15 Interventions for Portal Hypertension: BRTO and PARTO

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Abbreviations

BRTO	Balloon-occluded retrograde transvenous obliteration
PARTO	Plug-Assisted Retrograde Transvenous Obliteration
TIPS	Transjugular intrahepatic portosystemic shunt
HE	Hepatic encephalopathy
STS	Sodium tetradecyl sulfate
PVT	Portal vein thrombosis

15.1 Introduction

The major complications of portal hypertension include variceal bleeding, hypersplenism, hepatic encephalopathy (HE), ascites, and hydrothorax [1, 2]. Management of these complications requires a combination of medical, surgical, endoscopic, and interventional radiological procedures. In 1984, Olsen and coworkers described the procedure of transrenal vein reflux ethanol sclerosis [3]. In 1996, Kanagawa and colleagues revived this technique using ethanolamine oleate and named it balloon-occluded retrograde transvenous obliteration (BRTO). This technique aims to achieve the action of the sclerosing agent on the endothelial lining of the blood vessel by inducing stagnation within varix and to cause endothelial damage and vascular thrombosis [4].

The major cause of morbidity and mortality in patients with portal hypertension is spontaneous rupture of the gastric varices and massive hemorrhage. TIPS is effective in reducing the portal pressure, but may not be effective in controlling gastric variceal hemorrhage as these varices bleed even at low portal pressures. Moreover, portosystemic shunt may cause serious complications such as HE. Endoscopic interventions with glue injection and band ligation remain the first line of treatment in the case of actively bleeding gastric varices. BRTO/PARTO is used for prophylactic prevention as well in cases of failed endoscopic interventions.

Basic endovascular interventional techniques of PARTO and BRTO for treatment of gastric varices and HE, their indications, contraindications with emphasis on current data and future perspective on these procedures are discussed below:

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15.2 Indications and Contraindications

15.2.1 Indications for BRTO/PARTO

- Active uncontrolled gastric variceal bleeding
- Recurrent gastric variceal bleed in patients who have failed endoscopic and medical treatment
- Contraindications for performance TIPS in patients with gastric varices
- Prophylaxis against rebleeding after primary endoscopic therapy
- Management of recurrent HE secondary to portosystemic shunt

15.2.2 Contraindications for BRTO/PARTO

- Severe uncorrected coagulopathy
- Splenic vein thrombosis
- Portal vein thrombosis (where the gastrorenal shunt is the only outflow)
- Gross ascites
- High risk esophageal varices
- Gastric varices without a gastro/lienorenal shunt

15.2.3 Hardware Required

- 5F angiographic catheter (MPA/C2/SIM1/Picard)
- 6–12 F Flexor Check-Flo Introducer with large valve assembly
- 4-F angled or curved glide catheter/microcatheter
- Angled glide wire and stiff guide wire
- Compliant balloon catheter (size of the balloon is kept 1–2 mm larger than the diameter of the gastro/lienorenal shunt), Amplatzer vascular plug (for PARTO)
- Sclerosing agent/Gelatin sponge, Lipiodol

15.2.4 Sclerosing Agents [5]

Sclerosants are agents that act by denaturing biologic tissue. When they are injected into a vascular channel, they cause endothelial damage and fibrosis. Sclerosants (like ethanolamine oleate and detergent sclerosants) are made into foam or froth by agitating with gas (carbon dioxide or air). This process causes an increase in the volume-to-sclerosant ratio, thereby increasing potency and safety [5, 6].

15.2.5 Ethanolamine Oleate

Ten percent ethanolamine oleate is usually mixed with an equal volume of non-ionic contrast medium, like iopamidol, resulting in a 5% ethanolamine oleate–iopamidol mixture. Adverse effects of ethanolamine oleate include renal failure due to its hemolytic nature and hence other sclerosing agents are preferred over it [7].

15.2.6 Sodium Tetradecyl Sulfate

Sodium tetradecyl sulfate (STS) is the commonly used sclerosing agent in the BRTO. Sabri et al. [8] found that a smaller volume of STS is required as compared to ethanolamine oleate while performing BRTO with a good safety profile.

15.2.7 Polidocanol (Hydroxy Polyethoxydodecane)

It is a detergent and widely used in varicose vein sclerotherapy [9]. Polidocanol has been effectively used as a sclerosant for balloon-occluded retrograde transvenous obliteration [6].

