

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### Interventional procedure overview of transvenous obliteration for gastric varices

Varices are enlarged veins that can develop in the stomach (gastric) and can be caused by liver disease. They can burst, causing uncontrollable bleeding. In this procedure, a tube with a tiny balloon on the end is inserted into a vein (transvenous) in the thigh or neck and passed into the enlarged vein. The balloon is inflated to stop blood flowing into the vein. The vein is then blocked (obliterated) using one of several techniques. The aim is to reduce the risk of bleeding.

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## Abbreviations

Word or phrase	Abbreviation
Balloon-occluded retrograde transvenous obliteration	BRTO
Balloon-occluded antegrade transvenous obliteration	BATO
Coil-assisted retrograde transvenous obliteration	CARTO
Confidence interval	CI
Gastroesophageal varix	GOV
Grading of Recommendations Assessment, Development, and Evaluation	GRADE
Hazard ratio	HR
Isolated gastric varix	IGV
Model for end-stage liver disease	MELD
Odds ratio	OR
Plug-assisted retrograde transvenous obliteration	PARTO
Relative risk	RR
Transjugular intrahepatic portosystemic shunt	TIPS

## Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

## Date prepared

This overview was prepared in March 2022 and updated in November 2022.

## Procedure name

- Transvenous obliteration for gastric varices

## Professional societies

- British Association for the study of the liver (BASL)

- British Society of Interventional Radiology (BSIR)
- British Society of Gastroenterology (BSG)
- Royal College of Radiologists (RCR)

## Description of the procedure

### Indications and current treatment

Varices are dilated veins. Gastric varices form in approximately 20% of people with portal hypertension. Portal hypertension can occur in cirrhosis or in people without cirrhosis who develop thrombosis of the splanchnic circulation, such as portal vein thrombosis. Gastric varices are prone to bleeding, and this is associated with high mortality and poor prognosis.

Treatment for gastric varices includes non-selective beta-blockers, balloon tamponade, band ligation, endoscopic cyanoacrylate or thrombin injection, transjugular intrahepatic portosystemic shunt (TIPS), and transvenous obliteration.

### What the procedure involves

Cross-sectional imaging is done to identify and confirm the target shunt (gastrorenal shunt is usually present). Percutaneous venous access of the femoral or jugular vein using standard angiographic technique is done. An occlusion balloon catheter is inserted and navigated into the target shunt under fluoroscopic guidance. The balloon is inflated to occlude the shunt and venography is then done to define the variceal anatomy and type of varices. Sclerosant is slowly injected into the varices to fill the full extent of the varices, with the embolisation end point being minimal filling of the afferent vein or portal vasculature. The injection of sclerosant can be done with or without using a microcatheter for more selective injection. The occlusion balloon catheter is left in situ until satisfactory embolisation of the varices is achieved. This procedure is called balloon-occluded retrograde transvenous obliteration (BRTO). The aim is to obliterate the varices and manage acutely bleeding gastric varices or those at high risk of bleeding.

Modified techniques, such as balloon-occluded antegrade transvenous obliteration (BATO; a collective term for portal venous access routes to the varices), vascular plug-assisted retrograde transvenous obliteration (PARTO) and coil-assisted retrograde transvenous obliteration (CARTO), follow a similar procedure to BRTO. However, for PARTO and CARTO, shunt occlusion is achieved by vascular plugging or coiling. These 2 techniques can reduce procedure time and eliminate the risk of balloon rupture.

## Outcome measures

### Liver disease measures

#### Child-Pugh Score

System to predict mortality in people with cirrhosis. Scored based on assessment of severity of encephalopathy, severity of ascites, bilirubin concentration, albumin concentration, and prothrombin time or international normalised ratio. The severity of cirrhosis is then scored out of 15:

- Child-Pugh A: 5 to 6 points (least severe)
- Child-Pugh B: 7 to 9 points
- Child-Pugh C: 10 to 15 points (most severe)

#### Model for end-stage liver disease (MELD) score

Score to predict mortality in people with cirrhosis. Scored on assessment of aetiology, bilirubin concentration, creatinine concentration, sodium concentration, and prothrombin time or international normalised ratio. Higher scores indicate worse prognosis, in particular those with MELD score of less than 19.

### Classification of gastric varices

#### Sarin classification

System to classify gastric varices based on the relationship with oesophageal varices and their location in the stomach. Gastric varices are classified into 4 types:

- Gastroesophageal varix (GOV) type 1: varices in continuity with oesophageal varices along lesser curvature of the stomach.
- GOV type 2: extension of oesophageal varices along greater curvature of the stomach.
- Isolated gastric varix (IGV) type 1: isolated cluster of gastric varices in the gastric fundus.
- IGV type 2: isolated gastric varices in the other parts of the stomach.

#### Hashizume classification

System to classify gastric varices based on size, shape, location, and colour:

- Form: F1 (tortuous), F2 (nodular), F3 (tumorous).
- Location: La (anterior), Lp (posterior), Ll (lesser curvature), Lg (greater curvature), Lf (fundus).
- Colour: Cw (white), Cr (red).
- Red colour spot: Glossy, thin-walled focal redness on the varix.

## Hirota classification

System to classify gastric varices based on the results of balloon-occluded retrograde venography:

- Grade 1: gastric varices are well opacified without evidence of collateral veins.
- Grade 2: collateral veins were small and few, and the contrast medium remained in the gastric varices for 3 minutes or more.
- Grade 3: collateral veins were medium to large, there were few veins, and the contrast medium filled the gastric varices only partially and disappeared within 3 minutes.
- Grade 4: there were many large collateral veins, and the gastric varices were not opacified.
- Grade 5: the shunt could not be occluded with the balloon catheter because of the large size of the shunt and the rapid blood flow.

## Efficacy summary

### Technical success

#### BRTO

In a systematic review and meta-analysis of 21 studies (847 people), the pooled technical success rate was 96.4% (95% confidence interval [CI] 93.7 to 98.3;  $I^2=99.39$ ). Technical success was defined as complete thrombosis of gastric varices on immediate or short-term follow-up imaging, successful injection of sclerosing agent into gastric varices, and control of actively bleeding gastric varices (Park, 2015).

In a systematic review and meta-analysis of 6 studies (404 people [BRTO], 178 people [TIPS]), there was no difference in the technical success rate between the BRTO and TIPS groups: odds ratio (OR)=0.87 (95% CI 0.28 to 2.73,  $p=0.81$ , substantial heterogeneity  $I^2=50%$ ; Paleti, 2020).

In a retrospective case series of 183 people, technical success was achieved in 177 people (96.7%). Technical success was defined as the completion of the procedure after the confirmation of sufficient obliteration of gastric varices with sclerosant under retrograde venography, and without rebleeding at 2 days after BRTO (Jang, 2012).

In a retrospective case series of 100 people, complete obliteration was seen in 97 people (97%) and partial obliteration was seen in 2 people (2%). There was no statistically significant difference in technical success rates between bleeding and prophylactic cases (Naeshiro, 2014).

## **BATO**

In a retrospective case series of 71 people, complete obliteration, with all the gastric varices and their feeding veins obliterated, was achieved in 67 people (94.4%; Tian, 2011).

## **CARTO**

In a retrospective case series of 36 people, technical success was achieved in 36 people (100%). Technical success was defined as blood flow stagnation on venograms obtained immediately after final balloon deflation (this study used CARTO-II, which involves balloon occlusion; Yamamoto, 2020).

## **PARTO**

In a retrospective case series of 54 people, technical success was achieved in 54 people (100%) and gastric variceal eradication was seen in 50 people (92.6%). Technical success was defined by the complete occlusion of the efferent shunt and complete filling of gastric varix with a gelfoam slurry (Park, 2020).

In a retrospective cohort study of 95 people (74 BRTO; 21 PARTO) technical and clinical success was achieved in 90 people (94.7%). Technical success was defined as clotting of varices without blood aspiration and no variceal flow on the test injection of contrast media. Clinical success was defined as the absence of residual enhancement within the gastric varices on follow-up CT scan and cessation of gastric bleeding on endoscopic evaluation (Kim, 2016).

## **Clinical success**

### **BRTO**

In the systematic review and meta-analysis of 23 studies (902 people), the pooled clinical success rate was 97.3% (95% CI 95.2 to 98.8;  $I^2=99.29$ ). Clinical success was defined as no recurrence or rebleed of bleeding gastric varices (or in the case of at-risk gastric varices, no future bleed), or alternatively complete obliteration of varices on subsequent imaging (Park, 2015).

### **CARTO**

In a retrospective case series of 36 people, clinical success was achieved in 35 people (97.2%). Clinical success was defined as absence of recurrence (Yamamoto, 2020).

## Mortality or survival

### BRTO

In the systematic review and meta-analysis, the reported survival rates were (Park, 2015):

- 1-year survival: mean 92.6%  $\pm$  4.3% (13 studies; range from 83.1% to 100%)
- 3-year survival: mean 84.5%  $\pm$  10.1% (12 studies; range from 75% to 100%)
- 5-year survival: mean 65.4%  $\pm$  13.5% (10 studies; range from 39% to 85%)
- 7- or 8-year survival: mean 56.7%  $\pm$  15.4% (4 studies; range from 46% to 79%)

In the systematic review and meta-analysis of 3 studies (126 people [BRTO], 87 people [TIPS]), the mortality rate at 12 months was statistically significantly lower in the BRTO group compared with the TIPS group: OR=0.43 (95% CI 0.21 to 0.87,  $p=0.02$ , no heterogeneity  $I^2=0\%$ ; Paleti, 2020).

In a systematic review and network meta-analysis, there was no statistically significant difference in mortality between BRTO and beta-blockers, endoscopic techniques, and TIPS (Osman, 2022). BRTO was connected to the network by the Luo (2021) randomised controlled trial (RCT).

In a systematic review and meta-analysis of 5 studies (453 people), there was no statistically significant difference in mortality between BRTO and endoscopic injection therapy (OR 0.69, 95% CI 0.41 to 1.14,  $p=0.15$ ; Ahmad, 2019).

In an RCT of 32 people treated with BRTO versus 32 people treated with endoscopic cyanoacrylate injection, there was no statistically significant difference in mortality rates between the 2 groups, with 4 people dying in each ( $p=0.719$ ). Cumulative transplantation-free survival rates at 1 and 2 years were not statistically significantly different for cyanoacrylate injection versus BRTO groups (87.5% versus 84.0% and 93.8% versus 86.2% [ $p=0.649$ ], respectively). In multivariate analysis, hepatitis B-related cirrhosis (hazard ratio [HR] 0.076; 95% CI 0.014 to 0.412;  $p=0.003$ ), presence of ascites (HR 5.329; 95% CI 1.055 to 26.915;  $p=0.043$ ), and MELD score (HR 1.218, 95% CI 1.008 to 1.472;  $p=0.041$ ) were the prognostic factors associated with mortality (Luo, 2021).

In the retrospective case series of 183 people, the estimated 1-, 3- and 5-year overall survival rates were 86.2%, 71.0%, and 65.8%, respectively. In multivariate analysis, hepatocellular carcinoma (OR=2.897; 95% CI 1.612 to 5.204;  $p=0.001$ ) and Barcelona Clinic Liver Cancer criteria stage (a score system for grading liver cancer; OR=9.394, 95% CI 4.493 to 19.641;  $p<0.001$ ) were statistically significantly associated with mortality (Jang, 2012)

In the retrospective case series of 100 people, the overall cumulative survival rate was 50% at 5 years and 26% at 10 years after BRTO. There was no

statistically significant difference in survival rates between bleeding and prophylactic cases. In multivariate analysis, Child-Pugh classification (HR 2.371, 95% CI 1.457 to 3.860,  $p=0.001$ ) and hepatocellular carcinoma development (HR 4.782, 95% CI 2.331 to 9.810,  $p<0.001$ ) were statistically significant independent factors for overall survival (Naeshiro, 2014).

## **BATO**

In the retrospective case series of 71 people, 13 people (18.3%) died during follow up. The cumulative survival rate at 1 year was 96.9%, at 3 years was 68.9%, and at 5 years was 53.7% (Tian, 2011).

## **CARTO**

In a retrospective case series of 36 people, all survived the mean follow-up period of 207 days (Yamamoto, 2020).

## **Haemostasis**

### **BRTO**

In the systematic review and meta-analysis of 4 studies (283 people [BRTO], 106 people [TIPS]), there was no difference in the haemostasis rate in the BRTO and TIPS groups: OR=2.74 (95% CI 0.61 to 12.26,  $p=0.19$ , no heterogeneity  $I^2=0\%$ ; Paleti, 2020).

### **Rebleeding**

### **BRTO**

In the systematic review and meta-analysis of 7 studies (462 people [BRTO], 214 people [TIPS]), rebleeding rates were statistically significantly lower in the BRTO group compared with the TIPS group: OR=0.30 (95% CI 0.18 to 0.48,  $p<0.00001$ , no heterogeneity  $I^2=0\%$ ; Paleti, 2020).

In the systematic review and network meta-analysis, BRTO was associated with a statistically significantly lower risk of rebleeding when compared with beta-blockers (relative risk [RR]=0.04; 95% CI 0.01 to 0.26; low certainty) and endoscopic cyanoacrylate injection (RR=0.18; 95% CI 0.04 to 0.77; low certainty; Osman, 2022). BRTO was connected to the network by the Luo (2021) RCT.

In the systematic review of 5 studies (453 people), the rate of gastric variceal rebleeding was 3.6% in people who had BRTO and 23.5% in those who had endoscopic injection therapy (OR=0.11,  $p<0.00001$ , 95% CI 0.05 to 0.25;  $I^2=0\%$ ; Ahmad, 2019).

In the RCT of 32 people treated with BRTO versus 32 people treated with endoscopic cyanoacrylate injection, the probability of gastric variceal rebleeding



was significantly higher in the cyanoacrylate injection group than in the BRTO group ( $p=0.024$ ). The 1- and 2-year cumulative probability of remaining free of all-cause rebleeding was statistically significantly higher in the BRTO group than in the cyanoacrylate injection group: the probability after 1 and 2 years was 96.3% and 92.6% in the BRTO group and 77.0% and 65.2% in the cyanoacrylate injection group ( $p=0.004$ ). In multivariate analysis, BRTO (HR 0.155; 95% CI 0.034 to 0.702;  $p=0.016$ ) and MELD score (HR 1.24; 95% CI 1.012 to 1.519;  $p=0.038$ ) were prognostic factors of all-cause rebleeding (Luo, 2021).

