO prevented patients from developing post-BRTO ascites/hydrothorax as well as recurrent bleeding.

In patients with cavernous transformation of a chronically thrombosed main portal vein, a TIPS procedure could be technically difficult. If there is a gastroduodenal shunt on cross sectional images, BRTO could be performed in patients with bleeding GV (Fig. 2).

If there is a centrally located tumor and no window for the TIPS stent to land without violating the tumor, a BRTO would be a better option than TIPS (Fig. 3), so as to avoid tumor embolization.

For patients with GV and severe hepatic encephalopathy, BRTO would be a better option. One of the emerging indications for BRTO is hepatic encephalopathy with the presence of a gastroduodenal or splenorenal shunt.^{8,27,28,32–38} BRTO can preserve hepatic function and improve the hepatic encephalopathy. In five studies evaluating a total of 35 patients with encephalopathy there was resolution or significant reduction in encephalopathy in all patients.^{8,32,33,34,38}

BRTO is a good alternative in patients in whom a TIPS place-

ment is technically difficult, or if there is recurrent gastric variceal bleeding even after TIPS revision. According to Chao et al's study,³⁹ mean hepatic venous pressure gradient was 11.2 mmHg for GV and 15.5 mmHg for EV. So, there is a higher likelihood of having a diminished portal pressure (< 12 mmHg) in patients with GV. Thus, TIPS creation in these patients to further reduce the portosystemic gradient may not have a dramatically beneficial hemodynamic effect on the gastric variceal system, and can result in higher rebleeding rates than in patients with bleeding EV.^{39,40} Therefore, adding BRTO to TIPS can be effective in controlling gastric variceal bleeding (Fig. 4).

On the other hand, if the BRTO procedure is complicated by vein rupture or balloon rupture with subsequent clinical failure, TIPS could be placed (Fig. 5).

Conclusion

Both TIPS and BRTO can effectively treat bleeding GV with low rebleeding rates. Careful patient selection for TIPS and BRTO procedures is required to best treat the patient's individual clinical situation.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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Fig. 4. A 47-year-old man with underlying cirrhosis presenting with upper gastric variceal bleeding as seen on endoscopy. The patient underwent transjugular intrahepatic portosystemic shunts (TIPS) revision 4 months and 13 months after TIPS placement. (A) Initial portal venogram demonstrates patent TIPS stent with some collateral veins (arrow) filling varices. (B) Selective venogram from posterior gastric (arrow) vein shows retrograde filling of the gastric varices (GV). Balloon occlusion venogram of the gastroduodenal shunt shows retrograde filling of the GV along with a draining collateral vein. (C) The left inferior phrenic vein (arrow) is embolized using microcoils and the GV (dashed arrow) are then embolized using sodium tetradecyl sulfate (Sotradecol; AngioDynamics, Queensbury, NY, USA) mixed with Lipiodol (Ethiodol; Savage Laboratories, Melville, NY, USA). (D) Follow-up magnetic resonance imaging 3 1/2 years later shows complete obliteration of GV.

Fig. 5. A 63-year-old woman with underlying cirrhosis presenting with acute gastric variceal bleeding. (A) Coronal magnetic resonance (MR) image shows with large gastric varices (GV) with gastrorenal shunt (arrow). (B) After balloon inflation, GV (arrow) are then embolized using sodium tetradecyl sulfate (Sotradecol; AngioDynamics, Queensbury, NY, USA) mixed with Lipiodol (Ethiodol; Savage Laboratories, Melville, NY, USA). The occlusion balloon is found to be ruptured and she has continuous gastric variceal bleeding. Two days after balloon-occluded retrograde transvenous obliteration, she underwent transjugular intrahepatic portosystemic shunts (TIPS) procedure. (C) Initial portal venogram shows retrograde filling of the GV from the left gastric vein (arrow). (D) TIPS stent is successfully placed and left gastric vein is embolized with multiple coils (arrow). (E) Four months after TIPS procedure, she underwent TIPS reduction procedure due to hepatic encephalopathy with resulting central narrowing (arrow). (F) Twenty-seven months follow-up coronal MR image shows complete obliteration of GV.

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