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# Conventional versus selective balloon-occluded retrograde transvenous obliteration of gastric varices

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## Abstract

**Background:** Balloon-occluded retrograde transvenous obliteration (BRTO) is a well-established interventional radiological technique for treatment of isolated gastric varices (GV). The aim of this study is to compare outcome after different BRTO techniques, i.e., conventional, selective and superselective techniques.
Fifty-nine consecutive patients underwent BRTO as a primary prophylactic treatment for GV were retrospectively categorized into group A (38 patients underwent conventional BRTO) and group B (21 patients underwent selective or superselective BRTO). Group B was sub-grouped into group B1 (11 patients underwent selective BRTO) and group B2 (10 patients underwent superselective BRTO).

**Results:** Median volume of ethanol amine oleate iopamidol (EOI) was significantly higher in group A than in group B2 (14.8 Vs 7.4 ml, $p = 0.03$). Complete GV thrombosis was significantly lower in group B2 (50%) than in A (89.5%, $p = 0.01$) and B1 (100%, $p = 0.01$). GV bleeding rate after BRTO was significantly higher in group B2 than in group A (20% vs 0%, $p = 0.04$). GV recurrence rate was not significantly different between group A and B ($p = 0.5$) or between group A, B1 and B2 ($p = 0.1$). Cumulative ascites exacerbation rate was significantly higher in group A than B ($p = 0.005$), B1 ($p = 0.03$), and B2 ($p = 0.03$). Cumulative esophageal varices (Es.V) aggravation rate was significantly higher in group A than B ($p = 0.001$), B1 ($p = 0.01$), and B2 ($p = 0.03$). Volume of EOI was a significant risk factor for ascites exacerbation ($p = 0.008$) while shunt occlusion and pre-existing partial portal vein thrombosis were significant risk factors for Es.V aggravation ($p = 0.01$ and 0.03, respectively).

**Conclusion:** Selective and super-selective techniques had a lower ascites exacerbation, and Es.V aggravation rates than conventional technique. However, superselective BRTO had a lower GV complete thrombosis and higher GV bleeding rates after BRTO than other techniques.

**Keywords:** Selective BRTO, Superselective BRTO, Conventional BRTO, Gastric varices

## Background

Gastric varices (GV) are seen in 20% of patients with portal hypertension [1]. The cumulative risk of GV bleeding at 1, 3, and 5 years after diagnosis are 4.8%, 19.9%, and 23.2%, respectively [2]. GV have a lower bleeding incidence compared to esophageal varices (Es.V); however, bleeding GV tend to be more severe with a high mortality rate reaching up to 45% [1].

Balloon-occluded retrograde transvenous obliteration (BRTO) is an endovascular interventional radiological technique adopted and widely used in many countries including Japan for isolated GV treatment with high efficacy and safety [3–8].

"Conventional BRTO" technique as described by Kanagawa et al. [3] was to occlude the portosystemic shunt draining GV with a balloon occlusion catheter

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through systemic venous approach followed by retrograde injection of a sclerosant agent to fill the draining shunt and GV. However, there are some adverse effects reported with this technique related to the used sclerosant agent (mainly ethanolamine oleate) and related to the post-procedure aggravation of portal hypertension due to portosystemic shunt occlusion resulting in Es.V aggravation and ascites exacerbation [7, 9, 10].

The term "selective or superselective BRTO" was used by some authors when balloon occlusion catheter was advanced as near as possible to GV with selective injection of sclerosant agent within GV via a microcatheter [11, 12]. This technique can be considered as an "Anatomically selective technique" and aims to reduce the amount of sclerosant agent and to alleviate the need for collateral veins embolization. Detailed studies on GV anatomy have shown the possibility of presence of a direct connection between gastric veins and the shunt outside the gastric wall bypassing the GV [13–15], and it was termed as extra-gastric afferent efferent direct connection (EAEDC) [15]. Some authors used also the "selective or superselective" term when balloon occlusion catheter was advanced beyond that EAEDC to preserve the patency of the portosystemic shunt [11, 12, 16, 17]. This technique can be considered as a "hemodynamically selective technique." We prefer to use the term "selective BRTO" for the hemodynamically selective technique and the term "superselective BRTO" for anatomically selective technique with or without a hemodynamic selectivity at the same time.

This study aims to compare outcomes after these different described techniques, i.e., conventional, selective, and superselective techniques.

## Methods

### Patients

A total of 67 patients with GV had underwent BRTO between May 2005 and May 2018 in our department. We retrospectively included only 59 patients of them in this study after exclusion of 8 patients underwent BRTO as a secondary prophylactic measure after successful hemostatic endoscopic treatment of bleeding GV (Fig. 1). These 8 patients were excluded because the pre-BRTO endoscopic treatment may affect the post BRTO GV obliteration. The indication for BRTO in the included 59 patients was primary prophylactic treatment of high risk GV for rupture diagnosed by upper endoscopy (i.e., F2 = nodular form, F3 = tumorous form, or