In the retrospective case series of 183 people, the estimated 1-, 3- and 5-year rebleeding-free rates were 87.5%, 74.8%, and 68.9%, respectively. In multivariate analysis, Child-Pugh class was statistically significantly associated with rebleeding (OR=2.404; 95% CI 1.013 to 5.704;  $p=0.047$ ; Jang, 2012).

## **BATO**

In the retrospective case series of 71 people, rebleeding happened in 7 people (9.9%). The cumulative probability of remaining free of rebleeding at 1 year was 98.4%, at 3 years was 77.7%, and at 5 years was 77.7% (Tian, 2011).

## **PARTO**

In the retrospective case series of 54 people, there was 1 case of rebleeding (Park, 2020).

## **Eradication of gastric varices**

### **BRTO**

In the retrospective case series of 183 people, 79 (52.3%) had eradication of gastric varices, 110 (72.8%) had marked shrinkage, and 129 (85.4%) showed a decrease in size of gastric varices at follow up (Jang, 2012).

In the systematic review of 5 studies ( $n=453$ ) complete obliteration of gastric varices was reported in 95% of people who had BRTO and 72% of people who had endoscopic injection therapy (3 studies, OR 8.95,  $p<0.0001$ , 95% CI 3.16 to 25.35; Ahmad, 2019).

### **PARTO**

In the retrospective cohort study of 95 people (74 BRTO; 21 PARTO) there were 3 recurrent cases with BRTO and 4 cases with PARTO. People treated with PARTO had a statistically significantly higher rate of recurrence than the BRTO procedures ( $p<0.05$ ; Kim, 2016).

## Hepatic outcomes

### **PARTO**

In the retrospective case series of 54 people, there was a statistically significant increase in hepatic venous pressure gradient before and after PARTO ( $12.52 \pm 3.83$  to  $14.68 \pm 5.03$  mmHg,  $p < 0.001$ ; Park, 2020).

## Safety summary

Note: Gastric varices, liver cirrhosis, and portal hypertension can cause severe complications. It was not always clear from the studies included whether complications were attributable to the procedure or to the underlying illness.

### Overall complication rate

#### BRTO

In the systematic review and meta-analysis of 23 studies (938 people), the pooled major complication rate was 2.6% (95% CI 1.1, 4.6;  $I^2=99.34$ ). Major complications were defined as those needing therapy and minor hospitalisation (less than 48 hours); needing major therapy with unplanned increase in level of care and prolonged hospitalisation (more than 48 hours); resulting in permanent adverse sequelae, or resulting in death (Park, 2015).

In the systematic review and meta-analysis of 3 studies (56 people [BRTO], 67 people [TIPS]), there was no difference in the rates of procedure-related complications between the BRTO and TIPS groups: OR=1.95 (95% CI, 0.44 to 8.72,  $p=0.38$ , no heterogeneity  $I^2=0\%$ ; Paletti, 2020).

### Procedure-related death

#### BRTO

The systematic review and meta-analysis of 24 studies (1,016 people) reported 2 procedure-related deaths (less than 1%). The cause of death was uncertain for 1 person. For the other, it was presumed to be secondary to multi-organ failure. These deaths were considered to be procedure-related as they happened within 24 hours of BRTO (Park, 2015).

The retrospective cohort study of 95 people (74 BRTO; 21 PARTO) reported 1 death because of balloon rupture and subsequent migration of ethanolamine oleate into systemic circulation (Kim, 2016).

### Procedural complications

#### Balloon rupture

#### BRTO

The retrospective case series of 183 people reported 3 cases (1.6%) of pulmonary thromboembolism related to balloon rupture. The total number of balloon ruptures was not reported (Jang, 2012).

The retrospective cohort study of 95 people (74 BRTO; 21 PARTO) reported 1 death because of balloon rupture and subsequent migration of ethanolamine oleate into systemic circulation (Kim, 2016).

## **Migration of embolising material**

Note, there have also been reports of migration of coils and vascular plugs. Because these complications are broadly similar to sclerosant migration (that is, migration of embolising material), the case reports describing them have not been included in the key evidence.

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of foam migration to liver and 5 cases of systemic sclerosant extravasation (less than 1%; Park, 2015).

The retrospective cohort study of 95 people (74 BRTO; 21 PARTO) reported 1 death because of balloon rupture and subsequent migration of ethanolamine oleate into systemic circulation (Kim, 2016).

## **Gastrorenal shunt rupture**

### **BRTO**

The retrospective case series of 183 people reported 1 case of gastrorenal shunt rupture (Jang, 2012).

## **Iatrogenic injury**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of iatrogenic injury (Park, 2015).

## **Puncture site bleeding**

### **PARTO**

The retrospective case series of 54 people reported 1 case of puncture site bleeding (Park, 2020).

## **Microcoil embolisation**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 3 cases of microcoil embolisation (Park, 2015).

## Aggravation of cirrhotic complications

### Oesophageal varices

#### BRTO

The systematic review and meta-analysis of 20 studies reported a pooled oesophageal variceal recurrence rate of 33.3% (95% CI 24.6 to 42.6,  $I^2=99.74$ ; Park, 2015).

The RCT of 32 people treated with BRTO versus 32 people treated with endoscopic cyanoacrylate injection reported no difference in the overall cumulative oesophageal varices worsening rates between the groups (BRTO 1 year=26.1%, 2 years=41.3%; endoscopic cyanoacrylate injection 1 year=23.1%, 2 years=37.8%; Luo, 2021).

The retrospective case series of 183 people reported that oesophageal varices newly developed in 21 of 36 people without oesophageal varices before BRTO (58.3%), and that oesophageal varices progressed to a larger size in 33 of 100 people with oesophageal varices before BRTO (33.0%; Jang, 2012).

The retrospective case series of 100 people reported an overall cumulative aggravation rate of oesophageal varices of 21% at 1 year, 41% at 3 years, 50% at 5 years, and 54% 10 years after BRTO. In multivariate analysis, overall aggravating rates correlated statistically significantly and independently with existence of oesophageal varices before BRTO (HR 18.114, 95% CI 2.463 to 133.219,  $p=0.004$ ; Naeshiro, 2014).

#### BATO

The retrospective case series of 71 people reported 6 cases of aggravated oesophageal varices (8%; Tian, 2011).

#### PARTO

The retrospective case series of 54 people reported that oesophageal varices deteriorated in 26 people (53.1%; Park, 2020).

### Ascites

#### BRTO

The systematic review and meta-analysis of 11 studies reported a pooled ascites rate of 9.2% (95% CI 2.0 to 20.7,  $I^2=99.89$ ; Park, 2015).

The RCT of 32 people treated with BRTO reported 9 cases of ascites aggravation (28%; Luo, 2021).

The retrospective case series of 100 people reported 18 cases of ascites (18%; Naeshiro, 2014).

### **BATO**

The retrospective case series of 71 people reported 20 cases of ascites (28%; Tian, 2011).

### **PARTO**

The retrospective case series of 54 people reported that, of the 48 people with grade 1 or 2 ascites, an increase in the amount of ascites was detected in 8 people (16.7%) within 1 month and 0 people at 6 months after PARTO (Park, 2020).

## **Hepatic encephalopathy**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of procedure-related hepatic encephalopathy (Park, 2015).

In the systematic review and meta-analysis of 7 studies (462 people [BRTO], 214 people [TIPS]), the incidence of hepatic encephalopathy was statistically significantly lower in the BRTO group compared with the TIPS group, OR=0.06 (95% CI 0.02 to 0.15,  $p < 0.00001$ , low heterogeneity  $I^2 = 10\%$ ; Paleti, 2020).

### **PARTO**

The retrospective case series of 54 people reported that, of the 4 people with hepatic encephalopathy, hepatic encephalopathy improved to grade 0 at 1 month after PARTO. Such improvement continued until 6 months after PARTO (Park, 2020).

## **Thromboembolic events**

### **Pulmonary embolism**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 4 cases of pulmonary emboli (less than 1%). The pooled pulmonary embolus rate was 0.13% (23 studies, 95% CI 0.0049 to 0.42,  $I^2 = 97.12$ ; Park, 2015).

The retrospective case series of 183 people reported 5 cases (2.7%) of pulmonary thromboembolism (Jang, 2012).

## **Portal or splenic venous thrombus**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 11 cases of portal or splenic venous thrombus (1%; Park, 2015).

The RCT of 32 people treated with BRTO reported 2 cases of portal vein thrombosis (6%; Luo, 2021).

### **BATO**

The retrospective case series of 71 people reported 2 cases of portal vein thrombosis (3%; Tian, 2011).

## **Inferior vena cava or right iliac vein thrombus**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 6 cases of inferior vena cava or right iliac vein thrombus (less than 1%; Park, 2015).

## **Renal vein thrombus**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 3 cases of renal vein thrombus (less than 1%; Park, 2015).

## **Cardiac complications**

### **Ventricular fibrillation**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of ventricular fibrillation (Park, 2015).

### **Stress cardiomyopathy**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of stress cardiomyopathy (Park, 2015).

## **Liver complications**

### **Liver necrosis**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of liver necrosis (Park, 2015).

### **Jaundice**

#### **BRTO**

The retrospective case series of 100 people reported 9 cases of jaundice (9%; Naeshiro, 2014).

## **Urinary tract complications**

### **Acute renal failure**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 3 cases of microcoil embolisation (Park, 2015).

### **Renal infarction**

#### **BRTO**

The retrospective case series of 183 people reported 1 case of left renal infarction (Jang, 2012).

### **Haematuria**

#### **BRTO**

The systematic review and meta-analysis of 13 studies reported a pooled haematuria rate of 69.8% (95% CI 49.6 to 86.7,  $I^2=99.92$ ; Park, 2015).

The retrospective case series of 100 people reported 32 cases of gross haematuria (32%; Naeshiro, 2014).



## **Haemoglobinuria**

### **BRTO**

The retrospective cohort study of 95 people (74 BRTO, 21 PARTO) reported 1 case of haemoglobinuria in a person who had BRTO (Kim, 2016).

## **Pulmonary oedema**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of pulmonary oedema (Park, 2015).

## **Infection**

### **Bacteraemia**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of methicillin-sensitive staphylococcus aureus bacteraemia (Park, 2015).

#### **BATO**

The retrospective case series of 71 people reported 5 cases of bacteraemia (7%; Tian, 2011).

### **Pneumonia**

#### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of pneumonia (Park, 2015).

### **Bacterial peritonitis**

#### **BATO**

The retrospective case series of 71 people reported 6 cases of abdominal pain (8%; Tian, 2011).

## **Hepatic abscess**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 1 case of hepatic abscess (Park, 2015).

## **Haemorrhagic gastritis**

### **BRTO**

The systematic review and meta-analysis of 24 studies (1,016 people) reported 3 cases of haemorrhagic gastritis (Park, 2015).

## **Ulcer**

### **BATO**

The retrospective case series of 71 people reported 3 cases of ulcers (4%; Tian, 2011).

## **Fever**

### **BRTO**

The systematic review and meta-analysis of 14 studies reported a pooled fever rate of 51.1% (95% CI 39.2 to 62.9,  $I^2=99.92$ ; Park, 2015).

The RCT of 32 people treated with BRTO reported 2 cases of fever (6%; Luo, 2021).

The retrospective case series of 100 people reported 35 cases of fever (35%; Naeshiro, 2014).

### **BATO**

The retrospective case series of 71 people reported 32 cases of fever (45%; Tian, 2011).

### **PARTO**

The retrospective case series of 54 people reported 1 case of fever (Park, 2020).

## Pain

### BRTO

The RCT of 32 people treated with BRTO reported 3 cases of pain (9%; Luo, 2021).

The retrospective case series of 100 people reported 13 cases of pain (13%; Naeshiro, 2014).

The retrospective cohort study of 95 people (74 BRTO, 21 PARTO) reported 17 cases of abdominal pain, all in people who had BRTO (Kim, 2016).

### BATO

The retrospective case series of 71 people reported 25 cases of abdominal pain (35%; Tian, 2011).

## Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

For this procedure, professional experts listed the following anecdotal adverse events: pleural effusion, cardiogenic shock, and anaphylactic reaction.

## The evidence assessed

### Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transvenous obliteration for gastric varices. The following databases were searched, covering the period from their start to 15 September 2022: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The [inclusion criteria](#) were applied to the abstracts identified by the literature search. If selection criteria could not be determined from the abstracts the full paper was retrieved.

### Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	<p>Clinical studies were included. Emphasis was placed on identifying good quality studies.</p> <p>Abstracts were excluded if no clinical outcomes were reported, or if the paper was a review, editorial, or a laboratory or animal study.</p> <p>Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.</p>
Patient	People with gastric varices.
Intervention/test	Transvenous obliteration.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

### List of studies included in the IP overview

This IP overview is based on about 2,500 people from 4 systematic reviews and meta-analyses, 1 RCT, 1 cohort study, and 5 case series.

Other studies that were considered to be relevant to the procedure but were not included in the main [summary of the key evidence](#) are listed in the [appendix](#).

## Summary of key evidence on BRTO for gastric varices

### Study 1 Park JK (2015)

#### Study details

<b>Study type</b>	Systematic review and meta-analysis
<b>Country</b>	Japan (21 studies), Korea (2 studies), US (1 study)
<b>Recruitment period</b>	Study publication dates ranged from 1996 to 2012
<b>Study population and number</b>	n=1,016 People with bleeding or at-risk gastric varices.
<b>Age and sex</b>	Mean 61.2 years; 60.6% men
<b>Study selection criteria</b>	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>Population: 10 or more people with acute bleeding or at-risk gastric varices (at-risk gastric varices were defined as those demonstrating findings of erythema or enlargement)</li> <li>Intervention: BRTO</li> </ul> <p>Exclusion criteria: publications that were excluded were those suspected of containing people published in multiple papers (in which case the most recent paper or the paper with the most people was used), as well as studies that evaluated fewer than 10 people.</p>
<b>Technique</b>	BRTO with ethanolamine oleate (94.3%), STS foam (2.2%), or polidocanol foam (3.5%).
<b>Follow up</b>	Not reported for individual studies.
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors report that they have no conflict of interest. Source of funding: Not reported.

