The long-term outcome of patients with bleeding gastric varices after balloon-occluded retrograde transvenous obliteration

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Background. The purpose of our study was to evaluate the long-term outcome and complications of balloonoccluded retrograde transvenous obliteration (B-RTO) in patients with hemorrhage from gastric fundal varices. Methods. Thirty-four consecutive patients with bleeding from gastric varices who were treated with B-RTO were enrolled in this study between December 1994 and September 2005 (urgent cases, n = 12; elective cases, n = 22). The long-term outcome, complications, and various liver functions were evaluated. Results. Complete obliteration was achieved in 31 of 34 (91%) patients with an acute bleeding episode. In one of the remaining patients, there was a technical failure, and the other two had only partial obliteration. The two patients with partial obliteration did not obtain hemostasis. Thus, the rate of hemostasis was 94% (31/33). Gastric varices disappeared in all patients with complete obliteration during the treatment. The rate of gastric variceal eradication was 91%. Variceal rebleeding from esophageal varices occurred in three patients. The rate of rebleeding was 10% (3/31). Rebleeding from gastric varices was not observed after complete obliteration. None of the patients showed worsening of their Child-Pugh score. Although the 5-year cumulative worsening rate of esophageal varices was 52%, neither portal hypertensive gastropathy nor ectopic varices were observed. The patients with worsening esophageal varices were successfully treated with an endoscopic procedure. The 5-year survival rate was 68%. Conclusions. B-RTO is useful for treatment of bleeding gastric varices, achieving high eradication of gastric varices, a low rebleeding rate, and a fairly good prognosis with improved hepatic function.

Key words: balloon-occluded retrograde transvenous obliteration (B-RTO), gastric fundal varices, bleeding, ethanolamine oleate

Introduction

Gastric fundal varices with hemorrhage are associated with a higher mortality rate than esophageal variceal bleeding,¹⁻³ and optimal management of gastric varices therefore requires a multidisciplinary approach. Generally, various treatment modalities such as pharmacotherapy, balloon tamponade, endoscopic procedures, interventional radiologic treatment, and surgery have been widely performed. In uncontrolled hemorrhage or rebleeding from gastric varices, a transjugular intrahepatic portosystemic shunt (TIPS) is an important tool.⁴⁻¹³ However, even patients with gastric varices with portal pressure gradients of <12 mmHg can hemorrhage, and TIPS is not always effective in such patients with low initial portal pressure gradients.^{6,8} Balloon-occluded retrograde transvenous obliteration (B-RTO) is an interventional radiologic technique that was developed in Japan.¹⁴⁻¹⁶ This procedure involves occlusion of blood flow by inflation of a balloon catheter into an outflow shunt, such as a gastrorenal shunt, and injection of 5% ethanolamine oleate into gastric varices in a retrograde manner. B-RTO has been safely performed for gastric varices with almost complete eradication.

In patients with gastric varices, low portal pressure gradients are associated with the presence and size of a spontaneous gastrorenal shunt, which is present in up to 85% of such patients.^{3,17,18} If a large spontaneous shunt is present and the portal pressure gradient (as measured by hepatic vein wedge pressure gradient) is <12 mmHg, B-RTO should be considered.¹⁹ However, the majority of reports in the literature pertain to prophylactic treatment, and the long-term outcome after

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Patients and methods

Patients

Between December 1994 and September 2005, 133 patients diagnosed with cirrhosis of the liver underwent an urgent endoscopy for a history of hematemesis or melena. In 87 patients, the primary indication was esophageal variceal hemorrhage, in 38 patients, gastric variceal hemorrhage, and in eight patients, acute nonvariceal upper gastrointestinal bleeding, such as erosion or ulcer. Among 38 patients with gastric variceal bleeding, 18 had bleeding signs, such as spurting bleeding and adhesion clots. We treated four patients endoscopically for gastroesophageal varices. Among the remaining 14 patients with isolated gastric variceal bleeding, we treated eight by endoscopic hemostasis, such as endoscopic variceal ligation or clipping, or endoscopic procedures such as injection sclerotherapy using 5% ethanolamine oleate or tissue adhesives, and six by balloon tamponade. The other 20 patients had already stopped bleeding at endoscopy. Thus, 14 bleeding patients were treated with B-RTO after the abovementioned hemostasis, and 20 patients with isolated gastric varices were treated with B-RTO. In this study, these 34 consecutive patients with bleeding from gastric fundal varices were enrolled at Hiroshima University Hospital between December 1994 and September 2005 (Fig. 1). Patient characteristics are shown in Table 1.