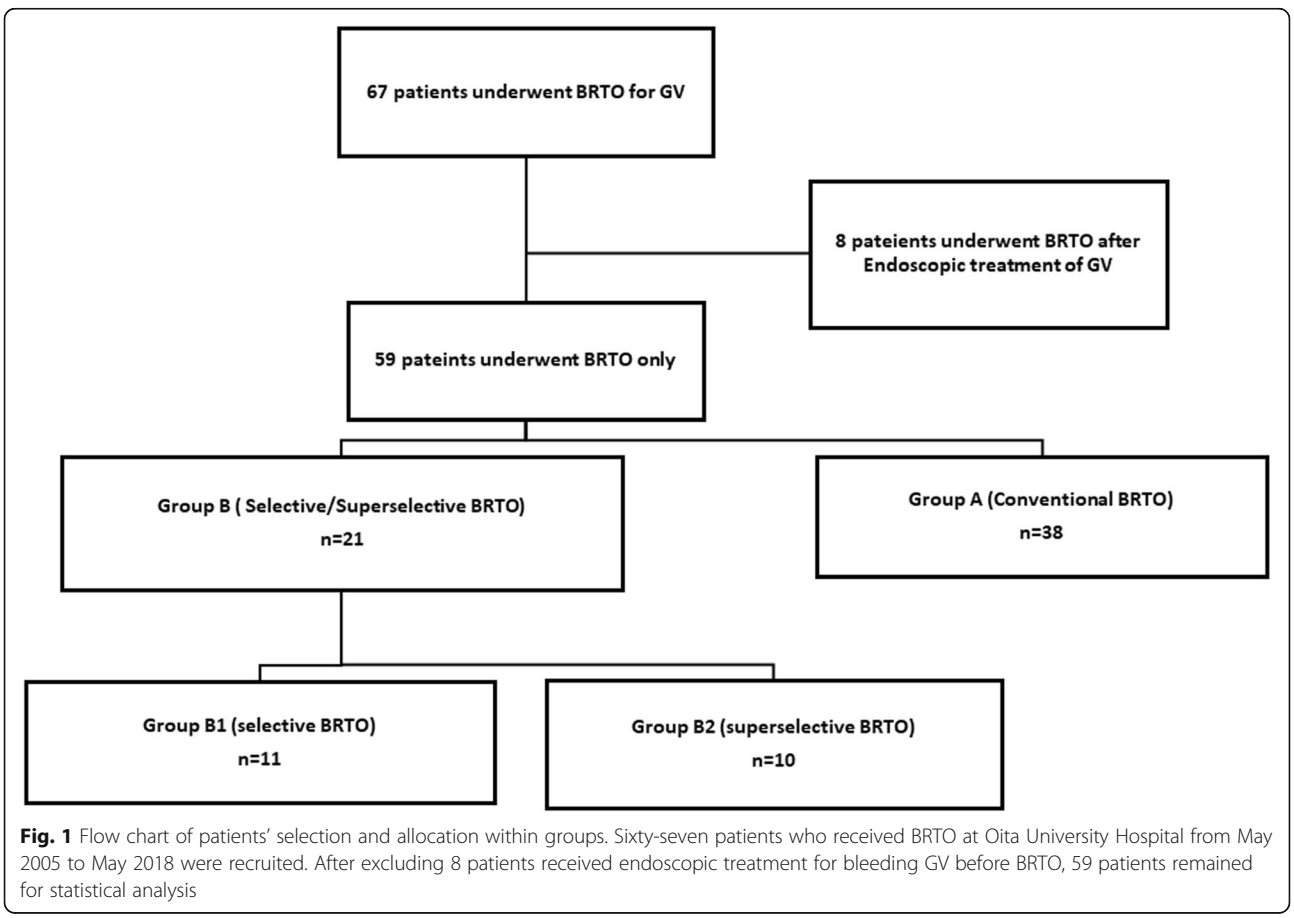


**Fig. 1** Flow chart of patients' selection and allocation within groups. Sixty-seven patients who received BRTO at Oita University Hospital from May 2005 to May 2018 were recruited. After excluding 8 patients received endoscopic treatment for bleeding GV before BRTO, 59 patients remained for statistical analysis

presence of red color spot sign) [18]. A written informed consent was obtained from all patients before all intervention procedures which were in accordance with the ethical standards of Helsinki Declaration. This retrospective study was approved by our institutional review board.

### Pre- and post-BRTO assessment

Contrast enhanced CT (CE-CT) was routinely done in all patients 1–2 weeks before BRTO for assessment of GV anatomy, planning of BRTO technique, and comparison with post-BRTO follow up imaging. CT images were acquired with a 32- or 64-CT scanner (Canon Medical Systems, Otawara, Japan) during arterial, portal, and equilibrium phases at 40, 70, and 150 seconds, respectively after bolus injection of contrast medium (Iopamidol 370, Bayer, Japan; 1.7 ml/kg, 150 ml maximum volume) at a rate of 3 ml/s. A Synapse Vincent V.5 (FUJIFILM Co., Japan) workstation was used to generate volume rendering (VR) images from the pre-BRTO axial portal phase images using manual selection of each afferent and efferent vein in a separate color-coded image [15].The baseline degree of ascites was categorized into G0: no ascites, G1: minimal–mild, G2: moderate, G3: marked.

Follow-up CE-CT was done 1 week, 1, 3, 6, 12, and 24 months after BRTO for assessment of GV thrombosis, GV recurrence, and ascites exacerbation. “Complete GV thrombosis” was defined as complete disappearance of the pre-BRTO enhanced intramural and submucosal GV. “ascites exacerbation” was defined as increase of ascites grade compared to baseline grade.

Upper endoscopy was done routinely within 1 week before BRTO for assessment of GV and Es.V and then after BRTO at 1 week, 1, 3, 6, 12, and 24 months for assessment of Es.V aggravation, and GV rebleeding or recurrence. “Es.V aggravation” was defined as increase of Es.V form and size compared to the baseline endoscopic findings, new appearance of red color spot or Es.V bleeding.

### BRTO technique

BRTO procedure was performed under Infinix Active DSA system (Canon medical system, Otawara, Japan) via a femoral vein access using a double coaxial balloon catheter system (Candis; Medikit, Miyazaki, Japan) formed of a 9F guiding balloon catheter (2 cm balloon diameter) and a coaxially inserted 5F balloon catheter (1 cm balloon diameter). Following balloon occlusion of the lower part of the gastrorenal shunt by the 9F balloon catheter, balloon-occluded retrograde venography (BORV) was performed with approximately 8 mL of contrast material (Iopamidol 370; Bayer, Osaka, Japan) with a frame rate of two per second to detect collateral draining veins. A microcatheter (Excelsior 1018; Boston Scientific, USA) was coaxially inserted within the 5F balloon catheter and advanced high up in the shunt close to or within GV. Then, the 5F balloon catheter was advanced over the microcatheter as high as possible to reduce the amount of needed sclerosant and to bypass collateral drainage veins or an EAEDC.

If 5F balloon catheter could not be advanced beyond collateral veins, they were obliterated using coils, gelfoam, or 50% glucose solution or the 5F balloon catheter was exchanged with a microballoon catheter (3F Attendant; 8 mm balloon diameter, Terumo) or (a 3.4 Masamune microballoon; 5.5 mm balloon diameter, Fuji Systems) which could be advanced more distally in the shunt very close to GV. After confirmation of contrast stagnation within GV, 5% ethanolamine oleate iopamidol (EOI) was injected via the microcatheter. The 5% EOI was formed of 10% ethanolamine oleate (Oldamin, Takeda Pharmaceutical, Japan) diluted with the same amount of Iopamidol. Intravenous administration of 4000 units of human haptoglobin (Green Cross) was started before infusing 5% EOI. After complete opacification of the GV with EOI, balloon catheters were kept inflated in place for 60 min. Then, as much as possible, sclerosant mixed with blood was aspirated via the balloon catheter. The balloon catheters were then deflated and withdrawn. In some cases where poor stagnation of EOI within GV was noted without definite collateral draining veins visualization, selective n-butyl cyanoacrylate (n-BCA) injection within GV was done.

An additional temporary balloon occlusion of the splenic artery was performed in some cases when GV were supplied by multiple gastric veins. The temporary splenic artery occlusion technique was done using a 5F balloon catheter (Clinical Supply Co.) to reduce the high pressure within the short or posterior gastric veins to prevent insufficient filling of GV with EOI.

“Conventional BRTO technique” was defined as complete filling of GV and shunt with EOI without preservation of EAEDC patency if present (Fig. 2). “Selective BRTO technique” was defined as complete filling of the GV and portion of the shunt beyond the level of EAEDC with preservation of EAEDC patency (Fig. 3). “Superselective BRTO technique” was defined as complete filling of GV only with EOI regardless of the presence or absence of an EAEDC (Fig. 4). In cases where n-BCA was super-selectively injected within GV via microcatheter, BRTO technique was categorized as “superselective” regardless of the position of the balloon catheter. The choice of which BRTO technique to be done was made by the operator according to his own assessment of the intra-procedural conditions and the available tools.