#### Analysis

**Study design issues:** This systematic review and meta-analysis evaluated the efficacy and safety of BRTO for bleeding or at-risk gastric varices. The meta-analysis was done to Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines. All studies included were uncontrolled and all but 1 were retrospective. The efficacy outcomes were:

- Technical success, defined as complete thrombosis of gastric varices on immediate or short-term follow-up imaging, successful injection of sclerosing agent into gastric varices, and control of actively bleeding gastric varices.
- Clinical success, defined as no recurrence or rebleed of bleeding gastric varices (or in the case of at-risk gastric varices, no future bleed), or alternatively complete obliteration of varices on subsequent imaging.
- Major complications, defined as those needing therapy and minor hospitalisation (less than 48 hours); needing major therapy with unplanned increase in level of care and prolonged hospitalisation (more than 48 hours); resulting in permanent adverse sequelae, or resulting in death.

Meta-analyses were done to estimate the pooled rates using the DerSimonian-Laird random effect for the studies, where the model assumes heterogeneity between the studies.

**Study population issues:** Of the people whose aetiology was provided, 124 (13.7%) had underlying hepatitis B virus, 467 (51.4%) had underlying hepatitis C virus, 205 (22.6%) had cirrhosis attributable to alcohol, and 112 (12.3%) had cirrhosis of other aetiology. Most studies assessed both patients with acutely bleeding and at-risk gastric varices without sub-stratifying their results. Of the studies that did specifically assess people with at-risk varices without active bleeding, rates of clinical success, technical success, and oesophageal varices recurrence were similar to the overall pooled rates. Two people (0.2%) had BRTO primarily for hepatic encephalopathy, with an additional 18 treated for hepatic encephalopathy in addition to gastric varices. Of studies citing the number of people with underlying hepatocellular carcinoma at the time of BRTO, 271 (31.8%) people had underlying hepatocellular carcinoma. Among studies citing the Child-Pugh classification, 424 people (42.8%) were class A, 452 (45.6%) were class B, and 115 (11.6%) were class C.

## Key efficacy findings

### Technical success

Number of people analysed: 21 studies, 847 people

- The pooled technical success rate was 96.4% (95% CI 93.7 to 98.3;  $I^2=99.39$ )

### Clinical success

Number of people analysed: 23 studies, 902 people

- The pooled clinical success rate was 97.3% (95% CI 95.2 to 98.8;  $I^2=99.29$ )

### Survival

Number of people analysed: various

- 1-year survival: mean 92.6%  $\pm$  4.3% (13 studies; range from 83.1% to 100%)
- 3-year survival: mean 84.5%  $\pm$  10.1% (12 studies; range from 75% to 100%)
- 5-year survival: mean 65.4%  $\pm$  13.5% (10 studies; range from 39% to 85%)
- 7- or 8-year survival: mean 56.7%  $\pm$  15.4% (4 studies; range from 45.8% to 79%)

## Key safety findings

### Major complications

Number of people analysed: 23 studies, 938 people

- The pooled major complication rate was 2.6% (95% CI 1.1 to 4.6;  $I^2=99.34$ )

#### Major complications (1,016 total people)

Complication	Number	Percentage
Procedure-related deaths <ul style="list-style-type: none"> <li>The cause of death was uncertain for 1 person. For the other, it was presumed to be secondary to multi-organ failure. These deaths were considered procedure-related as they occurred within 24 hours of BRTO.</li> </ul>	2	less than 1%
Pulmonary oedema	1	-

Pulmonary emboli	4	less than 1%
Portal or splenic venous thrombus	11	1%
Renal vein thrombus	3	less than 1%
Ventricular fibrillation	1	-
Procedure-related hepatic encephalopathy	1	-
Haemorrhagic gastritis	3	less than 1%
Liver necrosis	1	-
Foam migration to liver	1	-
Additional cases of systemic sclerosant extravasation	5	less than 1%
Methicillin-sensitive staphylococcus aureus bacteraemia	1	-
Pneumonia	1	-
Hepatic abscess	1	-
Iatrogenic injury	1	-
Microcoil embolisation	3	less than 1%
Stress cardiomyopathy	1	-
Acute renal failure	1	-
Inferior vena cava or right iliac vein thrombus	6	less than 1%
<b>Total</b>	<b>48</b>	<b>-</b>

### Other complication rates

- Oesophageal variceal recurrence rate = 33.3% (20 studies, 95% CI 24.6 to 42.6,  $I^2=99.74$ )
- Pulmonary embolus rate = 0.13% (23 studies, 95% CI 0.0049 to 0.42,  $I^2=97.12$ )
- Haematuria rate = 69.8% (13 studies, 95% CI 49.6 to 86.7,  $I^2=99.92$ )
- Ascites rate = 9.2% (11 studies, 95% CI 2.0 to 20.7,  $I^2=99.89$ )
- Fever rate = 51.1% (14 studies, 95% CI 39.2 to 62.9,  $I^2=99.92$ )

## Study 2 Paleti S (2020)

### Study details

<b>Study type</b>	Systematic review and meta-analysis
<b>Country</b>	Korea (5 studies), US (2 studies)
<b>Recruitment period</b>	Study publication dates ranged from 2003 to 2018
<b>Study population and number</b>	n=7 studies, 462 people (BRTO), 214 people (TIPS) People with gastric varices because of portal hypertension who were at high risk of bleeding or were bleeding.
<b>Age and sex</b>	Median age ranged from 52 to 59 years; Median proportion male ranged from 53% to 81%
<b>Study selection criteria</b>	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>• Population: people with a diagnosis of gastric varices because of portal hypertension who were at high risk of bleeding or were bleeding.</li> <li>• Intervention and comparator: comparison between people who had BRTO and people who had TIPS.</li> <li>• Outcomes: technical success rate, haemostasis rate, incidence rate of post-operative rebleeding, incidence rate of hepatic encephalopathy, postoperative procedure-related complication and mortality rate at 1 year.</li> </ul> <p>Exclusion criteria: any study that failed to include TIPS or BRTO as an intervention of management for gastric varices; all studies that did not directly compare BRTO with TIPS; review articles, nonhuman studies, also studies where the definition of procedures was not uniformly accepted.</p>
<b>Technique</b>	Technique details are not described for individual studies.
<b>Follow up</b>	Mean follow up ranged from 14.4 months to 30.6 months.
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors report that they have no conflict of interest. Source of funding: Not reported.

### Analysis

**Study design issues:** This systematic review and meta-analysis compared the efficacy and safety of BRTO versus TIPS for bleeding or at-risk gastric varices caused by portal hypertension. The meta-analysis was reported according to the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) statement. One study was an RCT (21 total patients) and 6 were cohort studies. Two studies were available only as conference abstracts. Risk of bias in all studies was assessed by the Newcastle–Ottawa quality assessment scale (6 of the studies were rated as ‘high’ quality). However, note that the Newcastle–Ottawa quality assessment scale is not designed to assess RCTs. The outcomes included mortality at 1 year, technical success, rebleeding, haemostasis, post-procedure complications, and hepatic encephalopathy. A definition for technical success was not reported.

Pooled ORs with CIs for the outcomes of interest were synthesised by meta-analysis using a random-effects model. Heterogeneity between the included studies was estimated using the inconsistency index ( $I^2$ ). Heterogeneity of less than 30%, 30% to 50%, 50% to 75%, and more than 75% was classified as low, moderate, substantial, and considerable heterogeneity, respectively.



## Key efficacy findings

### Mortality at 12 months

Number of people analysed: 3 studies, 126 people (BRTO), 87 people (TIPS)

- The mortality rate at 12 months was statistically significantly lower in the BRTO group compared with the TIPS group, OR=0.43 (95% CI 0.21 to 0.87, p=0.02, no heterogeneity I<sup>2</sup>=0%)

### Technical success

Number of people analysed: 6 studies, 404 people (BRTO), 178 people (TIPS)

- There was no difference in the technical success rate between the BRTO and TIPS groups, OR=0.87 (95% CI 0.28 to 2.73, p=0.81, substantial heterogeneity I<sup>2</sup>=50%)

### Haemostasis rate

Number of people analysed: 4 studies, 283 people (BRTO), 106 people (TIPS)

- There was no difference in the haemostasis rate in the BRTO and TIPS groups, OR=2.74 (95% CI 0.61 to 12.26, p=0.19, no heterogeneity I<sup>2</sup>=0%)

### Rebleeding rate

Number of people analysed: 7 studies, 462 people (BRTO), 214 people (TIPS)

- Rebleeding rates were statistically significantly lower in the BRTO group compared with the TIPS group, OR=0.30 (95% CI 0.18 to 0.48, p<0.00001, no heterogeneity I<sup>2</sup>=0%).

## Key safety findings

### Post-procedure complication rate

Number of people analysed: 3 studies, 56 people (BRTO), 67 people (TIPS)

- There was no difference in the rates of procedure-related complications between the BRTO and TIPS groups, OR=1.95 (95% CI, 0.44 to 8.72, p=0.38, no heterogeneity  $I^2=0\%$ ).

### Hepatic encephalopathy rate

Number of people analysed: 7 studies, 462 people (BRTO), 214 people (TIPS)

- The incidence of hepatic encephalopathy was statistically significantly lower in the BRTO group compared with the TIPS group, OR=0.06 (95% CI 0.02 to 0.15,  $p<0.00001$ , low heterogeneity  $I^2=10\%$ ).

## Study 3 Osman KT (2022)

### Study details

<b>Study type</b>	Systematic review and network meta-analysis
<b>Country</b>	Taiwan (4 studies), China (3 studies), India (2 studies)
<b>Recruitment period</b>	Recruitment periods ranged from 1995 to 2018
<b>Study population and number</b>	n=9 RCTs (1 included BRTO); 647 people (32 had BRTO)
<b>Age and sex</b>	Average age across all studies ranged from 39 to 61 years; 70.7% male
<b>Study selection criteria</b>	<p>Inclusion criteria:</p> <ul style="list-style-type: none"> <li>• Population: adults with portal hypertension and a history of prior gastric variceal bleeding (cohorts with a mixed population of primary prophylaxis, acute bleeding, and secondary prophylaxis were included if more than 90% were included for secondary prophylaxis).</li> <li>• Intervention and comparator: beta-blockers, endoscopic techniques, TIPS, BRTO, or any combination.</li> <li>• Outcomes: rebleeding and all-cause mortality.</li> <li>• Study design: RCTs with a minimum follow up of at least 6 weeks.</li> </ul> <p>Exclusion criteria: non-randomised or observational studies; less than 90% of population were included for secondary prophylaxis of gastric variceal bleeding; did not specify the presence of gastric varices; had a follow-up period of less than 6 weeks; were done in people younger than 18 or animals.</p>
<b>Technique</b>	Details of the technique used in Luo, 2021 (the BRTO study included in this network meta-analysis) are summarised in the Luo, 2021 study summary (Study 4).
<b>Follow up</b>	Median follow up across all studies was 26 months.
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors report no conflicts of interest. Source of funding: Not reported.

### Analysis

**Study design issues:** This systematic review and network meta-analysis compared the outcomes of several techniques (including BRTO) for secondary prophylaxis of gastric variceal bleeding. The meta-analysis was reported according to the PRISMA statement.

Only 1 study that used BRTO was included in the network meta-analysis – Luo, 2021 (included in this overview as study 4). Endoscopic cyanoacrylate injection was the common comparator across all RCTs. All comparisons were based on the results of 1 or 2 RCTs. Risk of bias in individual studies was assessed by using the Cochrane Risk of Bias assessment tool version 2.0. Studies were assessed as at low to moderate risk of bias. Due to the objective outcomes, the authors felt that single-blinded or unblinded trials were not at high risk of bias.

Outcomes were:

- Rebleeding
- Mortality

For pairwise comparisons, RR and 95% CIs were estimated. Heterogeneity was assessed using the  $I^2$ -statistic, with values greater than 50% suggesting substantial heterogeneity. Network meta-analysis was performed based on a random-effects consistency model following a multivariate meta-regression approach. Relative ranking of the interventions using P scores were calculated. P scores range between 0 when a treatment is certainly the worst and 1 when a treatment is certainly the best. The authors then classified the interventions based on P scores into the following 4 categories: P scores >0.75, 0.50 to 0.75, 0.25 to 0.50, and <0.25 corresponding to high, moderate, low, and very low mean probability of the intervention for being ranked the best, respectively. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to rate the certainty of evidence of estimates derived from the network meta-analysis was used.

**Study population issues:** Viral hepatitis was the main underlying cause of cirrhosis (56.27%), followed by alcohol (24.19%). People with cirrhosis had Child-Pugh class A (34.22%), class B (44.09%), and Class C (21.69%). The location of gastric varices was GOV1 in 20.35%, GOV2 in 57.73%, and IGV1 in 21.92%.

## Key efficacy findings

### Rebleeding

Number of people analysed: 32 (BRTO)

- BRTO was connected to the network through the Luo, 2021 RCT of BRTO versus endoscopic cyanoacrylate injection.
- BRTO was associated with a statistically significantly lower risk of rebleeding when compared with beta-blockers (RR=0.04; 95% CI 0.01 to 0.26; low certainty) and endoscopic cyanoacrylate injection (RR=0.18; 95% CI 0.04 to 0.77; low certainty).
- Endoscopic ultrasound cyanoacrylate injection (P score=0.90) and BRTO (P score=0.84) ranked the highest, whereas beta-blockers (P score=0.04) ranked the lowest in preventing rebleeding.

### Mortality

Number of people analysed: 32 (BRTO)

- BRTO was connected to the network through the Luo, 2021 RCT of BRTO versus endoscopic cyanoacrylate injection.
- There was no statistically significant difference in mortality between BRTO and the other interventions.
- Endoscopic ultrasound cyanoacrylate injection ranked the highest (P score=0.83) and beta-blockers ranked the lowest (P score=0.14) in preventing mortality. A P score for BRTO is not reported, but can be estimated at approximately 0.60 from the publication, ranking 5<sup>th</sup>.

## Key safety findings

Safety findings were not reported.