15.2.8 Foam Versus Liquid Sclerosant

The advantage of foam sclerosant is that it reduces the sclerosant-to-volume ratio, requiring less sclerosant per procedure [4]. In addition, the

foam sclerosant is thought to distribute better into the numerous varices and tortuousities of the gastric variceal system [4].

15.3 Pre-Procedural Evaluation of Patient

- Grade of encephalopathy, liver function tests, renal function tests, complete blood cell count, prothrombin time and international normalized ratio (INR)
- Arterial ammonia level
- Triple phase CECT of the abdomen is required to assess technical feasibility of BRTO in terms of afferent & efferent gastric variceal anatomy of the patient, size of the shunt, and normal variants (Fig. 15.1).

It is very important to understand the gastric variceal anatomy while planning a BRTO/PARTO procedure. The gastric varices along with gastro/lienorenal shunt have a complex anatomy mostly due to variation in the veins supplying as well as draining the gastric varices [10]. The gastric varices are supplied by either

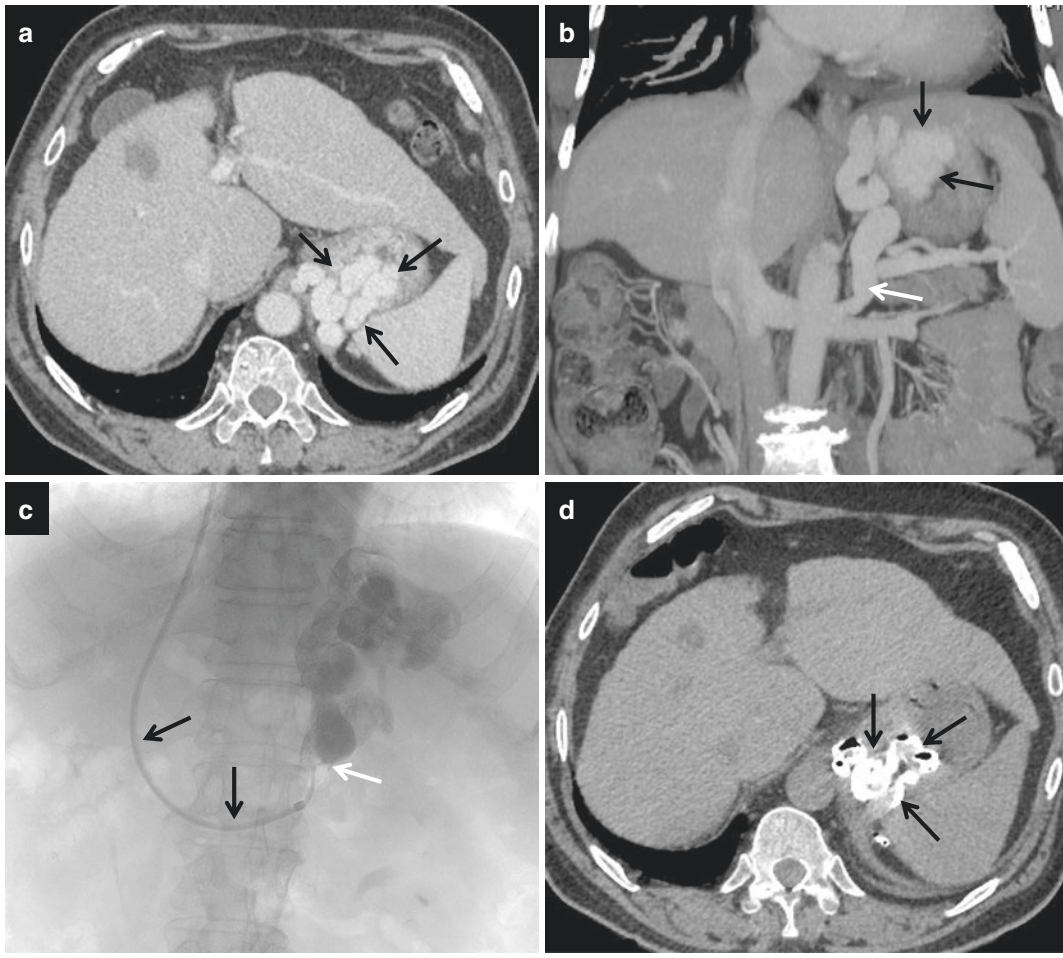

Fig. 15.1 CECT axial image (**a**) shows large gastric fundal varices protruding into the gastric lumen (black arrows), coronal reformatted image (**b**) shows large gastric varices (black arrows) with a lieno renal shunt (white arrow). Fluoroscopic image shows BRTO procedure with access taken from jugular route and vascular sheath placed within the left renal vein (black arrows) with a compliant balloon catheter inflated within the shunt (white arrow) and sclerosant mixture filling the shunt and the varices. Post-procedure CT image (**d**) showing complete obliteration of varices with formation of sclerosant cast (black arrows)

Fig. 15.2 Angiographic image (**a**) shows PARTO procedure being performed via femoral approach and vascular access sheath placed in the left renal vein (black arrows) with its tip within the lienorenal (LR) shunt and an angiographic catheter coaxially placed inside the LR shunt (white arrow). Image (**b**) shows placement of vascular plug (black arrows) within the shunt and a microcatheter coaxially placed deep within the shunt with contrast venogram being performed. Fluoroscopic image (**c**) shows deployed plug (black arrows) occluding the shunt with microcatheter (white arrow) being used to inject gel foam slurry, (**d**) shows final image with complete obliteration of the gastric varices and the LR shunt