According to BRTO technique, patients were categorized into group A (i.e., patients underwent conventional

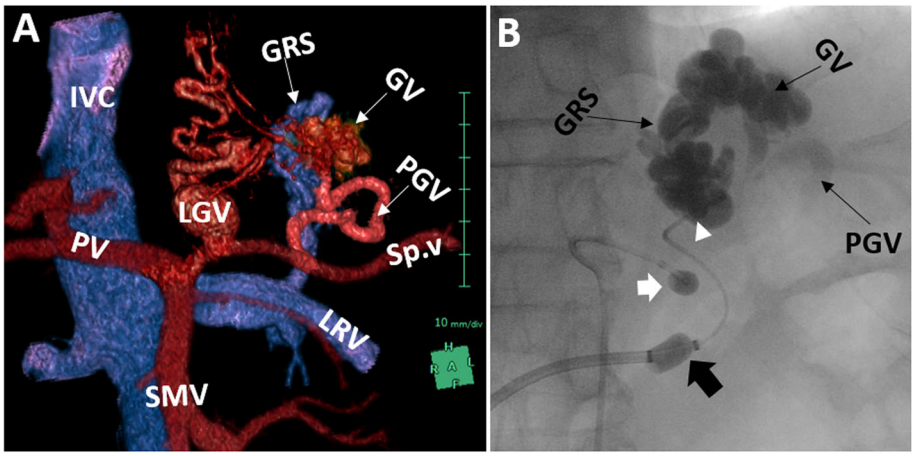


**Fig. 2** Conventional BRTO technique. **a C**olor-coded volume rendering image obtained from pre-BRTO CE-CT portal phase images shows gastric varices (GV) supplied mainly from posterior gastric vein (PGV) and small branch from left gastric vein (LGV) and drained by gastrorenal shunt (GRS). **b** Fluoroscopic image obtained at the end of BRTO shows 9F Balloon occlusion guiding catheter positioned at the base of the GRS (black solid arrow) through which a 5F balloon catheter was advanced till the mid part of the GRS (white arrowhead). The distal and mid parts of the GRS, GV, and part of the PGV were totally opacified with EOI. Noted splenic artery balloon occlusion catheter (white solid arrow)

BRTO technique) and group B (i.e., patients underwent selective or superselective technique). Group B patients were subcategorized into group B1 (i.e., patients underwent selective technique) and group B2 (i.e., patients underwent superselective technique).

### Statistical analysis

Comparison of categorical variables between study groups was performed using Fisher's exact test or Chi-square test. Comparison of continuous data was performed using Student's t-test or Mann-Whitney *U* test. Ascites exacerbation and Es.V aggravation rates were compared between study groups using Kaplan-Meier method with Log rank test for statistical significance. Univariate and multivariate analyses were conducted using a Cox proportional hazard regression model to determine risk factors for ascites exacerbation and Es.V aggravation.

All statistical analyses were performed with IBM SPSS V.21 statistical software. The statistical level of significance was set at $p < 0.05$.

## Results

### Patients' demographics

Out of the 59 patients included in this study, 24 were females (40.7%) and 35 were males (59.3%) with age ranging between 24 to 87 years old (mean 67 ± 12 years old). Patients' demographics are summarized in (Table 1). "Conventional BRTO technique" was successfully performed in 64.4% of patients (i.e. group A = 38 patients) while "selective or superselective BRTO technique" was successfully performed in 35.6% of patients (i.e. group B = 21 patients). Out of group B patients, "selective BRTO technique" was performed in 11 patients (group B1 = 18.6% of total patients) while "superselective BRTO technique" was performed in 10 patients (group B2 = 17% of total patients).

### EOI volume and procedure time

The median volume of EOI used in all patients was 13 ml (interquartile range = 6–20 ml). The median volume of EOI used in group B2 patients was significantly lower than in group A patients (7.4 ml vs 14.8 ml, $p = 0.03$). There was no statistically significant difference in median EOI volume used between groups B and A (10 ml vs 14.8 ml, $p = 0.06$), group B1 and B2 (13 ml vs 7.4 ml, $p = 0.05$), or group B1 and group A (13 ml vs 14.8 ml, $p = 0.5$) (Fig. 5). Mean procedure time was 242 ± 52 min in group A, 233 ± 43 min in group B1, 208 ± 38 min in group B2 without statistically significant difference between them ($p = 0.1$).

### GV thrombosis

Complete GV thrombosis was observed at 1 week follow-up CE-CT in 84.7% of patients ($n = 50$). Complete GV thrombosis was observed in 89.5% of group A patients ($n = 34/38$), 76.2% of group B patients ($n = 16/21$), 100% of group B1 patients ($n = 11/11$), and 50% of group B2 patients ($n = 5/10$). Complete GV thrombosis was significantly lower in group B2 than in group A (50% vs 89.5%, $p = 0.01$) and significantly lower than in group B1 (50% vs 100%, $p = 0.01$). There was no statistically significant difference in complete GV thrombosis rate between groups A and B (89.5% vs 76.2%, $p = 0.3$) or between group A and B1 (89.5% vs 100%, $p = 0.6$).