## Study 4 Ahmad (2019)

### Study details

<b>Study type</b>	Systematic review and meta-analysis
<b>Country</b>	Korea, Japan, US
<b>Recruitment period</b>	Search date: February 2019. Included trials were published between 2009 and 2016.
<b>Study population and number</b>	n=453 (5 studies) Patients with gastric variceal bleeding
<b>Age and sex</b>	Mean age in BRTO groups ranged from 50.7 to 62 years; 55% male (250/453)
<b>Study selection criteria</b>	Inclusion criteria: randomised and non-randomised trials and comparative studies that compared BRTO and endoscopic injection therapy in people with acute gastric variceal bleeding or with prior history of bleeding from gastric varices. Endoscopic criteria for gastric variceal bleeding included active spurting or oozing, or blood clot coating the GV.  Studies comparing the interventions in patient presenting with acute oesophageal variceal bleeding were excluded. Trials that compared BRTO, endoscopic injection therapy to other modalities such as TIPS were excluded. Non-comparative studies were also excluded. Abstracts were excluded if there were no available full text publications.
<b>Technique</b>	All studies used cyanoacrylate injection therapy as the primary and first modality to control active variceal bleeding and achieve haemostasis. In 2 studies, ethanolamine oleate was used after haemostasis was achieved to prevent rebleeding.
<b>Follow up</b>	Range 13.5 to 78.4 months
<b>Conflict of interest/source of funding</b>	None

### Analysis

**Study design issues:** There were no randomised controlled trials identified. The quality of non-randomised studies was assessed using the Newcastle–Ottawa scale. Of the 5 included studies, 2 were prospective and 3 were retrospective cohorts. The primary outcome was incidence of gastric variceal rebleeding.

**Study population issues:** patients with acute gastric variceal bleeding or with a history of bleeding from gastric varices were included.

### Key efficacy findings

Number of people analysed: 453

#### Gastric variceal rebleeding:

- BRTO=3.6%
- Endoscopic injection therapy=23.5%, OR=0.11,  $p<0.00001$  (95% CI 0.05 to 0.25). No heterogeneity was observed ( $I^2=0\%$ ,  $p=0.92$ ).

#### Complete obliteration of gastric varices:

- BRTO=95%
- Endoscopic injection therapy=72%, OR=8.95,  $p<0.0001$  (95% CI 3.16 to 25.35).

There was no statistically significant difference in the aggravation of oesophageal varices (OR 0.93, 95% CI 0.57 to 1.52,  $p=0.77$ ) or mortality (OR 0.69, 95% CI 0.41 to 1.14,  $p=0.15$ )

### **Key safety findings**

Safety findings were not reported.

## Study 5 Luo X (2021)

### Study details

<b>Study type</b>	RCT
<b>Country</b>	China
<b>Recruitment period</b>	2015 to 2018
<b>Study population and number</b>	n=32 (BRTO), 32 (endoscopic cyanoacrylate injection) People with cirrhosis who had acute or previous bleeding from fundal gastric varices.
<b>Age and sex</b>	BRTO group: Mean 58.3 years; 53.1% male
<b>Patient selection criteria</b>	Inclusion criteria: people aged 18 to 75 years with cirrhosis who were admitted to the institution because of acute bleeding from fundal gastric varices (stratum 1) or were transferred to the hospital after recovering from a previous acute gastric varices bleeding within 4 weeks (stratum 2). Exclusion criteria: (1) previous secondary prophylactic treatment of gastric varices; (2) absence of a portosystemic shunt; (3) noncirrhotic portal hypertension; (4) portal cavernoma; (5) advanced malignancy; (6) end-stage renal disease under renal replacement therapy; (7) cardiorespiratory failure; (8) pregnancy; and (9) refusing to participate.
<b>Technique</b>	BRTO done under local anaesthesia. A balloon catheter was inserted through the femoral or internal jugular vein into the portosystemic shunt. Venography was used to confirm the gastric varix. Varices were embolised by polidocanol until the feeding veins were visualised on venography.  For people who had endoscopic cyanoacrylate injection, an attempt was made to completely obliterate gastric varices in 1 session by injecting glue at multiple sites. Endoscopic cyanoacrylate was injected at 4-week intervals until gastric varices were obliterated.  For people with concomitant medium-to-large oesophageal varices, endoscopic band ligation was done using multiband ligators.
<b>Follow up</b>	BRTO group: Mean 27.6 months (SD 14.3 months)
<b>Conflict of interest/source of funding</b>	Conflict of interest: One author reports consulting for, and grants from, several companies. Source of funding: Supported by a grant from the National Natural Science Foundation of China.

### Analysis

**Follow up issues:** Five people (3 in the cyanoacrylate injection group and 2 in the BRTO group) had poor adherence to the treatment protocol. Three people could be contacted and the other 2 could not be contacted. It is not reported in which group the people who could not be contacted were in.

**Study design issues:** This RCT compared BRTO with cyanoacrylate injection for the secondary prophylaxis of gastric varices rebleeding after primary haemostasis. People in stratum 1 had treatment for 3 to 5 days. An emergency endoscopy was done within 24 hours, and cyanoacrylate injection was administered to control acute bleeding without obliterating all GVs. People in stratum 1 were then randomised on day 6 to either BRTO or endoscopic cyanoacrylate injection. People in stratum 2 were randomised after screening gastroscopy. The blinding of participants was done using sealed opaque envelopes. The primary outcome was gastric variceal rebleeding and all-cause rebleeding. Secondary outcomes included all-cause mortality and complications, including worsening of oesophageal varices.

Comparisons between the 2 groups were done using the student t-test for normally distributed continuous data and the chi-squared test or Fisher's exact test for categorical data. Gastric variceal rebleeding, all-cause rebleeding, and mortality were estimated using the Kaplan–Meier method and compared with the log-rank test. Primary analyses were conducted on an intention-to-treat basis. All tests were 2-tailed and  $p < 0.05$  was considered statistically significant.

**Study population issues:** There were no statistically significant differences between the baseline characteristics of the treatment groups. The aetiology of cirrhosis was hepatitis B infection in 39 people (61%), alcohol in 8 (13%), autoimmune liver disease in 5 (8%), and unspecified 'others' in 12 (19%). The mean Child-Pugh score for the BRTO group was  $7.2 \pm 2.2$  (class B) and for the cyanoacrylate group was  $7.4 \pm 1.7$  (class B). The mean MELD score was  $10.0 \pm 2.3$  in the BRTO group and  $10.7 \pm 2.9$  in the cyanoacrylate group. The location of gastric varices was GOV2 in 42 people (66%) and IGV 1 in 22 people (34%). A total of 42 people (66%) had concomitant oesophageal varices. No people were prescribed non-selective beta-blocker therapy.

## Key efficacy findings

### Rebleeding

Number of people analysed: 32 (BRTO), 32 (endoscopic cyanoacrylate injection)

- The probability of gastric variceal rebleeding was significantly higher in the cyanoacrylate injection group than in the BRTO group ( $p=0.024$ ).
- The 1- and 2-year cumulative probability of remaining free of all-cause rebleeding was statistically significantly higher in the BRTO group than in the cyanoacrylate injection group: the probability after 1 and 2 years was 96.3% and 92.6% in the BRTO group and 77.0% and 65.2% in the cyanoacrylate injection group ( $p=0.004$ ).
- In multivariate analysis, BRTO (HR 0.155; 95% CI 0.034 to 0.702;  $p=0.016$ ) and MELD score (HR 1.24; 95% CI 1.012 to 1.519;  $p=0.038$ ) were prognostic factors of all-cause rebleeding.

### Mortality

Number of people analysed: 32 (BRTO), 32 (endoscopic cyanoacrylate injection)

- There was no difference in mortality rates between the 2 groups, with 4 people dying in each ( $p=0.719$ ).
  - Liver failure, infection, and bleeding were the main causes of death.
- Cumulative transplantation-free survival rates at 1 and 2 years were not statistically significantly different for cyanoacrylate injection versus BRTO groups – 87.5% versus 84.0% and 93.8% versus 86.2% ( $p=0.649$ ).
- In multivariate analysis, hepatitis B-related cirrhosis (HR 0.076; 95% CI 0.014 to 0.412;  $p=0.003$ ), presence of ascites (HR 5.329; 95% CI 1.055 to 26.915;  $p=0.043$ ), and MELD score (HR 1.218, 95% CI 1.008 to 1.472;  $p=0.041$ ) were the prognostic factors associated with mortality.



## Key safety findings

### Complications

Number of people analysed: 32 (BRTO) 32 (endoscopic cyanoacrylate injection)

- There were no statistically significant differences between the complications of both procedures. The following complications happened:

	<b>Cyanoacrylate injection (N=32)</b>	<b>BRTO (N=32)</b>
<b>Complications</b>	16	17
Pain	4	3
Fever	4	2
Tachycardia	0	1
Portal vein thrombosis	1	2
Death	1	0
Worsening of ascites	6	9

### Aggravation of oesophageal varices

Number of people analysed: 32 (BRTO), 32 (endoscopic cyanoacrylate injection)

- Only people with associated small oesophageal varices were included to analyse worsening oesophageal varices. People with medium-to-large oesophageal varices where variceal band ligation was done were excluded.
- There was no difference in the overall cumulative oesophageal varices worsening rates, with 23.1% and 37.8% in the cyanoacrylate injection group and 26.1% and 41.3% in the BRTO group at 1 and 2 years, respectively (p=0.786).

## Study 6 Jang SY (2012)

### Study details

<b>Study type</b>	Retrospective, multicentre, case series
<b>Country</b>	Korea
<b>Recruitment period</b>	2001 to 2010
<b>Study population and number</b>	n=183 People with liver cirrhosis who had BRTO for bleeding gastric varices.
<b>Age and sex</b>	Mean 57.1; 76% male
<b>Patient selection criteria</b>	All people with liver cirrhosis who had BRTO for endoscopically confirmed gastric varices bleeding. People could not have had any other endoscopic, surgical or radiologic interventional treatments before BRTO.
<b>Technique</b>	A balloon catheter was inserted through the femoral or internal jugular vein, then advanced toward the gastorenal shunt through the left renal vein and subsequently placed in the proximal portion of a shunt by ballooning. The varices were visualised by venography. Ethanolamine oleate mixed with lipiodol was then injected to obliterate the varix.
<b>Follow up</b>	Mean 36 months (SD 29.2 months)
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors report that they have no conflicts of interest. Source of funding: The study was supported by Kyungpook National University Research Fund.

### Analysis

**Follow up issues:** Of 177 people who successfully completed BRTO, 151 people had the endoscopic or radiologic follow-up examinations.

**Study design issues:** This case series reported the outcomes of BRTO for bleeding gastric varices. People were identified retrospectively from medical records. Outcomes included:

- Technical success, defined as the completion of the procedure after the confirmation of sufficient obliteration of gastric varices with sclerosant under retrograde venography, and without rebleeding at 2 days after BRTO.
- Eradication of gastric varices, defined as complete obliteration of targeted varix on follow up. Varices were classified by the Hashizume classification as:
  - grade 0, non-visible
  - grade 1, small sized, tortuous winding varices
  - grade 2, medium sized, nodular-shaped varices
  - grade 3, large sized, tumorous varices
- Rebleeding, the presence of haematemesis (blood in vomit), melena (digested blood in faeces), or haematochezia (fresh blood in faeces) with a significant drop in haemoglobin level and blood transfusion of 2 or more units was needed.
- Mortality.

Procedure-related complications were defined as any untoward adverse events during or immediately after BRTO, which required active treatment or prolonged hospitalisation.

Quantitative variables were compared using Student's t-test, and qualitative variables were compared using Fisher's exact test. Kaplan–Meier analyses were applied to examine the time to the first episode of rebleeding,

or time to death. The log-rank test was used to examine the variation of rebleeding episodes and survival rates. All p-values were 2-tailed, and  $p < 0.05$  was considered statistically significant. People who were lost to follow up were right-censored at the time of drop out. People who failed to BRTO were excluded for the analysis of the rebleeding and mortality rates.

**Study population issues:** The aetiology of cirrhosis was hepatitis B in 90 people (49%), hepatitis C in 23 (13%), chronic alcohol abuse in 50 (27%), others (including autoimmune hepatitis, primary biliary cirrhosis, cryptogenic) in 13 (7%), and combined aetiologies in 7 (4%). According to the Child-Pugh classification, 48 people were class A (26%), 103 people were class B (56%), and 32 people were class C (17%). The location of gastric varices was GOV1 in 42 people (23%), GOV2 in 80 people (44%), and IGV1 in 61 people (33%). The sizes of gastric varices were grade 1 in 18 people (10%), grade 2 in 40 (22%), grade 3 in 124 (68%), and undetermined in 1. A total of 131 people (72%) had concomitant oesophageal varices at the time of BRTO. Fifty people (27%) had hepatocellular carcinoma.

## Key efficacy findings

### Technical success

Number of people analysed: 183

- Technical success was achieved in 177 of 183 people (96.7%).

### Eradication of gastric varices

Number of people analysed: 151

- Eradication: 79 people (52.3%)
  - The eradication rate of GOV1 was statistically significantly lower than IGV1/GOV2 ( $p=0.032$ ).
- Marked shrinkage to grade 0/1: 110 people (72.8%)
- Decrease in size: 129 people (85.4%)

### Rebleeding

Number of people analysed: 177

- The estimated 1-, 3- and 5-year rebleeding-free rates were 87.5%, 74.8%, and 68.9% respectively.
- Rebleeding occurred in 39 people (22.0%), of which:
  - Oesophageal varices,  $n=18$
  - Gastric varices,  $n=7$
  - Non-variceal bleedings,  $n=4$
  - Unknown,  $n=10$
- In multivariate analysis, Child-Pugh class was statistically significantly associated with rebleeding (OR=2.404; 95% CI 1.013 to 5.704;  $p=0.047$ ).

### Mortality

Number of people analysed: 177

- The estimated 1-, 3-, 5-year overall survival rates were 86.2%, 71.0%, and 65.8% respectively.
- A total of 52 people died during follow up, because of:
  - Hepatocellular carcinoma,  $n=15$
  - Rebleeding,  $n=13$
  - Hepatic failure,  $n=6$
  - Complications of portal hypertension except variceal bleedings,  $n=7$
  - Infections except spontaneous bacterial peritonitis (included in the above cause),  $n=3$

- Unspecified 'others', n=8
- In multivariate analysis, hepatocellular carcinoma (OR=2.897; 95% CI 1.612 to 5.204; p=0.001) and Barcelona Clinic Liver Cancer criteria stage (a score system for grading liver cancer; OR=9.394, 95% CI 4.493 to 19.641; p<0.001) were statistically significantly associated with mortality.

## Key safety findings

### Complications

Number of people analysed: 183

- Procedure-related complications (during or immediately after BRTO) happened in 8 people (4.4%).
  - Pulmonary thromboembolism, n=5 (2.7%)
    - Three of these cases were associated with balloon rupture during BRTO procedure.
  - Transient mental change, n=1
  - Left renal infarction, n=1
  - Gastrorenal shunt rupture, n=1

### Aggravation of oesophageal varices

Number of people analysed: 136

- Oesophageal varices newly developed in 21 of 36 people without oesophageal varices before BRTO (58.3%).
- Oesophageal varices progressed to a larger size in 33 of 100 people with oesophageal varices before BRTO (33.0%).