left gastric/short gastric/posterior gastric vein or combination of any two or all three veins. The gastric varices are then drained by gastro-renal/lienorenal/gastro-lieno-renal shunt into the left renal vein and/or IVC or rarely into other systemic veins [10]. There may be variations in draining channels as well. These variations should be recognized prior to the procedure for the successful obliteration of varices (Fig. 15.2).

15.4 Technique

15.4.1 BRTO Procedure

1. BRTO is performed under local anesthesia or conscious sedation.
2. The left renal vein is accessed via femoral vein approach, alternatively internal jugular vein approach can also be used. Alternative routes are utilized for gastric varices when there is no gastrorenal shunt (alternative routes are more commonly required with duodenal and mesenteric varices compared with gastric varices).
3. A 6 to 12-French vascular sheath is placed in the left renal vein.
4. The target shunt (typically gastrorenal shunt via left renal vein) is catheterized using a selective catheter [e.g., Simmons or Cobra; (Cook, Bloomington, IN) selective catheter].
5. Compliant balloon is advanced into the shunt and inflated to occlude the shunt. (The size of the balloon is kept 1–2 mm larger than the diameter of the gastro/lienorenal shunt).
6. After occluding the shunt, contrast is injected upstream of the occlusion via the distal lumen port of occlusion balloon to evaluate variceal anatomy and identify collateral vein, if any.
7. Significant efferent collateral vessels are embolized using coils, and/or gel foam and sclerosant. It is necessary to confirm the complete occlusion of the shunt before the sclerosant agent is injected.
8. Sclerosant is injected upstream of the balloon into the gastric varices, with the occlusive balloon remaining in place for 6–12 h. During this period, the patient is kept in the angiography suite or in the recovery area beside the angiography suite.
9. Care should be taken to decide the endpoint which consists of complete coverage of the varices with sclerosant without any spill of sclerosant into the spleno-portal axis. Conebeam CT may be used to confirm complete occlusion.
10. Post-procedural follow-up imaging at 24–48 h can be done with plain CT scan of the abdomen to ensure complete obliteration of the shunt and the varices.
11. Thereafter, regular clinical and imaging follow-up is scheduled with the hepatologist and interventional radiologist.