An urgent case of bleeding gastric varices is defined as bleeding within 24h of the initial hemostasis, and an elective case of bleeding gastric varices is defined as bleeding after 24h of initial hemostasis.37 Twelve patients had urgent cases, and 22 had elective cases. The patients comprised 26 men and eight women with a mean age of 60 years. Among the 33 patients with liver cirrhosis, the causes were viral liver cirrhosis (n = 17: hepatitis B surface antigen-positive, n = 2; anti-hepatitis C virus antibody-positive, n = 15), alcoholic liver cirrhosis (n = 10), primary biliary cirrhosis (n = 1), autoimmune hepatitis (n = 1), and unknown (n = 4: negative for viral markers). Child-Pugh classifications were grade A (n = 12), grade B (n = 18), and grade C (n = 3). The one remaining patient was diagnosed with an extrahepatic presinusoidal obstruction (EHO). Endoscopic findings for gastric varices were evaluated according to the general rules for recording endoscopic findings of esophagogastric varices.^{37,38} Briefly, gastric varices were classified according to their relationship to the cardiac orifice: Lg-c if they were adjacent to the cardiac orifice, Lg-f if they were distant from the cardiac orifice, and Lg-cf if they extended from the cardiac orifice to the fornix. Among 27 patients, the location of the gastric varices was Lg-f, and it was Lg-cf in seven patients. The gastric varices were classified by morphology into F1, tortuous; F2, nodular; or F3, tumorous. The morphol-

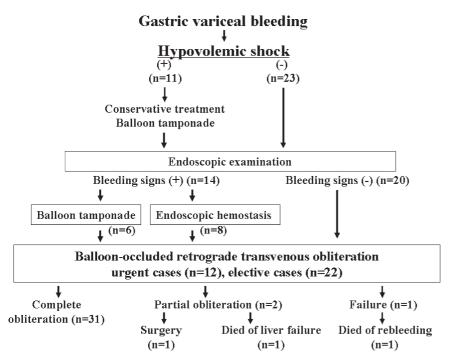


Fig. 1. Schematic flow diagram showing clinical courses and results of patients with bleeding from gastric fundal varices

Table 1. Characteristics of patients

	Urgent cases	Elective cases	P value
Number	12	22	
Age (years) ^a	56 (26-80)	60 (24-82)	0.239
Sex (male/female)	9/3	17/5	0.637
Etiology (viral/alcohol/other)	7/3/2	10/7/5	0.781
Child's grade (A/B/C)	4 ^b /5/3	9/13/0	0.071
Location of GV ^c (Lg-f/Lg-c/Lg-cf)	10/0/2	17/0/5	0.521
Form of GV ^c (F1/F2/F3)	0/8/4	0/10/12	0.205
Hirota ²¹ grade ^d $(1/2/3/4/5)$	3/3/2/4/0	1/4/8/8/1	0.480

B-RTO, balloon-occluded retrograde transvenous obliteration; GV, gastric varices; Lg-f, gastric varices separated from the cardiac orifice; Lg-c, gastric varices adjacent to the cardiac orifice; Lg-cf, gastric varices continuing from the cardiac orifice to the gastric fundus; F1, straight small-caliber varices; F2, moderately enlarged, beady varices; F3, markedly enlarged, nodular, or tumor-shaped varices

^aData are mean values (range)

^bThe patient with extrahepatic presinusoidal obstruction was included as Child's grade A

^cEndoscopic findings for gastric varices were evaluated according to the general rules for recording endoscopic findings of esophagogastric varices^{37,38}

^dCriteria for difficulty of retrograde transvenous obliteration according to retrograde venography under balloon occlusion²¹

ogy was F1 in no patients, F2 in 18 patients, and F3 in 16 patients. When patients showed signs of bleeding on endoscopic examination (Fig. 2a), temporary hemostasis was achieved with balloon tamponade or endoscopic procedures such as injection sclerotherapy using 5% ethanolamine oleate or tissue adhesives, or endoscopic variceal ligation or clipping (Fig. 2b). Portosystemic collaterals such as a gastrorenal shunt were evaluated by contrast-enhanced computed tomography (CT) (Fig. 2c). The study was approved by the institutional review boards of the participating clinical sites before study initiation, and the study was conducted according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients at the time of enrollment.