## Study 7 Naeshiro N (2014)

### Study details

<b>Study type</b>	Retrospective, single centre, case series
<b>Country</b>	Japan
<b>Recruitment period</b>	1994 to 2013
<b>Study population and number</b>	n=100 People with gastric varices treated by BRTO.
<b>Age and sex</b>	Median 72 years; 59% male
<b>Patient selection criteria</b>	Consecutive people with gastric varices who had BRTO. People were classified into 2 groups: the prophylactic cases (n=39) and the bleeding cases (n=61).
<b>Technique</b>	BRTO performed under local anaesthesia. A balloon catheter was inserted through the femoral or internal jugular vein into the portosystemic shunt. When needed, minor collateral vessels of the shunts were embolised by 50% glucose solution and microcoils before EOI injection. The varices were visualised by venography. BRTO was done using 5% ethanolamine oleate mixed with iopamidol.
<b>Follow up</b>	Median 60 months (range 0 to 191 months)
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors declared no conflict of interest. Source of funding: Not reported.

### Analysis

**Study design issues:** This retrospective case series evaluated the long-term outcomes of BRTO for gastric varices. People were identified retrospectively from medical records. Outcomes included:

- Short-term:
  - Technical success. Complete obliteration was defined as when the contrast-enhanced CT showed gastric varices with low attenuation, including the afferent veins or the draining veins of the gastric varices.
  - Complications. Minor complication was defined as not to need medical attention. Major complication was defined as therapy is needed, permanent adverse sequelae, or death.
- Long-term:
  - Survival.
  - Aggravation of oesophageal varices.

The cumulative survival rates and aggravation rates of oesophageal varices were determined using the Kaplan–Meier method. The Cox’s proportional hazards model was used to estimate the significance of independent variables.  $p < 0.05$  was statistically significant.

**Study population issues:** There was no difference in baseline characteristics between bleeding and prophylactic cases except gender (male/female;  $p = 0.041$ ). The aetiology was hepatitis B in 4 people (4%), hepatitis C in 54 (54%), alcohol in 24 (24%), and unspecified ‘others’ in 18 (18%). There were 39 people (39%) classified as Child-Pugh grade A, 48 (48%) as grade B, and 13 (13%) as grade C. Fifty people (50%) had grade F2 variceal size and 50 (50%) had grade F3. A total of 68 people (68%) had concomitant oesophageal varices at the time of BRTO. A total of 61 people (61%) had hepatocellular carcinoma.

## Key efficacy findings

### Technical success

Number of people analysed: 100

- Complete obliteration was achieved in 97 (97%) people.
- Partial obliteration was seen in 2 (2%) people.
- Failure was seen in 1 (1%) person.
- There was no statistically significant difference in technical success rates between bleeding and prophylactic cases.

### Survival

Number of people analysed: 97 (only those people who had complete obliteration)

- The overall cumulative survival rate was 50% at 5 years and 26% at 10 years after BRTO.
- A total of 31 people died during follow up. The causes of death were:
  - Hepatocellular carcinoma, n=8
  - Hepatic failure, n=20
  - Oesophageal variceal bleeding, n=3
  - Extrahepatic diseases, n=15.
- There was no statistically significant difference in survival rates between bleeding and prophylactic cases.
- In multivariate analysis, Child-Pugh classification (HR 2.371, 95% CI 1.457 to 3.860, p=0.001) and hepatocellular carcinoma development (HR 4.782, 95% CI 2.331 to 9.810, p<0.001) were statistically significant independent factors for overall survival.

## Key safety findings

### Complications

Number of people analysed: 100

- Major complications were not observed.
- Minor complications included:
  - Pain, n=13 (13%)
  - Fever, n=35 (35%)
  - Gross haematuria, n=32 (32%)
  - Transaminase elevation, n=29 (29%)
  - Jaundice, n=9 (9%)
  - Renal dysfunction, n=6 (6%)
  - Ascites, n=18 (18%)

### Aggravation of oesophageal varices

Number of people analysed: 100

- Overall cumulative aggravation rates of oesophageal varices were 21% at 1 year, 41% at 3 years, 50% at 5 years, and 54% 10 years after BRTO.
- In multivariate analysis, overall aggravating rates correlated statistically significantly and independently with existence of oesophageal varices before BRTO (HR 18.114, 95% CI 2.463 to 133.219, p=0.004).



## Summary of key evidence on BATO for gastric varices

### Study 8 Tian X (2011)

#### Study details

<b>Study type</b>	Retrospective, single centre, case series
<b>Country</b>	China
<b>Recruitment period</b>	2003 to 2009
<b>Study population and number</b>	n=73 (71 followed up) People with acute or recent gastric varices bleeding who had percutaneous transhepatic obliteration.
<b>Age and sex</b>	Mean 50.3 years; 62% male
<b>Patient selection criteria</b>	Inclusion criteria: acute gastric variceal bleeding or a history of gastric variceal bleeding within 6 months of hospital admission.  Exclusion criteria: serum bilirubin level of more than 100 mg/L, serum creatinine value of greater than 2 mg/dL, platelet count of less than 20,000/mm <sup>3</sup> , complete obstruction of the portal vein because of thrombosis, hepatic encephalopathy greater than stage II, hepatorenal syndrome, and cardiorespiratory failure.
<b>Technique</b>	Percutaneous transhepatic obliteration under local anaesthesia. Percutaneous transhepatic puncture of the intrahepatic branch of the portal vein was performed. Splenoportography was done to evaluate the gastric varices, the feeding veins, and the draining veins.  In people without large gastrorenal shunts, cyanoacrylate was injected directly into the gastric varices. For people with large gastrorenal shunts, a balloon catheter was inserted into the left renal vein via the right femoral vein to reduce the gastrorenal shunt blood flow. Afterward, cyanoacrylate was injected into the gastric varices.
<b>Follow up</b>	Mean 24.2 months (SD 12.4 months)
<b>Conflict of interest/source of funding</b>	Conflict of interest: Not reported. Source of funding: Not reported.

#### Analysis

**Follow up issues:** The procedure was unsuccessful in 2 people – both were excluded from the analysis.

**Study design issues:** This retrospective case series reported the outcomes of percutaneous transhepatic obliteration for gastric varices. People were identified retrospectively from medical records. People in which the procedure failed were excluded from the analysis. Outcomes included technique outcomes (extent of obliteration), rebleeding rates, survival, and complications.

The Kaplan–Meier method was used to examine the rebleeding rate and survival rate value.  $p < 0.05$  was considered statistically significant.

**Study population issues:** The aetiology was hepatitis B in 40 people (56%), hepatitis C in 13 (18%), alcohol in 13 (18%), and unspecified 'others' in 5 (7%). There were 24 people (34%) classified as Child-Pugh grade A, 31 (44%) as grade B, and 16 (23%) as grade C. The location of gastric varices was GOV2 in 41 people (58%) and IGV1 in 30 people (42%). The form of gastric varices was F1 in 18 people (25%), F2 in 26 (37%), and F3 in 32 (45%). A total of 15 people (21%) had hepatocellular carcinoma.



## Key efficacy findings

### Technique outcomes

Number of people analysed: 71

- Complete obliteration, with all the gastric varices and their feeding veins obliterated, was achieved in 67 people (94.4%).
- Partial obliteration, with only the feeding veins obliterated, was achieved in the remaining 4 people (5.6%).

### Rebleeding

Number of people analysed: 71

- During the follow up period, rebleeding occurred in 7 people (9.9%). Rebleeding was due to:
  - Gastric varices, n=4 (5.6%)
  - Oesophageal varices, n=2 (2.8%)
  - Portal hypertensive gastropathy, n=1 (1.4%)
- The cumulative probability of remaining free of rebleeding at 1 year was 98.4%, at 3 years was 77.7%, and at 5 years was 77.7%.

### Survival

Number of people analysed: 71

- During the follow-up, 13 people (18.3%) died:
  - Hepatocellular carcinoma, n=7
  - Progression of hepatic failure, n=5
  - Uncontrolled rebleeding, n=1
- The cumulative survival rate at 1 year was 96.9%, at 3 years was 68.9%, and at 5 years was 53.7%.

## Key safety findings

### Complications

Number of people analysed: 71

The following complications were reported:

- Bacteraemia, n=5 (7%)
- Transient fever greater than 38°C, n=32 (45%)
- Abdominal pain, n=25 (35%)
- Ulcer, n=3 (4%)
- Spontaneous bacterial peritonitis, n=6 (8%)
- Ascites, n=20 (28%)
- Portal vein thrombosis, n=2 (3%)
- Aggravated oesophageal varices, n=6 (8%)

## Summary of key evidence on CARTO for gastric varices

### Study 9 Yamamoto A (2020)

#### Study details

<b>Study type</b>	Retrospective, single centre, case series
<b>Country</b>	Japan
<b>Recruitment period</b>	2016 to 2018
<b>Study population and number</b>	n=36 Consecutive people with gastric varices who had CARTO-II (see Technique below)
<b>Age and sex</b>	Mean 64.7 years; 56% male
<b>Patient selection criteria</b>	Consecutive people with gastric varices who had CARTO-II.  People were excluded for: emergent BRTO (n=3), high wedge pressure of the hepatic vein (45 mmHg) after temporary occlusion of the gastrosplenic shunt (n=1), did not undergo BRTO because of visualisation of apparent portopulmonary vein anastomosis during the procedure (n=1).
<b>Technique</b>	CARTO-II is a modified BRTO technique in which coils and a balloon catheter are used.  Under local anaesthesia, a balloon catheter is inserted into the gastrosplenic shunt. Venography was performed to visualise the varices. Ethanolamine oleate and iopamidol was used to embolise the varices. Then, coil embolisation of the drainage vein was performed through the balloon catheter.
<b>Follow up</b>	Mean 207 days (range 3 to 675 days)
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors declare that they have no conflict of interest. Source of funding: Not reported.

#### Analysis

**Study design issues:** This retrospective case series assessed the outcomes of a modified CARTO procedure, CARTO-II, for the treatment of gastric varices. Consecutive people were identified retrospectively from medical records. Outcomes included:

- Technical success, defined as blood flow stagnation on venograms obtained immediately after final balloon deflation.
- Clinical success, defined as absence of recurrence after CARTO-II.
- Survival.
- Complications.

No statistical analysis was performed.

**Study population issues:** The aetiology was alcohol in 13 (36%), non-alcoholic fatty liver disease in 7 (19%), hepatitis B in 5 (14%), hepatitis C in 4 (11%), Fontan-associated liver disease in 1 (3%), primary biliary cirrhosis in 1 (3%), Wilson disease in 1 (3%), extrahepatic portal vein obstruction in 1 (3%), and unknown in 3 (8%). There were 28 people classified as Child-Pugh grade A and 8 as grade B. The form of gastric varices was F1 in 1 person (2%), F2 in 29 (82%), and F3 in 6 (16%). The Hirota grade of varices was 1 in 5 people (14%), 2 in 12 (33%), 3 in 11 (31%), and 4 in 8 (22%).

## Key efficacy findings

### Technical success

Number of people analysed: 36

- The technical success rate was 100% (36/36).

### Clinical success

Number of people analysed: 36

- The clinical success rate was 97.2% (35/36).
  - One person experienced recurrence of varices in the follow up period.

### Survival

Number of people analysed: 36

- All people survived the follow-up period.

## Key safety findings

### Complications

Number of people analysed: 36

No severe complications were observed.

## Summary of key evidence on PARTO for gastric varices

### Study 10 Park JW (2020)

#### Study details

<b>Study type</b>	Retrospective, single centre, case series
<b>Country</b>	Korea
<b>Recruitment period</b>	2012 to 2018
<b>Study population and number</b>	n=73 (54 followed up) People who had PARTO for bleeding gastric varices or for prophylaxis
<b>Age and sex</b>	Mean 56.6 years; 68.5% male
<b>Patient selection criteria</b>	People who had PARTO for bleeding gastric varices (active or recent bleeding) or for primary prophylaxis. One person was included who had PARTO for hepatic encephalopathy.
<b>Technique</b>	PARTO. The catheter was inserted to the gastorenal shunt via the femoral or jugular vein. Venograms were obtained to visualise the varices. The size of the vascular plug was selected according to the diameter of the narrowest gastorenal shunt. The plug was deployed at the most dilated gastorenal shunt to facilitate the entry into the gastorenal shunt proximal to the vascular plug. A gelfoam slurry was used.
<b>Follow up</b>	Mean 28 months (SD 19.8 months)
<b>Conflict of interest/source of funding</b>	Conflict of interest: The authors declare that they have no conflict of interest. Source of funding: This study was supported by the Soonchunhyang University Research Fund.

#### Analysis

**Follow up issues:** Of the 73 people who had PARTO, 15 were lost to follow up, and 4 died within a month after PARTO. The causes of death were deterioration of liver function (n=2), the oesophageal varices bleeding (n=1), and infection (n=1). It is not reported whether these deaths were assessed as related to the efficacy or safety of PARTO. These people were excluded from the analysis.

**Study design issues:** This retrospective case series evaluated the outcomes of PARTO for the treatment of gastric varices. People were identified retrospectively from medical records. As noted above, 19 people were excluded from the analysis. Outcomes included:

- Technical success, defined by the complete occlusion of the efferent shunt and complete filling of gastric varices with a gelfoam slurry.
- Eradication of gastric varices, defined by complete or marked shrinkage of gastric varices on follow-up endoscopy or CT scan.
- Hepatic function and bleeding.
- Complications, including aggravation of oesophageal varices.

**Study population issues:** PARTO was performed for various indications: active bleeding, 11/54 (20.4%); recent bleeding, 13/54 (24.1%); primary prophylaxis for impending rupture 29/54 (53.7%); and just for hepatic encephalopathy control without gastric varices, 1/54 (1.9%). The aetiology was alcohol in 24 people (44.4%), hepatitis B in 14 (25.9%), hepatitis C in 2 (3.7%), and unspecified 'others' in 14 (25.9%). The mean MELD score was  $11.46 \pm 4.35$ . The location of gastric varices was GOV1 in 12 people, GOV2 in 36 people, and undefined 'others' in 5 people.

## Key efficacy findings

### Technical success

Number of people analysed: 54

- The technical success rate was 100%.
- The gastric variceal eradication rate was 92.6% (50/54).