15.4.2 PARTO Procedure

1. The procedure is performed under local anesthesia or conscious sedation after written informed consent is obtained.
2. The choice of access is femoral vein approach; alternatively, internal jugular vein approach can be used in difficult anatomy.
3. A 6 to 12-French vascular sheath is advanced and placed within the target shunt for deployment of the vascular plug.
4. A microcatheter is advanced deep within the shunt beyond the specified location planned for the placement of the vascular plug.
5. The vascular plug is inserted co-axially through the sheath and deployed to occlude the shunt. (The size of the plug is kept 2–4 mm larger than the diameter of the gastro−/lienorenal shunt and varied from 10 to 22 mm, Amplatzer vascular plug type 2 (AVP; St. Jude Medical, Inc., St. Paul, MN, USA).
6. Once the vascular plug is placed at the desired location contrast is injected upstream of the occlusion with the microcatheter (retrograde venography) to confirm adequacy of the occlusion. In case any significant efferent vein is identified then it should be embolized using embolization coils/gel foam slurry.
7. After complete occlusion of the shunt is confirmed gel foam slurry mixed with contrast is injected through the microcatheter to completely fill the shunt and varices.
8. Care should be taken to decide the endpoint which consists of complete coverage of the varices with gel foam slurry/sclerosant without any spill of sclerosant into the spleno-portal axis. Conebeam CT may be used to confirm complete occlusion.

9. Post-procedural follow-up imaging at 24–48 h can be done with plain CT scan of the abdomen to ensure complete obliteration of the shunt and the varices.
10. Thereafter, regular clinical and imaging follow-up is scheduled with the hepatologist and interventional radiologist.

15.4.3 Complications

1. Typically, transient and self-limited epigastric/back pain, fever, hematuria, nausea [11–17]
2. Worsening of esophageal varices due to increased portal pressures.
3. Temporary worsening of ascites or hydrothorax [12]
4. Altered respiratory function (presumably secondary to altered pulmonary perfusion) [18].
5. Chances of balloon rupture are minimal but such rupture can cause rapid migration of sclerosant into the right ventricle and pulmonary embolism [19].
6. Recurrent gastric variceal bleeding.
7. Gelfoam embolization to pulmonary arteries though the collateral veins.

15.5 Success Rate

The procedural success rate of BRTO in patients with portosystemic shunts and gastric varices ranges from 79% to 100% according to various studies [20–25]. In these studies, gastric variceal rebleeding rate ranges between 0% and 20% [20–28] after a successful BRTO. In a recent meta-analysis [29] including 1016 patients from 24 studies, the technical success rate was found to be 96.4%. The clinical success rate was 97.3% at a mean follow-up of 487 days, with clinical success defined as no recurrence or rebleeding from gastric varices or complete obliteration of varices on subsequent imaging. The flow velocity and flow volume in the varices have been correlated with outcomes after BRTO, with slow flow and low volume being associated with a higher success rate [30].

15.6 BRTO and Complications

The most important long-term concern after BRTO remains aggravation of non-gastric (i.e., esophageal or duodenal) varices. In four studies evaluating 160 patients who underwent BRTO with continuous post-BRTO endoscopic follow-up, the esophageal variceal aggravation rates at 1, 2, and 3 years were: 27% to 35%, 45% to 66%, and 45% to 91% respectively [11, 31–33]. In the meta-analysis by Park et al. [31], the esophageal variceal recurrence rate was 33.3%. The risk of esophageal varices aggravation has been shown to correlate significantly with the total bilirubin level and a portosystemic gradient >13 [34]. Thus, pre-BRTO prophylactic esophageal variceal eradication, portosystemic gradient measurement, laboratory analysis, and post-BRTO surveillance may be helpful to avoid subsequent esophageal variceal hemorrhage. Other complications due to raised portal pressure following BRTO include occurrence of portal hypertensive gastropathy (in 5%–13%), ascites (in 0%–44%), and hydrothorax/pleural effusion (in 0%–8%) [23, 25, 28, 31, 33]. Performance of TIPS in patients undergoing BRTO has been correlated with significantly lower ascites/hydrothorax rates and lower recurrent hemorrhage rates, although survival remains similar [35]. Furthermore, concomitant performance of partial splenic embolization also can mitigate esophageal variceal aggravation.

15.7 BRTO Versus TIPS

The retrospective studies that included intra-institutional comparison between BRTO and TIPS had a total of 133 BRTO cases and 94 TIPS cases [20, 36]. Ninoi et al. [20], compared patients undergoing only TIPS versus BRTO, reported a 1-year rebleeding rate of 20% after TIPS, while just 2% after BRTO ($P < 0.01$). Furthermore, the 1-, 3-, and 5-year survival rates after BRTO were better than those after uncovered stent TIPS 96%, 83%, and 76% versus 81%, 64%, and 40%, respectively ($P = 0.01$). However, a more recent study comparing covered TIPS

with BRTO revealed statistically similar rebleeding rates. Sabri et al. [36] reported a 1-year rebleeding rate of 11% in the TIPS group and 0% in the BRTO group (P = 0.25) with a hepatic encephalopathy rate of 15% and 0% (P = 0.12). Kim et al. [37] reported a 7% and 8% rebleeding rate throughout the study duration, respectively, but with a higher rate of hepatic encephalopathy after TIPS (22% versus 0%, P = 0.01).