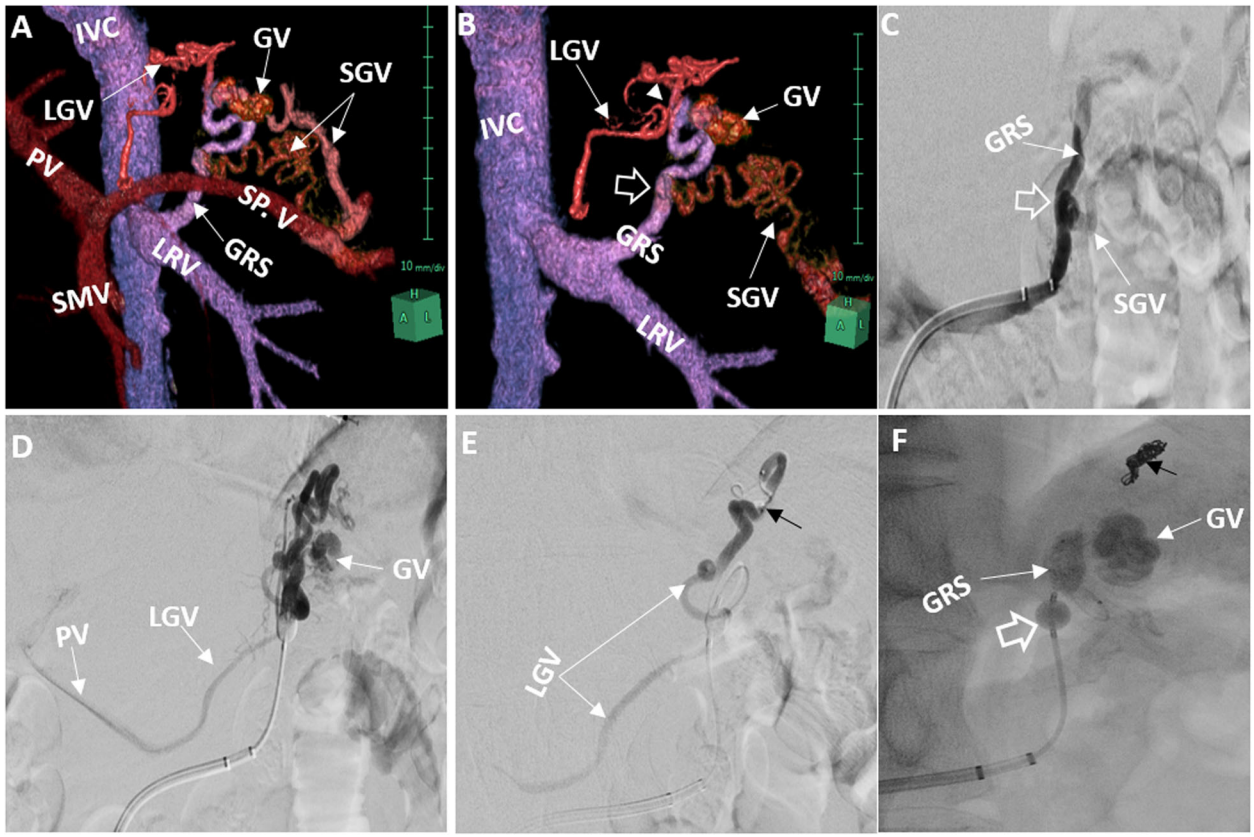


**Fig. 3** Selective BRTO technique. **a** Oblique volume rendering (VR) image obtained from pre-BRTO CE-CT portal phase images shows gastric varices (GV) supplied from short gastric vein (SGV) and drained by gastrorenal shunt (GRS). **b** The same oblique VR image in **a** but after subtraction of the feeding SGV, splenic vein (Sp.V), and portal vein (PV) to clearly visualize the direct connection between the other SGV and the proximal part of GRS (hollow white arrow) and the direct connection between left gastric vein (LGV) and the distal part of GRS very near to GV (arrowhead). **c D**SA image during retrograde venography of the GRS shows the connection between SGV and the proximal GRS (hollow white arrow). **d** DSA during balloon occluded retrograde venography of GRS shows partial visualization of GV with contrast reflux through the direct connection of LGV with the distal GRS (EAEDC) toward portal vein (PV). **e** Selective venography within the LGV EAEDC after successful catheterization of the EAEDC using microcatheter (black arrow) for EAEDC coiling to prevent EOI reflux into the PV. **f** Fluoroscopic image at the end of BRTO shows balloon catheter (hollow white arrow) positioned at the middle part of the GRS above the level of SGV EAEDC while LGV EAEDC was coiled (black arrow) with total opacification of the distal part of GRS and GV with EOI

Out of the nine patients with incomplete GV thrombosis after one BRTO session, seven patients underwent subsequent BRTO sessions and complete GV thrombosis was obtained in six of them. Consequently, overall GV complete thrombosis was achieved in 56 patients (94.9%).

### GV bleeding

GV bleeding after BRTO had occurred in 2 patients (3.4%); both were in group B2 patients. In the first patient, partially thrombosed GV had ruptured 6 months after superselective BRTO technique and urgent second session of BRTO combined with percutaneous transhepatic obliteration technique (PTO) was performed resulting in complete GV thrombosis. In the second patient, partially thrombosed GV had ruptured 16 months after superselective BRTO and subsequent session of conventional BRTO was done successfully resulting in complete GV thrombosis. GV bleeding rate after BRTO was significantly higher in group B2 than in group A (20% vs 0%, $p = 0.04$). However, GV bleeding rate after BRTO was not significantly different between groups A and B ($p = 0.1$) or between groups B1 and B2 ($p = 0.2$).

### GV recurrence

Out of the 50 patients with complete GV thrombosis after one BRTO session, GV recurrence occurred in 2 cases (4%). In the 1st case, GV recurrence was observed 5 months after a superselective BRTO and a 2nd conventional BRTO session was performed resulting in complete GV thrombosis. In the 2nd case, GV recurrence was observed 8 months after conventional BRTO in the cardiac region in continuity with Es.V (i.e., gastroesophageal varices). So, both Es.V and GV were successfully

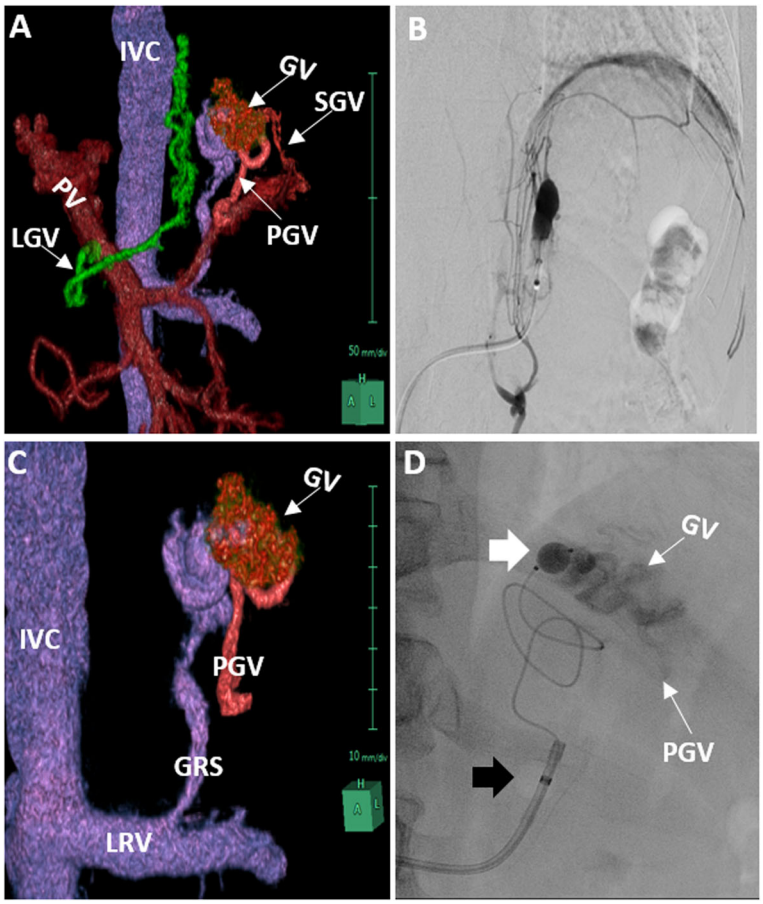


**Fig. 4** Superselective BRTO technique. **a** Oblique volume rendering (VR) image obtained from pre-BRTO CE-CT portal phase images shows GV supplied by posterior gastric vein (PGV) and small short gastric vein (SGV) and drained by gastrorenal shunt (GRS). **b** DSA image during balloon occluded retrograde venography of the GRS shows multiple medium sized collateral veins without contrast opacification of the GV. **c** The same as VR image in **a** but magnified showing only GRS, GV and PGV as a reference image for image **d**. **d** Fluoroscopic image at the end of BRTO shows 9F balloon guiding catheter positioned at lower GRS (solid black arrow) while microballoon catheter (white solid arrow) was positioned at the junction point between GRS and GV. There is complete opacification of GV and part of PGV with EOI

obliterated by endoscopic variceal ligation. GV recurrence rate was not significantly different between groups A and B ($p$ = 0.5) or between groups A, B1, and B2 ($p$ = 0.1).

### Portosystemic shunt patency

Portosystemic shunt patency was detected after BRTO in 37.3% of patients ($n$ = 22) including; all patients in group B1 ($n$ = 11/11), 70% of group B2 patients ($n$ = 7/10) and 10.5% of group A patients ($n$ = 4/38, i.e., patients in whom GV were not completely thrombosed after conventional BRTO technique).