### Rebleeding

Number of people analysed: 54

- Data on rebleeding is not well described.
- In Table 2 of the publication, there is 1 case of rebleeding classified as a complication.
- The results section describes 2 people who were refractory to PARTO as having 'additional' gastric varices bleeding.
- Further in the results section, the oesophageal varices outcomes are described. In 25 people in whom the portal pressure was measured, oesophageal varices deterioration was found in 10. Of those 10, 2 people experienced rebleeding of oesophageal varices.

### Hepatic outcomes

Number of people analysed: 54

- There was a statistically significant increase in the hepatic venous pressure gradient before and after PARTO ( $12.52 \pm 3.83$  to  $14.68 \pm 5.03$  mmHg,  $p < 0.001$ ).
- The Child-Pugh score after PARTO showed statistically significant improvements at 1 and 6 months (both  $p < 0.05$ ), but did not show improve significantly during the overall follow-up period ( $p > 0.05$ ).

## Key safety findings

### Complications

Number of people analysed: 54

- Fever,  $n=1$
- Puncture site bleeding,  $n=1$

### Aggravation of oesophageal varices

Number of people analysed: 49

- Oesophageal varices deterioration was observed in 26 people (53.1%).
  - Portal pressure after PARTO was statistically significantly associated with aggravation of oesophageal varices.

### Aggravation of ascites

Number of people analysed: 48

- Among 48 people with mild/moderate ascites except for 6 people with severe ascites, an increase in the amount of ascites was detected in 8 people (16.7%) within 1 month and 0 people at 6 months after PARTO.

## **Improvement of hepatic encephalopathy**

Number of people analysed: 4

- In 4 people, hepatic encephalopathy improved to grade 0 at 1 month after PARTO. Such improvement continued until 6 months after PARTO.

## Study 11 Kim YH (2016)

### Study details

<b>Study type</b>	Retrospective, single centre, cohort
<b>Country</b>	Korea
<b>Recruitment period</b>	2004 to 2015
<b>Study population and number</b>	n=95 (70 followed up) People with gastric varices
<b>Age and sex</b>	Mean 62.9 years; 77% male
<b>Patient selection criteria</b>	People with recent haematemesis, who had gastric varices, associated portal hypertension, and a gastroduodenal shunt.
<b>Technique</b>	<p>3 groups were studied:</p> <ol style="list-style-type: none"> <li>1. BRTO with ethanolamine oleate (n=49)</li> <li>2. BRTO with sodium tetradecyl sulfate foam (n=25)</li> <li>3. PARTO (n=21)</li> </ol> <p>BRTO: under local anaesthesia, balloon catheter was inserted via the femoral vein to the gastroduodenal shunt. Varices were visualised. Embolisation was performed with ethanolamine oleate or sodium tetradecyl sulfate foam until the variceal flow was stopped.</p> <p>PARTO: Same basic procedure as BRTO but use of a vascular plug and gelfoam slurry to embolise the varix.</p>
<b>Follow up</b>	No mean reported, follow up recurrence rates reported to 2 years
<b>Conflict of interest/source of funding</b>	Conflict of interest: the authors declare that they have no conflict of interest. Source of funding: Not reported.

### Analysis

**Follow up issues:** Of the 95 people identified, follow-up data was available for 70.

**Study design issues:** This retrospective cohort study compared the outcomes of BRTO with ethanolamine oleate, BRTO with sodium tetradecyl sulfate foam, and PARTO for the treatment of recently bleeding gastric varices. People were identified retrospectively from medical records. Outcomes included:

- Technical success, defined as clotting of varices without blood aspiration and no variceal flow on the test injection of contrast media.
- Clinical success, defined as the absence of residual enhancement within the gastric varices on follow-up CT scan and cessation of gastric bleeding on endoscopic evaluation.
- Recurrence of gastric varices was defined as enlargement of gastric varices on endoscopy or CT, or rebleeding was occurred.
- Procedure time.
- Major complications were defined as any undesired event that requires major therapy, prolonged hospitalisation or has permanent adverse sequelae or results in death. Pain as a minor complication was evaluated as mild, moderate, or severe.

The Chi-square test and Fisher's exact test were used to compare abdominal pain. The Kruskal–Wallis test and Mann–Whitney U test were used to verify relationship between procedure time and each procedure group. The Kaplan–Meier method and log-rank test were used to compare expected 1- and 2-year recurrence rates.  $p < 0.05$  was considered statistically significant.

**Study population issues:** There were no statistically significant differences in the baseline characteristics of the 3 groups. The aetiology of cirrhosis was hepatitis B in 26 people and hepatitis C in 5 people (other causes were not reported). There were 38 people (54%) who were classed as Child-Pugh grade A, 29 people (41%) were grade B, and 3 (4%) were grade C. Nineteen people (27%) had hepatocellular carcinoma.

## Key efficacy findings

### Technical outcomes

Number of people analysed: 95

- Technical and clinical success was achieved in 90 people (94.7%).
- Technical failure happened in only BRTO cases, causes included:
  - Severe angulation of left adrenal vein, n=2
  - Hirota grade 5 gastric varices, n=2
  - Rupture of the balloon during sclerotherapy, n=1
- The procedure time of PARTO was statistically significantly shorter than the procedure time of the BRTO procedures ( $p < 0.017$ ).

### Recurrence of gastric varices

Number of people analysed: 70 (34 BRTO with ethanolamine oleate, 18 BRTO with sodium tetradecyl sulfate, and 18 PARTO)

- There were 3 recurrent cases with BRTO with EO and 4 cases with PARTO.
- People treated with PARTO had a statistically significantly higher rate of recurrence than the BRTO procedures ( $p < 0.05$ ).
- Rebleeding happened in 2 cases, both with PARTO.

	Expected 6-month recurrence rate (%)	Expected 1-year recurrence rate (%)	Expected 2-year recurrence rate (%)
BRTO using EO	3.2	3.2	16.5
BRTO using STS foam	0	0	0
PARTO	16.0	32.8	55.2



## Key safety findings

### Complications

Number of people analysed: 95

- Death, n=1 (BRTO with ethanolamine oleate)
  - The balloon ruptured, causing migration of ethanolamine oleate into systemic circulation, which led to disseminated intravascular coagulation.
- Haemoglobinuria, n=1 (BRTO with ethanolamine oleate)
- Abdominal pain, n=17 (all BRTO with ethanolamine oleate)
  - Mild, n=13
  - Moderate, n=1
  - Severe, n=3

## Validity and generalisability of the studies

- The patient populations of included studies were generally comparable in terms of age, sex, location and form of gastric varices, and severity of liver disease.
- Transvenous obliteration was used for primary or secondary prophylaxis, or in actively bleeding gastric varices.
- Four types of transvenous obliteration were considered (BRTO, BATO, CARTO, and PARTO). However, there is very limited comparative evidence.
- There are technical differences in how each procedure is performed. For example, the sclerosant used. Different sclerosing agents may have different risk/benefit profiles.
- In the Ahmad (2019) systematic review, 2 studies were prospective and the other 3 were retrospective. In the Park (2015) systematic review and meta-analysis (BRTO outcomes), all studies except 1 were retrospective. In the Paleti (2020) systematic review and meta-analysis (BRTO vs. TIPS), all studies except 1 were non-randomised. One RCT was included in the Osman (2022) network meta-analysis – Luo (2021; BRTO vs. endoscopic cyanoacrylate injection) – and Luo (2021) was also included in the key evidence section of this overview (Study 4). All other studies were retrospective, non-randomised case series or cohort studies.
- There may be limited generalisability to a UK clinical practice context. This is due to:
  - Studies were conducted primarily in Korea, China, and Japan.
  - Non-selective beta-blockers were not used in almost all the studies. These agents are commonly used in people with previous variceal bleeding in the UK.
  - In most studies, the predominant aetiology of liver disease was viral hepatitis. This differs from the UK, where alcohol-related liver disease is most prominent.
- The longest follow up was 191 months (upper bound of Naeshiro, 2014), with the longest median follow up of 60 months (Naeshiro, 2014).

## Existing assessments of this procedure

In 2022, the Baveno VII Faculty published ‘Baveno VII – Renewing consensus in portal hypertension’, endorsed by the European Association for the Study of the Liver (de Franchis, 2022). The recommendations are based on a review of the literature (methods to identify literature are not reported) and expert opinion. The level of existing evidence was evaluated, and the recommendations were ranked according to the GRADE system, from A (high) to D (very low). The strength of

the recommendations was graded 1 (strong) or 2 (weak). The following recommendations relevant to BRTO were made:

- '5.22: There is no indication at present for balloon-occluded retrograde (antegrade) transvenous obliteration (BRTO or BATO) or TIPS in primary prophylaxis of gastric variceal bleeding in compensated patients. (D.1; New)'
- '6.40: In patients with GOV2, IGV1, and ectopic varices, BRTO could be considered as an alternative to endoscopic treatment or TIPS, provided it is feasible (type and diameter of shunt) and local expertise is available, as it has been shown to be safe and effective. (D.2; New)'

In 2021, the American Gastroenterological Association published a clinical practice update on the management of bleeding gastric varices (Henry, 2021). The recommendations are based on a review of the literature (methods to identify literature are not reported) and expert opinion. As per the best practice advice:

- 'Best practice advice 11: When a gastroduodenal shunt is present, local expertise is available, and when severe comorbid complications of portal hypertension are absent, BRTO is the optimal endovascular therapy for management of bleeding gastric varices.'

In 2016, the American Association for the Study of Liver Diseases published practice guidance on the risk stratification, diagnosis, and management of portal hypertensive bleeding in cirrhosis (Garcia-Tsao, 2016). Relevant literature was identified by a literature review (methods are not reported). Statements are based on literature, the outputs of previous consensus conferences, and expert opinion. The following guidance statements relevant to BRTO for gastric varices are made:

- 'Neither TIPS nor BRTO are recommended to prevent first haemorrhage in patients with fundal varices that have not bled.'
- 'In patients who have recovered from GOV2 or IGV1 haemorrhage, TIPS or BRTO are first-line treatments in the prevention of rebleeding.'

In 2015, the British Society of Gastroenterology published UK guidelines on the management of variceal haemorrhage in cirrhotic people (Tripathi, 2015). Relevant literature was identified by an 'exhaustive' literature review (methods are not reported). Recommendations were graded based on the supporting evidence, from level 1 (highest quality evidence; systematic reviews of RCTs) to level 5 (lowest quality evidence; expert opinion) and from grade A (consistent level 1 studies) to grade D (level 5 evidence or inconsistent or inconclusive studies). The guidelines give the following recommendation regarding BRTO:

- If control of bleeding fails with endoscopic therapy or TIPS:

- 'B-RTO or surgical shunting can be considered if TIPSS is not possible (for example, portal vein thrombosis present) and depending on local resources (level 3a, grade B).'

In 2016, the Japanese Society of Gastroenterology published clinical practice guidelines for liver cirrhosis (Fukui, 2016). Literature was identified by a literature search (full methods are not reported). The quality of evidence was graded from A (high) to D (very low). The strength of a recommendation was indicated as either 1 (strong) or 2 (weak). The guidelines give the following recommendations regarding BRTO:

- 'BRTO is proposed as an elective therapy after haemostasis of initial gastric variceal bleeding using cyanoacrylate and as a prophylactic therapy in the management of high-risk gastric varices (Evidence level C, strength 2).'

## Related NICE guidance

Below is a list of NICE guidance related to this procedure.

### Interventional procedures

- [Stent insertion for bleeding oesophageal varices](#) (2011) NICE interventional procedures guidance 392

### Medical technologies

- [Danis stent for acute oesophageal variceal bleeding](#) (2021) NICE medical technologies guidance MTG57

### NICE guidelines

- [Acute upper gastrointestinal bleeding in over 16s: management](#) (2012) NICE guideline CG141
- [Cirrhosis in over 16s: assessment and management](#) (2016) NICE guideline NG50

## Additional information considered by IPAC

### Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, when comments are considered voluminous, or publication would be unlawful or inappropriate.

Four professional expert questionnaires for transvenous obliteration for gastric varices were submitted and can be found on the [NICE website](#).

### **Company engagement**

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received no completed submissions.

### **Issues for consideration by IPAC**

- Four different techniques are included.

## References

1. Park JK, Saab S, Kee ST et al. (2015) Balloon-Occluded Retrograde Transvenous Obliteration (BRTO) for Treatment of Gastric Varices: Review and Meta-Analysis. *Digestive diseases and sciences* 60(6):1543-53.
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5. Luo X, Xiang T, Wu J et al. (2021) Endoscopic Cyanoacrylate Injection Versus Balloon-Occluded Retrograde Transvenous Obliteration for Prevention of Gastric Variceal Bleeding: A Randomized Controlled Trial. *Hepatology (Baltimore, Md.)* 74(4):2074-84.
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## Literature search strategy

Databases	Date searched	Version/files
MEDLINE (Ovid)	15/09/22	1946 to September 13, 2022
MEDLINE In-Process (Ovid)	15/09/22	1946 to September 13, 2022
MEDLINE Epubs ahead of print (Ovid)	15/09/22	September 13, 2022
EMBASE (Ovid)	15/09/22	1974 to 2022 September 14
EMBASE Conference (Ovid)	15/09/22	1974 to 2022 September 14
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	15/09/22	Issue 9 of 12, September 2022 1
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	15/09/22	Issue 9 of 12, September 2022 1
International HTA database (INAHTA)	15/09/22	-

### Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

### Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

## MEDLINE search strategy

The MEDLINE search strategy was translated for use in the other sources.

- 1 ((transven\* or vein\* or venous\*) adj4 (Obliterat\* or Emboli?\* or Embolotherap\*)).tw. 10790
- 2 Balloon Occlusion/ 3685
- 3 (Balloon adj4 (Tamponade or occlu\* or emboli?\*)).tw. 5928
- 4 (BRTO or BATO or PARTO or CARTO).tw. 1282
- 5 1 or 2 or 3 or 4 19233
- 6 "Esophageal and Gastric Varices"/ 13899
- 7 ((stomach or gastr\* or GI) adj4 ((vein\* or venous\*) adj4 (large or swollen or enlarge\*))).tw. 37
- 8 ((stomach or gastr\* or GI) adj4 (varices or variceal)).tw. 3305
- 9 or/6-8 14969
- 10 5 and 9 713
- 11 (Fogarty\* adj4 occlu\*).tw. 34
- 12 10 or 11 747
- 13 Animals/ not Humans/ 4914420



14 12 not 13 740

## Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the [summary of the key evidence](#). It is by no means an exhaustive list of potentially relevant studies. Studies that used BRTO only and included fewer than 50 people were not included in this appendix.

### Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
<b>BRTO</b>			
Akahoshi T, Hashizume M, Tomikawa M et al. (2008) Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: a 10-year experience. Journal of gastroenterology and hepatology 23(11):1702-9	n=68  FU=8 years	BRTO is beneficial over the long-term, despite worsening oesophageal varices in some patients, because of excellent treatment efficacy and improved mortality. BRTO can become a first-choice radical treatment following haemostasis for gastric variceal bleeding and prophylactic treatment for risky gastric varices.	Studies with more people or longer follow up included.
Arai H, Abe T, Takagi H and Mori M. (2006) Efficacy of balloon-occluded retrograde transvenous obliteration, percutaneous transhepatic obliteration and combined techniques for the management of gastric fundal varices. World journal of gastroenterology 12(24):3866-73	n=75 BRTO, 8 PTO, 10 combined  FU=2.6 years	Combined BRTO and PTO therapy may rescue cases with uncontrollable gastric fundal varices that remained even after treatment with BRTO and/or PTO.	Studies with more people or longer follow up included.
Cho SK, Shin SW, Do YS et al. (2008) Development of thrombus in the major systemic and portal veins after balloon-occluded retrograde transvenous obliteration for treating	n=60  FU=5 to 25 months	The frequency of thrombus development in the major systemic and portal veins after BRTO was 15%.	Safety outcome captured in included publications.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
gastric variceal bleeding: its frequency and outcome evaluation with CT. Journal of vascular and interventional radiology: JVIR 19 (4):529-38			
Chu HH, Kim M, Kim HC et al. (2018) Long-Term Outcomes of Balloon-Occluded Retrograde Transvenous Obliteration for the Treatment of Gastric Varices: A Comparison of Ethanolamine Oleate and Sodium Tetradecyl Sulfate. Cardiovascular and interventional radiology 41(4):578-86	n=142 FU=19.9 months to 23.9 months (group means)	BRTO using sodium tetradecyl sulfate has comparable long-term outcomes to BRTO using ethanolamine oleate for gastric varices.	Studies with more people or longer follow up included.
Gimm G, Chang Y, Kim HC et al. (2018) Balloon-Occluded Retrograde Transvenous Obliteration versus Transjugular Intrahepatic Portosystemic Shunt for the Management of Gastric Variceal Bleeding. Gut and liver 12(6):704-713	n=157 FU=8 years	BRTO provides better bleeding control, rebleeding-free survival, and OS than TIPS for patients with bleeding gastric varices.	Included in the Paleti (2020) systematic review and meta-analysis.
Imai Y, Nakazawa M, Ando S et al. (2016) Long-term outcome of 154 patients receiving balloon-occluded retrograde transvenous obliteration for gastric fundal varices. Journal of gastroenterology and hepatology 31(11):1844-50	n=154 FU=30 months	Therapeutic strategies including B-RTO with a microballoon catheter were useful to achieve a favourable outcome in patients with gastric fundal varices especially in those manifesting Child-Pugh class-A liver damage and/or those without hepatocellular carcinoma complication.	Studies with more people or longer follow up included.
Jogo A, Nishida N, Yamamoto A et al. (2019)	n=104	Selective BRTO for GV could minimise the risk of	Studies with more people or

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Selective Balloon-occluded Retrograde Transvenous Obliteration for Gastric Varices. Internal medicine (Tokyo, Japan) 58 (16):2291-2297	FU=15 months to 23 months (group means)	a worsening of EV or reduce the amount of sclerosants; however, the rate of recurrence was high in comparison to conventional BRTO.	longer follow up included.
Jogo A, Nishida N, Yamamoto A et al. (2014) Factors associated with aggravation of esophageal varices after B-RTO for gastric varices. Cardiovascular and interventional radiology 37(5):1243-50	n=67 FU=1 year	Total bilirubin and hepatic venous pressure gradient were significant independent risk factors for oesophageal varices aggravation after BRTO.	Studies with more people or longer follow up included. Oesophageal varices aggravation well described in the literature.
Jogo A, Yamamoto A, Kaminoh T et al. Utility of low-dose gelatin sponge particles and 5% ethanolamine oleate iopamidol mixture in retrograde transvenous obliteration (GERTO) for gastric varices. The British journal of radiology 93(1108):20190751	n=57 FU=12 to 16 months (group means)	GERTO was performed in lower amount of sclerosants and in less time compared to conventional BRTO in Hirota's grade 2 or more.	Studies with more people or longer follow up included.
Kamezaki H, Maruyama H, Shimada T et al. (2013) Short- and long-term clinical outcome after balloon-occluded retrograde transvenous obliteration: Is pretreatment portal flow direction a predictive factor? Hepatology International 7(1):241-7.	n=103 FU=2.1 to 3.4 years (group means)	Haemodynamic assessment of portal flow direction is important before BRTO, and care should be taken to manage thrombotic disorders in the perioperative period in patients with reversed portal flow after BRTO. Another treatment option might be preferred for gastric varices in Child classes B and C patients with reversed portal flow instead of B-RTO, which may have a poor prognosis.	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Kiyosue H, Mori H, Maruno M et al. (2020) Conventional versus selective balloon-occluded retrograde transvenous obliteration of gastric varices. Egyptian Journal of Radiology and Nuclear Medicine 51(1):101	n=59	Selective and superselective techniques had a lower ascites exacerbation, and oesophageal varices aggravation rates than conventional technique. However, superselective BRTO had a lower gastric varices complete thrombosis and higher gastric varices bleeding rates after BRTO than other techniques	Studies with more people or longer follow up included.
Lee HA, Kwak J, Cho SB et al. (2022) Endoscopic variceal obturation and retrograde transvenous obliteration for acute gastric cardiofundal variceal bleeding in liver cirrhosis. BMC gastroenterology 22(1); 355	n=86 (RTO) FU=18 months	Both EVO and RTO effectively controlled acute cardiofundal variceal bleeding. RTO was superior to EVO in preventing all-variceal and GV rebleeding after treatment, with similar survival outcomes.	Larger studies included.
Lee SJ, Kim SU, Kim M-D et al. (2017) Comparison of treatment outcomes between balloon-occluded retrograde transvenous obliteration and transjugular intrahepatic portosystemic shunt for gastric variceal bleeding hemostasis. Journal of gastroenterology and hepatology 32(8):1487-1494	n=95 FU=3 years	BRTO proved more effective than TIPS in haemostasis of gastric variceal bleeding, associated with significantly less risk of rebleeding.	Included in the Paleti (2020) systematic review and meta-analysis.
Maruyama H, Okugawa H, Kobayashi S et al. (2010) Pre-treatment hemodynamic features involved with long-term survival of cirrhotic patients after embolization of gastric fundal varices.	n=81 FU=3.5 years	Pretreatment flow volume ratio between gastric vein and portal trunk before BRTO may be a predictive indicator for prognosis in cirrhotic patients with gastric fundal varices after BRTO.	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
European journal of radiology 75(2):e32-7			
Mizutani T, Nirei K, Kanda T et al. (2022) Left Gastric Vein Width Is an Important Risk Factor for Exacerbation of Esophageal Varices Post Balloon-Occluded Retrograde Transvenous Obliteration for Gastric Varices in Cirrhotic Patients. Medicina (Kaunas, Lithuania) 58(2)	n=50	Careful attention should be paid to the LGV width when BRTO is performed for gastric varices.	Larger studies included.
Mukund A, Rangarh P, Patidar Y et al (2020) Salvage Balloon Occluded Retrograde Transvenous Obliteration for Gastric Variceal Bleed in Cirrhotic Patients With Endoscopic Failure to Control Bleed/Very Early Rebleed: Long-term Outcomes. Journal of Clinical and Experimental Hepatology; 10(5):421-8	n=52 FU= 2 years	Salvage BRTO is a safe and effective procedure for patients with acute gastric variceal bleed with failure to control bleed with endotherapy or very early rebleed after endotherapy. Salvage BRTO has good short/long-term outcomes with lower rebleed, higher survival, and improved liver disease severity.	Studies with more people or longer follow up included.
Nakazawa M, Imai Y, Uchiya H et al. (2017) Balloon-occluded retrograde transvenous obliteration as a procedure to improve liver function in patients with decompensated cirrhosis. JGH Open 1(4):127-33	n=112 FU=6 months	BRTO is a useful therapeutic procedure for improving liver function even in patients without gastric varices by increasing the portal venous flow with successfully targeted, uncommon portosystemic shunts.	Studies with more people or longer follow up included.
Ninoi T, Nishida N, Kaminou T et al. (2005) Balloon-occluded retrograde transvenous obliteration of gastric varices with gastrosplenic shunt: long-term follow-up in 78 patients. American	n=78 FU=1.9 years	BRTO is an effective method for gastric varices with gastrosplenic shunt and provides lower recurrence and bleeding rates.	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
journal of roentgenology 184(4):1340-6			
Ninoi T, Nakamura K, Kaminou T et al. (2004) TIPS versus transcatheter scleroththerapy for gastric varices. American Journal of Roentgenology 183(2):369–76	n=58 BRTO, 28 PTS  FU=41.2 months	Transcatheter scleroththerapy may provide better control of gastric variceal bleeding than TIPS. Transcatheter scleroththerapy may contribute to a higher survival rate than TIPS in patients with Child-Pugh class A disease.	Studies with more people or longer follow up included.
Oshita K, Ohira M, Honmyo N et al. (2020) Treatment outcomes after splenectomy with gastric devascularization or balloon-occluded retrograde transvenous obliteration for gastric varices: a propensity score-weighted analysis from a single institution. Journal of gastroenterology 55(9):877-87	n=55  FU=3 years	Splenectomy with gastric devascularization showed better overall survival and improvement of liver function compared with BRTO for the treatment of gastric varices caused by portal hypertension.	Studies with more people or longer follow up included.
Park SJ, Chung JW, Kim H-C et al. (2010) The prevalence, risk factors, and clinical outcome of balloon rupture in balloon-occluded retrograde transvenous obliteration of gastric varices. Journal of vascular and interventional radiology: JVIR 21(4):503-7	n=69	Balloon rupture during BRTO occurred in 8.7% of patients. Balloon rupture may cause rapid migration of sclerosant, pulmonary embolism, and recurrent gastric variceal bleeding.	Safety outcome captured in included publications.
Saad WEA, Nicholson D, Lippert A et al (2012) Balloon-occlusion catheter rupture during balloon-occluded retrograde transvenous obliteration of gastric varices utilizing sodium	n=40	The incidence of balloon-occlusion catheter rupture utilizing 3% sodium tetradecyl sulfate (STS) and inventory unique to the United States is significantly higher than in Asia (<8% rupture rate).	Safety outcome captured in included publications.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
tetradecyl sulfate: incidence and consequences. Vascular and endovascular surgery 46(8):664-70		However, these ruptures have no significant technical or clinical consequences.	
Shinkai K, Sakamori R, Yamada R et al. (2022) Prognostic impact of worsening of esophageal varices after balloon-occluded retrograde transvenous obliteration. Journal of gastroenterology and hepatology 37(6):1148-1155	n=258	Early worsening of EV after BRTO was associated with poor prognosis after BRTO.	No new outcomes.
Sonomura T, Ono W, Sato M et al. (2012) Three benefits of microcatheters for retrograde transvenous obliteration of gastric varices. World journal of gastroenterology 18(12):1373-8	n=56 FU=10.5 months	The microcatheter techniques are very effective methods for achieving a higher success rate of BRTO procedure.	Studies with more people or longer follow up included.
Shiba M, Higuchi K, Nakamura K, et al. (2002) Efficacy and safety of balloon-occluded endoscopic injection sclerotherapy as a prophylactic treatment for high-risk gastric fundal varices: a prospective, randomized, comparative clinical trial. Gastrointest Endosc. 56(4):522-8	n=20 (BRTO and sclerotherapy groups)	The gastric varices in all people except one in the BRTO group were eradicated with either treatment. Balloon-occluded endoscopic injection sclerotherapy is a safe and effective for treatment of high-risk gastric fundal varices. In contrast to BRTO, it can be used even in patients without a gastroduodenal shunt.	Larger RCT (Luo, 2021) included.
Stein DJ, Salinas C, Sabri S et al. (2019) Balloon Retrograde Transvenous Obliteration Versus Endoscopic Cyanoacrylate in Bleeding	n=71 FU=1 year	BRTO is associated with a lower rate of rebleeding but no change in mortality.	Studies with more people or longer follow up included.



Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Gastric Varices: Comparison of Rebleeding and Mortality with Extended Follow-up. Journal of vascular and interventional radiology: JVIR 30(2):187-194			
Takaji R, Kiyosue H, Matsumoto S et al. (2011) Partial thrombosis of gastric varices after balloon-occluded retrograde transvenous obliteration: CT findings and endoscopic correlation. American journal of roentgenology 96(3):686-91	n=69 FU=32 months	Partial thrombosis after BRTO can occur in complex-type gastric varices, which have a higher risk of regrowth. Additional techniques that achieve complete thrombosis are required for long-term efficacy for complex-type gastric varices.	Studies with more people or longer follow up included.
Waguri N, Osaki A, Watanabe Y et al. (2021) Balloon-occluded retrograde transvenous obliteration for gastric varices improves hepatic functional reserve in long-term follow-up. JGH Open 5(12):1328-34	n=60 FU=3 years (up to 10 year survival analysis)	BRTO for gastric fundal varices has a favourable effect on long-term hepatic functional reserve.	Studies with more people or longer follow up included.
Wang YB, Zhang JY, Gong JP et al. (2016) Balloon-occluded retrograde transvenous obliteration versus transjugular intrahepatic portosystemic shunt for treatment of gastric varices due to portal hypertension: A meta-analysis. Journal of gastroenterology and hepatology 31(4):727-33	n=5 studies, 210 patients	BRTO was a technically feasible as well as a secure method for the treatment of gastric varices originated from portal hypertension. It may have the potential to be an alternative shunt approach of TIPS, when suitable patients selected.	More recent systematic review and meta-analysis included.
Wang ZW, Liu JC, Zhao F et al. (2020) Comparison of the Effects of TIPS versus BRTO on Bleeding Gastric Varices: A Meta-	n=9 studies	In this meta-analysis, BRTO brought more benefits to patients, with a higher OS rate and lower rebleeding rate. BRTO is	Lower-quality systematic review and meta-analysis than Paleti,

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Analysis. Canadian journal of gastroenterology & hepatology: 5143013		a feasible method for gastric varices.	2020. Similar findings.
Yamagami T, Yoshimatsu R, Miura H et al. (2013) The role of divided injections of a sclerotic agent over two days in balloon-occluded retrograde transvenous obliteration for large gastric varices. Korean journal of radiology 14(3):439-45	n=50 FU=51.2 months	When gastric varices are very large, a strategy involving thrombosis of only the drainage vein on the first day followed by infusing the sclerotic agent on the following day might be effective and feasible.	Studies with more people or longer follow up included.
Yamamoto A, Nishida N, Morikawa H et al. (2016) Prediction for Improvement of Liver Function after Balloon-Occluded Retrograde Transvenous Obliteration for Gastric Varices to Manage Portosystemic Shunt Syndrome. Journal of vascular and interventional radiology: JVIR 27(8):1160-7	n=50	The predictive factor for improvement in albumin after BRTO was lower liver stiffness measurement (22.9 kPa or more) using transient elastography.	Studies with more people or longer follow up included.
Yoshimatsu R, Yamagami T, Miura H, and Hashiba M. (2015) Factors related to thrombosis of gastric varix during balloon-occluded retrograde transvenous obliteration. Acta radiologica (Stockholm, Sweden: 1987) 56(5):592-7	n=65	Liver function might influence the development of thrombosis of gastric varices in BRTO. Serum albumin and prothrombin time-international normalised ratio levels would provide information for deciding on the duration of retention of the BRTO catheter to obtain sufficient therapeutic effectiveness.	Studies with more people or longer follow up included.
Yu Q, Liu C, and Raissi D. (2021) Balloon-occluded Retrograde Transvenous Obliteration Versus	n=5 studies, 308 patients	Both BRTO and TIPS are safe and effective interventions in the management algorithm of	More comprehensive systematic review and

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Transjugular Intrahepatic Portosystemic Shunt for Gastric Varices: A Meta-Analysis. Journal of clinical gastroenterology 55(2):147-158		portal hypertensive gastric variceal bleeding. Although BRTO may be more effective at the prevention of future variceal rebleeding, the choice of BRTO versus TIPS should be tailored according to patient's comorbidities.	meta-analysis included.
<b>BATO</b>			
Ambati C, Boshell D, Ende J et al. (2021) The Promise of Percutaneous Transhepatic Variceal Embolization for Both Gastroesophageal and Ectopic Varices-An Australian Case Series. Journal of Clinical Interventional Radiology ISVIR 5(1):3-10	n=8 FU=44 days	Percutaneous transhepatic variceal embolization is an effective treatment option for patients with uncontrolled variceal bleeding (ectopic as well as gastroesophageal) especially when the traditional therapies such as transjugular intrahepatic portosystemic shunts, endoscopic variceal ligation, and BRTO are contraindicated or ineffective.	Studies with more people or longer follow up included.
Chikamori F, Kuniyoshi N, Kawashima T et al. (2006) Percutaneous transhepatic obliteration for isolated gastric varices with gastropericardiac shunt: case report. Abdominal imaging 31(2):249-52	n=1	Percutaneous transhepatic obliteration using a microcatheter is a rational, effective, and safe therapy for isolated gastric varices with a gastropericardiac shunt.	Studies with more people or longer follow up included.
Hirose S, Hasegawa N, Endo M et al. (2021) Percutaneous transhepatic obliteration-related procedures for isolated gastric varices: experience of three cases. Clinical Journal of Gastroenterology	n=3	PTO-related procedures are good treatment options for isolated gastric varices, but clinicians should be aware of the risk of treatment failure, especially the cases which have multiple feeding veins.	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Ishikawa T, Imai M, Ko M et al. (2017) Percutaneous transhepatic obliteration and percutaneous transhepatic sclerotherapy for intractable hepatic encephalopathy and gastric varices improves the hepatic function reserve Biomedical Reports 6(1):99-102	n=26  FU=6 months	For patients with various gastroduodenal shunts or those with BRTO-intractable hepatic encephalopathy and gastric varices without gastroduodenal shunts, PTO/PTS can improve the antegrade blood flow to the liver, as demonstrated by improvement in the hepatic function reserve.	Studies with more people or longer follow up included.
Kakio T, Ito T, Sue K et al. (1993) Hemostasis of gastric variceal hemorrhage by transileocolic and transhepatic obliteration. Acta medica Okayama 47(1):39-43	n=8	TIO and PTO seem to be safe, effective procedures to stop bleeding from ectopic varices, gastric or duodenal. This therapy is useful either to obtain accurate information about the varices or to obliterate the collateral veins in patients with ruptured ectopic varices.	Studies with more people or longer follow up included.
Kawai N, Minamiguchi H, Sato M et al. (2013) Percutaneous transportal outflow-vessel-occluded sclerotherapy for gastric varices unmanageable by balloon-occluded retrograde transvenous obliteration. Hepatology Research 43(4):430-5	n=2  FU=1 year	Although PTOS is slightly more invasive than BRTO, PTOS can be used as an alternative catheter treatment procedure for gastric varices that are unmanageable by BRTO	Studies with more people or longer follow up included.
Kwak HS and Han YM. (2008) Percutaneous transportal sclerotherapy with N-butyl-2-cyanoacrylate for gastric varices: technique and clinical efficacy. Korean journal of radiology 9(6):526-33	n=7  FU=14.8 months	Percutaneous transportal sclerotherapy with N-butyl-2-cyanoacrylate is useful to obliterate gastric varices if it is not possible to perform BRTO.	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Liu J, Yang C, Huang S et al. (2020) The combination of balloon-assisted antegrade transvenous obliteration and transjugular intrahepatic portosystemic shunt for the management of cardiofundal varices hemorrhage. <i>European journal of gastroenterology &amp; hepatology</i> 32(5):656-62	n=15  FU=6 months	For the treatment of gastric varices, the new technique balloon-assisted antegrade transvenous obliteration is feasible, safe and effective, and it may be a more convenient and economical method than conventional BRTO.	Combination of techniques used.
Mohan PP, Ahlman PP and Beltran-Perez J. (2019) Gastric variceal hemorrhage treated with percutaneous transhepatic embolization with balloon-occluded antegrade transvenous obliteration. <i>International Journal of Gastrointestinal Intervention</i> 8(4):165-7	n=1	The patient was successfully managed by percutaneous transhepatic coil embolization combined with BRTO. It is of great importance to obtain an accurate cross-sectional image to evaluate the anatomical variances of gastric varices that will lead to appropriate vascular access and to choose a suitable embolisation method.	Studies with more people or longer follow up included.
Uchiyama F, Murata S, Onozawa S et al. (2013) Management of gastric varices unsuccessfully treated by balloon-occluded retrograde transvenous obliteration: long-term follow-up and outcomes. <i>The Scientific World Journal</i> : 498535	n=13  FU=90 months	Both PTO and combined PTO and BRTO seem as safe and effective procedures for the treatment of gastroesophageal varices refractory to BRTO alone.	Studies with more people or longer follow up included.
Wang J, Tian XG, Li Y et al. (2013) Comparison of modified percutaneous transhepatic variceal embolization and endoscopic cyanoacrylate	n=32  FU=21.5 months	With extensive and permanent obliteration of gastric varices and its feeding veins, percutaneous transhepatic variceal embolisation with 2-OCA	Studies with more people or longer follow up included.

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
injection for gastric variceal rebleeding. World journal of gastroenterology 19(5)		is superior to endoscopic 2-OCA injection for preventing gastric variceal rebleeding.	
Yoshimatsu R, Yamagami T, Miura H, and Okuda K. Percutaneous transhepatic sclerotherapy with embolization of the drainage vein for a gastric varix. Acta Radiologica Short Reports 3(7)	n=1	A case with a gastric varix that did not have a catheterizable main drainage vein and had multiple afferent veins. For this case we successfully performed percutaneous transhepatic sclerotherapy.	Studies with more people or longer follow up included.
<b>CARTO</b>			
Lee EW, Saab S, Gomes AS et al. (2014) Coil-Assisted Retrograde Transvenous Obliteration (CARTO) for the Treatment of Portal Hypertensive Variceal Bleeding: Preliminary Results. Clinical and translational gastroenterology 5	n=20 FU=384 days	CARTO appears to be a technically feasible and safe alternative to traditional balloon-occluded retrograde transvenous obliteration or transjugular intrahepatic portosystemic shunt, with excellent clinical outcomes in treating portal hypertensive non-oesophageal variceal bleeding.	Non-gastric varices included.
Liu C, Han X, Ding P, and Lee EW. (2021) Coil-assisted retrograde transvenous obliteration for gastric varices in a Chinese case. Journal of Interventional Medicine 4 (2):94-6	n=1 FU=3 months	A Chinese case of portal hypertensive GV bleeding treated using CARTO with a coil and gelfoam slurry. Advantages of this technique include avoiding indwelling balloon catheters and complications related to sclerosant use. CARTO may have great potential to be widely accepted for the treatment of bleeding gastric varices in China.	Studies with more people or longer follow up included.

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Soape MP, Lichliter A, Asrani SK et al. (2018) Uncoiling the Coil: Coil Extrusion After Coil Assisted Retrograde Transvenous Obliteration for Gastric Variceal Bleeding. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association 16(5):e59	n=1	Case report of a migration of a coil into the stomach after CARTO.	Studies with more people or longer follow up included. Migration of embolising material already captured as an outcome.
Terada K, Ogi T, Yoneda N et al. (2020) Coil-assisted retrograde transvenous obliteration (CARTO) for the treatment of gastric varices via a single access route using steerable microcatheter: a case report. CVIR Endovascular 3(1):30	n=1	CARTO has advantages over BRTO in cases where performing BRTO is difficult, while CARTO is more expensive than BRTO. Using a steerable microcatheter simplifies the procedure by reducing the required access routes in CARTO.	Studies with more people or longer follow up included.
Uotani K, Matsushiro E, Hamanaka A et al. (2020) Modified Coil-Assisted Retrograde Transvenous Obliteration (m-CARTO) for Gastric Varices. CardioVascular and Interventional Radiology 43(7):1100-2	n=4 FU=24.8 months	M-CARTO enabled downgrading in cases in which advancing balloon catheters deep into the gastrorenal shunt was difficult. The disadvantages of m-CARTO are the cost of the microcoils and the second microcatheter, and prolonged procedure time compared with conventional BRTO.	Studies with more people or longer follow up included.
<b>PARTO</b>			
Chang MY, Kim MD, Kim T et al. (2016) Plug-Assisted Retrograde Transvenous Obliteration for the Treatment of	n=19 FU=11 months	PARTO is technically feasible, safe, and effective for gastric variceal haemorrhage in	Studies with more people or longer follow up included.

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Gastric Variceal Hemorrhage. Korean journal of radiology 17(2):230-8		patients with portal hypertension.	
Gwon DI, Ko GY, Kwon YB et al. (2018) Plug-Assisted Retrograde Transvenous Obliteration for the Treatment of Gastric Varices: The Role of Intra-Procedural Cone-Beam Computed Tomography. Korean journal of radiology 19(2): 223-9	n=17 FU=193 days	PARTO is technically and clinically effective for the treatment of GV.	Studies with more people or longer follow up included.
Gwon DI, Ko GY, Yoon HK et al. (2013) Gastric varices and hepatic encephalopathy: treatment with vascular plug and gelatin sponge-assisted retrograde transvenous obliteration-- a primary report. Radiology 268(1):281-7	n=13 FU=422 days	Vascular plug-assisted RTO is technically simple and safe and seems to be clinically effective for treatment of gastric varices.	Studies with more people or longer follow up included.
Gwon DI, Kim YH, Ko GY et al. (2015) Vascular Plug-Assisted Retrograde Transvenous Obliteration for the Treatment of Gastric Varices and Hepatic Encephalopathy: A Prospective Multicenter Study. Journal of vascular and interventional radiology: JVIR 26(11):1589-95	n=57 FU=544 days	PARTO can be rapidly performed with high technical success and durable clinical efficacy for the treatment of gastric varices and hepatic encephalopathy in the presence of a portosystemic shunt. Therefore, PARTO might be considered a first-line treatment in appropriate patients.	Outcomes for people with gastric varices and for people with hepatic encephalopathy are not presented separately.
Jang JY, Jeon UB, Kim JH et al. (2021) Plug-assisted retrograde transvenous obliteration via gastrocaval shunt for the gastric variceal bleeding: A case report.	n=1 FU=9 months	The gastric varix completely disappeared. The patient did not experience any additional bleeding events. PARTO via a gastrocaval shunt is safe and effective.	Studies with more people or longer follow up included.



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Medicine (United States) 100(49):e28107			
Kim T, Yang H, Lee CK, and Kim GB. (2016) Vascular Plug Assisted Retrograde Transvenous Obliteration (PARTO) for Gastric Varix Bleeding Patients in the Emergent Clinical Setting. Yonsei medical journal 57(4):973-9	n=9  FU=17 months	Emergent PARTO is technically feasible and safe, with acceptable mid-term clinical results, in treating active gastric varix bleeding.	Studies with more people or longer follow up included.
Mukund A, Anandpara KM, Ramalingam R et al. (2020) Plug-Assisted Retrograde Transvenous Obliteration (PARTO): Anatomical Factors Determining Procedure Outcome. Cardiovascular and interventional radiology 43 (10):1548-56	n=50	Knowledge of various anatomical factors of gastro-lieno-renal shunt may help in deciding the access route for PARTO and may determine technical success/failure. Alternate methods like BRTO or CARTO or anterograde obliteration of the shunt via transhepatic/splenic route might be needed in such circumstances.	Studies with more people or longer follow up included.
Tsauo J, Noh SY, Shin JH et al. (2021) Retrograde transvenous obliteration for the prevention of variceal rebleeding in patients with portal vein thrombosis: a multicenter study. European radiology 31(1):559-66	n=45 (27 PARTO, 18 BRTO)  FU=5.4 months	RTO may be effective for the prevention of variceal rebleeding in cirrhotic patients with portal vein thrombosis.	Studies with more people or longer follow up included.
Tsauo J, Noh SY, Shin JH et al. (2021) Retrograde transvenous obliteration for the prevention of variceal rebleeding in patients with hepatocellular carcinoma: a multicentre retrospective study.	n=79 (32 BRTO, 40 PARTO, 1 CARTO)  FU=6.3 months	RTO was effective and safe in preventing variceal rebleeding in patients with hepatocellular carcinoma.	Studies with more people or longer follow up included.

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Clinical radiology 76(9):681-7			