15.8 BRTO and Portal Venous Thrombosis

There is a paucity of literature on BRTO with portal vein occlusion. Generally, BRTO in this setting can be associated with grave consequences, as the gastric varices may be the sole or dominant outflow for the entire spleno-mesenteric circulation; thus, occlusion of this outflow could result not only in splenic engorgement and infarction, it could also result in mesenteric venous congestion and leading to venous mesenteric ischemia [38]. One small case series of 2 patients described successful BRTO in a non-cirrhotic patient with subacute portal vein thrombosis with complete resolution of gastric varices on endoscopy 105 days post-procedure and on CT 5 months post-procedure. The second patient had chronic portal vein occlusion with cavernous transformation and splenic vein thrombosis that was due to necrotizing pancreatitis with multiple failed endoscopic treatments of her gastric varices [39]. BRTO was again successfully performed, with resolution of variceal bleeding and continued complete obliteration of varices at 6 months.

15.9 BRTO Versus PARTO

PARTO has certain advantage over BRTO. First, there is no risk of balloon rupture and subsequent pulmonary embolism, which can be fatal. The rupture of the balloon is attributed to the corrosive nature of the lipiodol used in sclerosant foam. Second, the dose limitation of sclerosants is not an obstacle for PARTO, because gel foam slurry is used instead of sclerosant mixture. Moreover, gel foam is safer embolic material than ethanolamine oleate or STS [28]. Third, PARTO does not require a long procedure time with indwelling balloon catheter and monitoring. The disadvantage of PARTO includes inability to access the shunt in case of recanalization/partial obliteration due to the presence of vascular plug.

15.10 Modifications of BRTO

Modifications of BRTO/PARTO use coils (CARTO, Coil assisted retrograde transvenous obliteration) for the occlusion of efferent flow in larger shunts followed by embolization of the varices. The advantage of CARTO is that deployment of coils does not require placement of sheath into the shunt hence making easier in cases of extreme tortuosity of shunt/varices. However, it is difficult to occlude large shunt with bunch of coils and may lead to partial occlusion. Modified techniques of BRTO include antegrade approach through portal vein [trans-TIPS or percutaneous trans-hepatic obliteration (PTO)] or a BRTO from an unconventional systemic vein. These modifications can be used in selective cases depending on factors like vascular anatomy seen on multiphasic CECT, presence or absence of ascites, INR of the patient and the location of the varices (duodenal, and other ectopic varices). It is postulated that obliteration of the portosystemic shunt by BRTO/PARTO leads to an increased portal pressure and portal hepatic blood flow with resultant improvement in hepatic function and enhanced ammonia detoxification by the liver.

15.10.1 Future Directions

There are endless innovative procedures that can be performed, incorporating the principal behind the BRTO procedure. There have been few case reports demonstrating such applications of this technique, including treatment of small-bowel varices, parastomal varices, and spontaneous mesenteric portosystemic shunts [40–44].

Management of gastric varices with modified techniques of BRTO, like BATO, CARTO, PARTO, or a combination of these is being practiced with greater frequency and is well documented in the literature [45–48]. Techniques using both endoscopic and percutaneous approaches, known as balloon-occluded endoscopic injection sclerotherapy are also being applied to prevent hemorrhage from gastric varices located in short gastric or posterior gastric territories.

15.11 Conclusion

BRTO and PARTO are endovascular procedures performed in patients with portosystemic shunts leading to gastric variceal bleeding and hepatic encephalopathy. These procedures are time tested and reliable at achieving the desired outcome with fewer associated risks and complications. PARTO is a step ahead of BRTO and lacks the risk of balloon rupture. Further modifications and variations of these procedures are being consistently employed in challenging cases with anatomic variations.

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