### Procedure complications and hospital stay

Post-procedure complications were observed in 9 patients (5 in group A, 3 in group B1, and 1 in group B2) without statistically significant difference ($p$ = 0.5). In group A, multi-organ failure was encountered in two patients and newly developed portal vein thrombosis was seen in one patient. Renal dysfunction (improved with medical treatment) was encountered in one patient in group A and 1 patient in group B1. Grade 1 hepatic encephalopathy (improved with medical treatment) was encountered in one patient in group A, two patients in group B1, one patient in group B2. Median hospital stay was 9 days (IQR = 5) in group A, 8 days (IQR = 6) in group B1 and 13 days (IQR = 9) in group B2, without statistically significant difference ($p$ = 0.4).

### Ascites exacerbation

Cumulative ascites exacerbation rates 1, 3, 6, 12, and 24 months after BRTO occurred in 21%, 28%, 39%, 41%, and 41% of patients, respectively. The rates were (32%, 42%, 50%, 54%, and 54%, respectively) in group A patients, (0%, 0%, 17%, 17%, and 17%, respectively) in group B patients, (0%, 0%, 17%, 17% and 17%,

**Table 1** Demographic data of total 59 patients

| | Total ($n$ = 59) | Group A ($n$ = 38) | Group B ($n$ = 21) | $p$ value |
|---|---|---|---|---|
| Age in years (mean ± SD) | 67 ± 11.6 | 68 ± 11.5 | 67 ± 12 | 0.8[t] |
| Sex (male:female) | 35:24 | 23:15 | 12:9 | 1[f] |
| Underlying disease | | | | 0.2[x] |
| Viral hepatitis (B or C) | 19 | 12 | 7 | |
| Alcoholic hepatitis | 27 | 20 | 7 | |
| Others | 13 | 6 | 7 | |
| Child class (A:B:C) | 35:22:2 | 25:12:1 | 10:10:1 | 0.4[x] |
| Pre-existing PVT | 7 | 6 | 1 | 0.4[f] |
| Co-existing Es.V | 37 | 24 | 13 | 1[f] |
| GV form (F2:F3) | 30:29 | 18:20 | 12:9 | 0.6[f] |
| HCC | 22 | 13 | 9 | 0.6[f] |
| Ascites | | | | 0.2[x] |
| No | 38 | 28 | 10 | |
| Minimal-mild | 16 | 7 | 9 | |
| Moderate | 3 | 2 | 1 | |
| Marked | 2 | 1 | 1 | |
| Albumin level (mean ± SD) | 3.6 ± 0.6 | 3.6 ± 0.5 | 3.5 ± 0.7 | 0.6[t] |
| Bilirubin level (mean ± SD) | 1.3 ± 0.7 | 1.2 ± 0.6 | 1.5 ± 0.7 | 0.1[t] |

[t]Student's *t* test
[f]Fisher's exact test
[x]Chi-square test
*F2* nodular form, *F3* tumorous form, *PVT* partial portal vein thrombosis, *HCC* hepatocellular carcinoma

respectively) in group B1, and (0%, 0%, 17%, 17%, and 17%, respectively) in group B2 (Fig. 6). It was significantly higher in group A than in group B1 ($p$ = 0.03), group B2 ($p$ = 0.03), and whole group B ($p$ = 0.005) but there was no statistically significant difference between group B1 and group B2 ($p$ = 1). Cumulative ascites exacerbation rate 1, 3, 6, 12, and 24 months after BRTO was lower in patients with patent shunt (0%, 0%, 31%, 31%, and 31%, respectively) than in patients with occluded shunt (25%, 35%, 43%, 47% and 47%, respectively) but without statistical significance ($p$ = 0.3).

A Cox-proportional hazards model was used to evaluate possible risk factors for ascites exacerbation after BRTO (Table 2) including shunt occlusion, baseline albumin level, baseline bilirubin level, baseline prothrombin concentration (PC), baseline Child class, EOI amount used during BRTO and presence of partial portal vein thrombosis before BRTO. In a multivariate analysis model, high volume of EOI used was a significant risk factor for ascites exacerbation with hazard ratio of ascites exacerbation with EOI dose > 23 ml was 4 (95% CI = 1.6–11, $p$ = 0.004). A cut-off value of 23.4 ml of EOI for prediction of ascites exacerbation has been calculated from ROC curve using Youden's index with 45% sensitivity and 97.4% specificity (AUC = 0.7, CI 0.5–0.9, $p$ = 0.01).

### Es.V aggravation

Cumulative Es.V aggravation rates at 1, 3, 6, 12, and 24 months after BRTO were 24.6%, 36%, 47%, 63%, and 78%, respectively. It was 39%, 56.3%, 69.4%, 69.4%, and 79.6%, respectively in group A; 0%, 0%, 0%, 43%, and 71.4%, respectively in group B; 0%, 0%, 0%, 50%, and

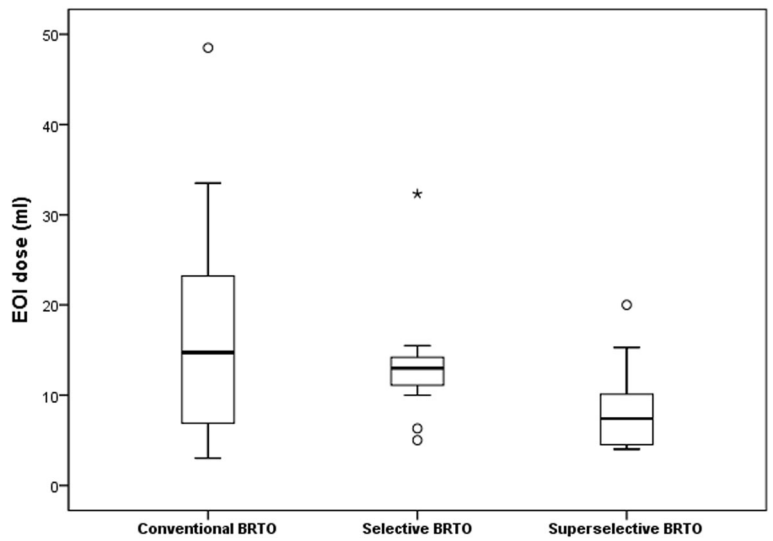


**Fig. 5** EOI volume used during different BRTO techniques. Box Plot shows that EOI volume used in superselective BRTO technique was lower than selective BRTO ($p$ = 0.05) and conventional BRTO ($p$ = 0.03)

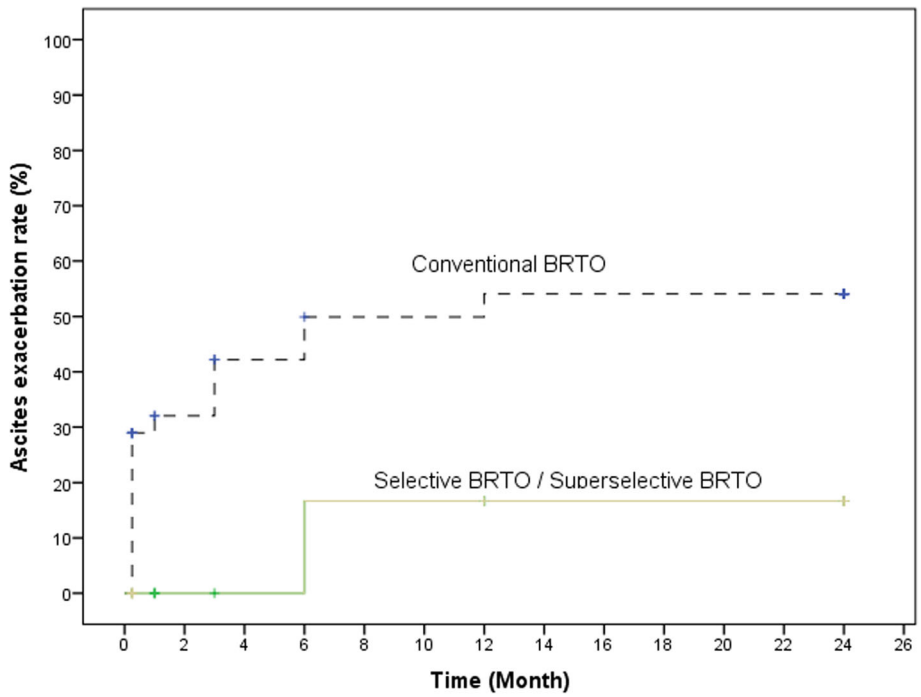


**Fig. 6** Ascites exacerbation after conventional, selective, and superselective BRTO.Kaplan-Meier curves show that ascites exacerbation rates after conventional BRTO were significantly higher than both selective and superselective BRTO ($p = 0.03$)

50%, respectively in group B1; and 0%, 0%, 0%, 33.3%, and 66.7%, respectively in group B2 (Fig. 7). It was significantly higher in group A than in group B1 ($p = 0.01$), group B2 ($p = 0.03$) and whole group B patients ($p = 0.001$) but there was no statistically significant difference between groups B1 and B2 ($p = 0.7$). Cumulative Es.V aggravation 1, 3, 6, 12, and 24 months after BRTO was significantly higher in patients with occluded shunt (37.8%, 51.2%, 64.5%, 71.6%, 78.7%) than in patients with preserved shunt (0%, 8.3%, 8.3%, 45%, 100%) ($p = 0.008$).

A Cox-proportional hazards model was used to evaluate possible risk factors for Es.V aggravation after BRTO (Table 3) including; shunt occlusion, co-existence of esophageal varices with GV before BRTO, GV form, baseline Child class, baseline bilirubin level, presence of partial portal vein thrombosis before BRTO, and amount of EOI used. In a multivariate analysis model, shunt occlusion after BRTO and presence of partial portal vein thrombosis before BRTO were statistically significant risk factors for Es.V aggravation ($p = 0.01$ and 0.03, respectively).

## Discussion

In this study, we preferred to use the term "superselective BRTO" for anatomically selective technique and the term "selective BRTO" for the hemodynamically selective technique. However, in cases where an EAEDC is present, superselective BRTO technique with

**Table 2** Univariate and multivariate analysis of prognostic factors for ascites exacerbation after BRTO

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | Hazard ratio (95% CI) | *p* value | Hazard ratio (95%CI) | *p* value |
| Low baseline albumin | 0.6 (0.3–1.2) | 0.1 | 0.5 (0.2–1.2) | 0.1 |
| Low baseline PC | 0.99 (0.98–1.01) | 0.3 | 0.98 (0.96–1) | 0.05 |
| High baseline bilirubin | 1.3 (0.7–2.4) | 0.4 | – | – |
| Child class (B or C) | 1.2 (0.5–2.8) | 0.8 | – | – |
| Pre-existing PVT | 2.7 (0.9–8) | 0.09 | 1.9 (0.6–5.7) | 0.3 |
| Occluded shunt | 1.7 (0.6–4.8) | 0.3 | 2.6 (0.8–8.2) | 0.1 |
| High EOI-dose | 1.06 (1.02–1.1) | 0.004 | 1.1 (1.02–1.1) | 0.008 |

*PC* prothrombin concentration (%), *PVT* partial portal vein thrombosis

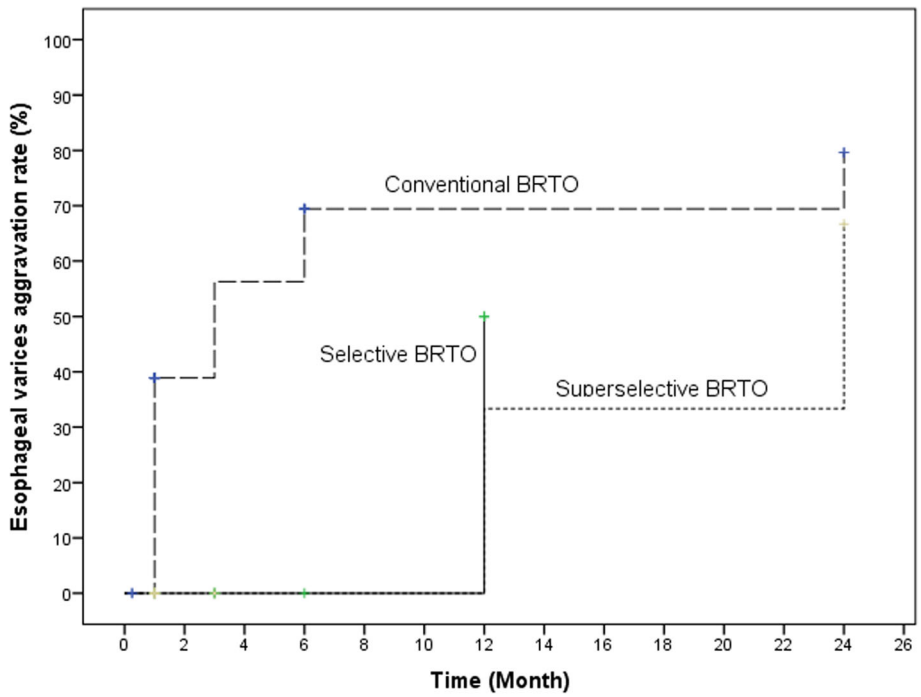


**Fig. 7** Esophageal varices aggravation after conventional, selective. and superselective BRTO.Kaplan-Meier curves show that Es.V aggravation rates were significantly higher after conventional BRTO than both selective and superselective BRTO ($p = 0.01$ and 0.03, respectively).

obliteration of the GV only will result in both "Hemodynamically and anatomically selective BRTO" at the same time. Because of this, overlap between the hemodynamically selective BRTO and the anatomically selective BRTO, we grouped both selective and superselective BRTO techniques in group B patients and then sub-grouped them into group B1 (selective BRTO) and group B2 (superselective BRTO).

Jogo et al. [17] compared the outcome after conventional and selective BRTO techniques. They defined the selective BRTO technique as selective embolization of GV with shunt preservation which is consistent with our definition of superselective BRTO technique but only in the presence of an EAEDC. They reported that EOI volume, ascites exacerbation rate within 6 months, Es.V aggravation rate within 1 year and GV complete eradication rate after their selective BRTO technique were significantly lower than after conventional BRTO. Our results are in agreement with their results regarding the significantly lower EOI volume, ascites exacerbation rate, Es.V aggravation rate, and complete GV obliteration rate after "superselective BRTO technique" than after "conventional BRTO technique."

In our study, there was no significant difference in EOI volume between "selective technique" and "conventional technique" which can be explained by the fact that our selective BRTO technique is only hemodynamically selective and can be achieved with balloon catheter positioned in the lower or middle portions of the shunt above the level of a low lying (proximally located)

**Table 3** Univariate and multivariate analysis of prognostic factors for Es.V aggravation after BRTO

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | Hazard ratio (95% CI) | *p* value | Hazard ratio (95% CI) | *p* value |
| Shunt occlusion | 3.4 (1.2–10) | 0.03 | 4 (1.3–12) | 0.01 |
| Pre-existing PVT | 3 (1–9.3) | 0.05 | 3.4 (1.1–10.7) | 0.03 |
| Pre-existing ES.V | 1.6 (0.7–3.6) | 0.3 | 2 (0.8–4.7) | 0.1 |
| Child class (B or C) | 1.2 (0.6–2.7) | 0.6 | – | – |
| High GV form | 1 (0.5–2.2) | 0.98 | – | – |
| High EOI amount | 1.03 (1–1.06) | 0.05 | 1.03 (0.995–1.1) | 0.1 |
| High baseline bilirubin | 1.2 (0.6–2) | 0.6 | – | – |

*PVT* partial portal vein thrombosis

EAEDC. Also, we considered the technique to be conventional when the balloon occlusion catheter was positioned at lower or middle part of the shunt but there was no EAEDC to be preserved.

In our study, complete GV thrombosis after only one session was significantly lower in superselective technique than both conventional and selective techniques but it was not significantly different between selective and conventional techniques. This may be explained by the fact that GV may drain into the shunt through multiple perforator veins in separate sites [14]. So, there is a higher possibility to miss one of these perforator veins during superselective technique. In contrast, a considerable segment of the shunt is occluded in "selective and conventional techniques" which reduces the possibility to miss one of these perforator veins.

Ascites exacerbation was reported in 34–82% of patients including minimal ascites detected only by imaging within the first 2 weeks after BRTO [9, 10], and it was assumed to be related to the temporary increase in portal hypertension immediately after BRTO and poor baseline liver functions [10, 19]. Many authors believe that ascites occurrence several months after BRTO is mostly related to the natural progress of hepatic cirrhosis [10, 19]. Watanabe et al. [10] reported that hypoalbuminemia, hyperbilirubinemia, low PC, and high Child score were possible factors that may affect the incidence of ascites exacerbation. Saad et al. [19] reported that transjugular intrahepatic portosystemic shunt (TIPS) may have a protective effect against the development or exacerbation of ascites and/or hydrothorax after BRTO. In our study, the cumulative rate of ascites exacerbation after BRTO was higher in patients with occluded shunt than in patients with patent shunt, but without statistical significance. The only significant independent risk factor for ascites exacerbation in our study was the volume of EOI used. This can be explained by the fact that EOI binds with albumin in the blood [20] with subsequent temporary reduction of albumin level in the early post-BRTO period [8] which may predispose to ascites exacerbation. However, this is only temporary because of the well documented improvement in albumin level within 1–6 months after BRTO [21–23]. So, we agree with other authors regarding that ascites exacerbation after BRTO is multifactorial and could not be totally explained or predicted by one factor [10, 19].

Es.V aggravation rate after BRTO varies between studies reaching up to 61.5% [7, 24–27]. Multiple independent risk factors for Es.V aggravation after BRTO were reported including; presence of Es.V before BRTO [7, 24], presence of multiple high grade collateral veins during BRTO [25], elevation of the portal systemic pressure gradient (PSPG) > 5 mmHg immediately after BRTO [26], high baseline wedged hepatic venous pressure gradient > 13 mmHg [27], hyperbilirubinemia > 1.6 mg/dl [27], high EOI volume used [27], and high Child-Pugh class (i.e., B or C) [24]. In our study, shunt occlusion after BRTO and presence of partial portal vein thrombosis before BRTO were statistically significant risk factors for Es.V aggravation based on multivariate analysis. Shunt occlusion after BRTO has been linked with the occurrence of significant increase in the portal venous blood flow and pressure within 1-week after BRTO predisposing to Es.V aggravation [22, 26, 28, 29]. The effect of partial portal vein thrombosis on Es.V aggravation can be explained by the inability of the partially thrombosed portal vein to accommodate the sudden increased blood flow and pressure after shunt occlusion resulting in shifting of the increased blood flow toward the esophageal variceal portosystemic pathway.

Limitations to this study include its retrospective design, small number of patients underwent selective and superselective BRTO compared to conventional BRTO and small number of Child C patients. Further studies on the usefulness of performing selective or superselective techniques versus conventional technique in high risk patients (i.e., Child C patients or patients with portal vein thrombosis) are recommended.

## Conclusion

Selective and superselective BRTO techniques have several advantages over conventional technique including the lower EOI dose, ascites exacerbation rate and Es.V aggravation rate. However, superselective technique may have a lower GV complete thrombosis rate and consequently a higher GV rebleeding rate than both selective and conventional techniques. We recommend the use of selective BRTO technique with occlusion of a considerable length of the shunt in patients where shunt preservation is desired.

### Abbreviations

BRTO: Balloon-occluded retrograde transvenous obliteration; BORV: Balloon occluded retrograde venography; CE-CT: Contrast-enhanced computed tomography; EAEDC: Extra-gastric afferent efferent direct connection; EOI: Ethanolamine oleate iopamidol; Es.V: Esophageal varices; GV: Gastric varices; n-BCA: n-butyl cyanoacrylate; PC: Prothrombin concentration; PTO: Percutaneous transhepatic obliteration; TIPS: Transjugular intrahepatic portosystemic shunt; VR: Volume rendering

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### Authors' contributions

R.A collected the data from medical records, performed statistical analysis, and wrote the initial draft. H.K and M.M performed BRTO techniques. M.O and SH.A assessed imaging findings pre- and post-BRTO, respectively. H.M, S.A, and S.M revised and edited the manuscript. The authors read and approved the final manuscript.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Ethics approval and consent to participate

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. A written informed consent was obtained from all patients before all intervention procedures done in this study. This retrospective study was approved by our institutional review board. This article does not contain any studies with animals performed by any of the authors.

### Consent for publication

Not applicable; retrospective study.

### Competing interests

The authors declare that they have no competing interests.

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### References

1. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK (1992) Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology. 16(6):1343–1349. https://doi.org/10.1002/hep.1840160607
2. Lee CH, Lee JH, Choi YS, Paik SW, Sinn DH, Lee CY et al (2008) Natural history of gastric varices and risk factors for bleeding. Korean J Hepatol. 14(3):331–341. https://doi.org/10.3350/kjhep.2008.14.3.331
3. Kanagawa H, Mima S, Kouyama H, Gotoh K, Uchida T, Okuda K (1996) Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol. 11(1):51–58. https://doi.org/10.1111/j.1440-1746.1996.tb00010.x
4. Hiraga N, Aikata H, Takaki S, Kodama H, Shirakawa H, Imamura M et al (2007) The long-term outcome of patients with bleeding gastric varices after balloon-occluded retrograde transvenous obliteration. J Gastroenterol. 42(8):663–672. https://doi.org/10.1007/s00535-007-2077-1
5. Kitamoto M, Imamura M, Kamada K, Aikata H, Kawakami Y, Matsumoto A et al (2002) Balloon-occluded retrograde transvenous obliteration of gastric fundal varices with hemorrhage. AJR Am J Roentgenol. 178(5):1167–1174. https://doi.org/10.2214/ajr.178.5.1781167
6. Sonomura T, Sato M, Kishi K, Terada M, Shioyama Y, Kimura M et al (1998) Balloon-occluded retrograde transvenous obliteration for gastric varices: a feasibility study. Cardiovasc Intervent Radiol. 21(1):27–30. https://doi.org/10.1007/s002709900206
7. Ninoi T, Nishida N, Kaminou T, Sakai Y, Kitayama T, Hamuro M et al (2005) Balloon-occluded retrograde transvenous obliteration of gastric varices with gastrorenal shunt: long-term follow-up in 78 patients. AJR Am J Roentgenol. 184(4):1340–1346. https://doi.org/10.2214/ajr.184.4.01841340
8. Kobayakawa M, Kokubu S, Hirota S, Koizumi J, Nishida N, Yasumoto T et al (2018) Short-term safety and efficacy of balloon-occluded retrograde transvenous obliteration using ethanolamine oleate: results of a prospective, multicenter, single-arm trial. J Vasc Interv Radiol. 28(8):1108–1115. https://doi.org/10.1016/j.jvir.2017.03.041
9. Cho SK, Shin SW, Yoo EY, Do YS, Park KB, Choo SW et al (2007) The short-term effects of balloon-occluded retrograde transvenous obliteration, for treating gastric variceal bleeding, on portal hypertensive changes: a CT evaluation. Korean J Radiol. 8(6):520–530. https://doi.org/10.3348/kjr.2007.8.6.520
10. Watanabe M, Shiozawa K, Ikehara T, Nakano S, Kougame M, Otsuka T et al (2012) Short-term effects and early complications of balloon-occluded retrograde transvenous obliteration for gastric varices. ISRN Gastroenterol. 2012:919371. https://doi.org/10.5402/2012/919371
11. Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y (2003) Transcatheter obliteration of gastric varices: Part 2. Strategy and techniques based on hemodynamic features. Radiographics 23(4):921–937. https://doi.org/10.1148/rg.234025135
12. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y (2001) Eight years of experience with transjugular retrograde obliteration for gastric varices with gastrorenal shunts. Surgery 129(4):414–420. https://doi.org/10.1067/msy.2001.112000
13. Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y (2003) Transcatheter Obliteration of Gastric Varices: Part 1. Anatomic Classification. Radiographics 23(4):911–920. https://doi.org/10.1148/rg.234025044
14. Saad WEA. Vascular anatomy and the morphologic and hemodynamic classifications of gastric varices and spontaneous portosystemic shunts relevant to the brto procedure. (2013) Tech Vasc Interv Radiol 16(2):60–100. https://doi.org/10.1053/j.tvir.2013.02.002
15. Ahmed R, Kiyosue H, Maruno M, Matsumoto S, Mori H (2019) Coexistence of "extra-gastric afferent-efferent direct connection" with gastric varices: CT evaluation and clinical significance. Abdom Radiol (New York). 44(8):2699–2707. https://doi.org/10.1007/s00261-019-02033-z
16. Nishida N, Ninoi T, Kitayama T, Tokunaga M, Sakai Y, Hamuro M et al (2006) Selective balloon-occluded retrograde transvenous obliteration of gastric varix with preservation of major portacaval shunt. AJR Am J Roentgenol 186(4):1155–1157. https://doi.org/10.2214/AJR.04.1971
17. Jogo A, Nishida N, Yamamoto A, Kageyama K, Nakano M, Sohgawa E et al (2019) Selective balloon-occluded retrograde transvenous obliteration for gastric varices. Intern Med. 58(16):2291–2297. https://doi.org/10.2169/internalmedicine.2356-18
18. Tajiri T, Yoshida H, Obara K, Onji M, Kage M, Kitano S et al (2010) General rules for recording endoscopic findings of esophagogastric varices (2nd edition). Dig Endosc. 22(1):1–9. https://doi.org/10.1111/j.1443-1661.2009.00929.x
19. Saad WE, Wagner CC, Lippert A, Al-Osaimi A, Davies MG, Matsumoto AH et al (2013) Protective value of TIPS against the development of hydrothorax/ascites and upper gastrointestinal bleeding after balloon-occluded retrograde transvenous obliteration (BRTO). Am J Gastroenterol. 108(10):1612–1619. https://doi.org/10.1038/ajg.2013.232
20. Ohta M, Hashizume M, Ueno K, Tanoue K, Sugimachi K (1993) Albumin inhibits hemolysis of erythrocytes induced by ethanolamine oleate during endoscopic injection sclerotherapy. Hepatogastroenterology 40(1):65–68
21. Yamamoto A, Nishida N, Morikawa H, Jogo A, Kageyama K, Sohgawa E et al (2016) Prediction for improvement of liver function after balloon-occluded retrograde transvenous obliteration for gastric varices to manage portosystemic shunt syndrome. J Vasc Interv Radiol. 27(8):1160–1167. https://doi.org/10.1016/j.jvir.2016.03.031
22. Nakazawa M, Imai Y, Uchiya H, Ando S, Sugawara K, Nakayama N et al (2017) Balloon-occluded retrograde transvenous obliteration as a procedure to improve liver function in patients with decompensated cirrhosis. JGH open an open access. J Gastroenterol Hepatol. 1(4):127–133. https://doi.org/10.1002/jgh3.12020
23. Uehara H, Akahoshi T, Tomikawa M, Kinjo N, Hashimoto N, Nagao Y et al (2012) Prediction of improved liver function after balloon-occluded retrograde transvenous obliteration: relation to hepatic vein pressure gradient. J Gastroenterol Hepatol. 27(1):137–141. https://doi.org/10.1111/j.1440-1746.2011.06835.x
24. Elsamman MK, Fujiwara Y, Kameda N, Okazaki H, Tanigawa T, Shiba M et al (2009) Predictive factors of worsening of esophageal varices after balloon-occluded retrograde transvenous obliteration in patients with gastric varices. Am J Gastroenterol. 104(9):2214–2221
25. Fukuda T, Hirota S, Sugimura K (2001) Long-term results of balloon-occluded retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy. J Vasc Interv Radiol. 12(3):327–336. https://doi.org/10.1016/S1051-0443(07)61912-5
26. Tanihata H, Minamiguchi H, Sato M, Kawai N, Sonomura T, Takasaka I et al (2009) Changes in portal systemic pressure gradient after balloon-occluded retrograde transvenous obliteration of gastric varices and aggravation of esophageal varices. Cardiovasc Intervent Radiol. 32(6):1209–1216. https://doi.org/10.1007/s00270-009-9679-3
27. Jogo A, Nishida N, Yamamoto A, Matsui H, Takeshita T, Sakai Y et al (2014) Factors associated with aggravation of esophageal varices after B-RTO for gastric varices. Cardiovasc Intervent Radiol 37(5):1243–1250. https://doi.org/10.1007/s00270-013-0809-6
28. Kako Y, Yamakado K, Jomoto W, Nasada T, Asada K, Takaki H et al (2017) Changes in liver perfusion and function before and after percutaneous occlusion of spontaneous portosystemic shunt. Jpn J Radiol. 35(7):366–672. https://doi.org/10.1007/s11604-017-0647-6
29. Miyamoto Y, Oho K, Kumamoto M, Toyonaga A, Sata M (2003) Balloon-occluded retrograde transvenous obliteration improves liver function in patients with cirrhosis and portal hypertension. J Gastroenterol Hepatol. 18(8):934–942. https://doi.org/10.1046/j.1440-1746.2003.03087.x

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