Balloon-occluded retrograde transvenous obliteration

After we confirmed that gastric variceal bleeding was controlled, we performed angiography and B-RTO. Selective angiography of the celiac and superior mesenteric arteries was performed before B-RTO to evaluate portosystemic collaterals. All patients were in stable condition at the time of treatment. In patients with a gastrorenal shunt, a 6-French balloon catheter (Selecon MP Catheter; Clinical Supply, Gifu, Japan) was inserted into the inferior vena cava through the right femoral vein. In those without a gastrorenal shunt, other catheterizable main draining veins such as a gastrocaval shunt were examined using a 5.5-French balloon catheter (Artec Balloon Catheter, B-RTO type II SML; Create Medic, Tokyo, Japan). The catheter was advanced into any outflow vessels such as a gastrorenal shunt or gastrocaval shunt. If necessary, both shunts were occluded

using two balloon catheters. During balloon occlusion of outflow vessels, retrograde venography was performed to determine the hemodynamics of the gastric varices and collateral veins. On the basis of the adrenal venogram obtained during balloon occlusion, the degree of progression of the gastric varices and collateral veins was graded in accordance with Hirota et al.²¹ Then, B-RTO was performed by injecting 5% ethanolamine oleate (Oldamin; Grelan Pharmaceutical, Tokyo, Japan) through the outflow vessels during balloon occlusion. Especially in the case of Hirota's grade 3 or 4 varices,²¹ additional specialized techniques to treat minor collaterals were utilized.^{15,18,21,23,28,30,39,40} If occlusion of minor collateral vessels was necessary, a 50% glucose solution, ethanol, and embolic coils were used. With or without these interventions, a 2.8-French microcatheter (Rapid transit; Johnson and Johnson, New Brunswick, NJ, USA) was introduced through a balloon catheter to the gastric varices, and 2.5-5 ml of 5% ethanolamine oleate was injected intermittently into the gastric varices under fluoroscopy (Fig. 2d). When varices and inflow vessels such as a short gastric vein or a posterior gastric vein could be visualized in their entirety, injection was suspended. Human haptoglobin was administered to prevent renal dysfunction related to hemolysis occurring as a systemic effect of 5% ethanolamine oleate before B-RTO. To avoid incomplete therapeutic efficacy and pulmonary infarction due to an unstable thrombus, we left the catheter in the vein with the balloon inflated for about 20h and removed it after retrograde venography. If obliteration of gastric varices was insufficient on retrograde venography, additional B-RTO was subsequently performed until opacification of inflow vessels. All patients underwent gastrointesti-

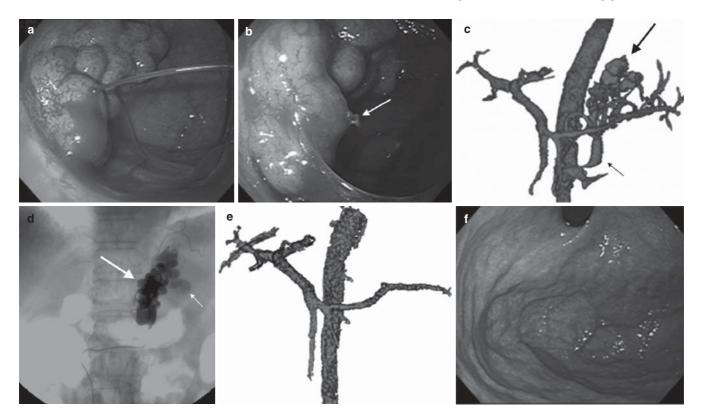


Fig. 2a–f. A 78-year-old man with alcoholic liver cirrhosis. **a** Endoscopic examination reveals huge gastric fundal varices with spurting bleeding. **b** After cyanoacrylate glue was injected intravariceally, gastric variceal bleeding stopped and the glue spilled from the rupture site (*arrow*). **c** Three-dimensional computed tomography (CT) portogram a few hours after endoscopic treatment reveals gastric varices (*large arrow*) and a gastrorenal shunt (*small arrow*). **d** Venogram shows retrograde obliteration. Gastric fundic varices (*large arrow*) were completely obliterated by 5% ethanolamine oleate injected in retrograde manner during balloon occlusion. Subsequently, the posterior gastric vein (*small arrow*) was opacified in retrograde manner. **e** Three-dimensional CT portogram obtained 1 week after balloon-occluded retrograde transvenous obliteration (B-RTO) reveals disappearance of the gastric varices and gastrorenal shunt. **f** Endoscopic examination obtained 1 year after B-RTO reveals complete eradication of the gastric varices

nal endoscopy and contrast-enhanced CT approximately 1 week after B-RTO (Fig. 2e). When the contrastenhanced CT scan showed gastric varices with low attenuation, including of the afferent veins or the draining veins of the gastric varices, we considered obliteration to be complete. On the other hand, when contrast-enhanced CT showed gastric varices with partial enhancement, we considered the obliteration to be partial. Two radiologists interpreted the angiograms and retrograde venograms during balloon occlusion.

Follow-up and statistical analysis

The hepatic functional reserve was estimated based on the Child-Pugh score. Follow-up diagnostic imaging, such as gastrointestinal endoscopy or contrast-enhanced CT, and examination of hepatic function were performed consecutively at 1, 3, 6, and 12 months, and then every 6 months or 1 year after B-RTO. Any patients who died of causes unrelated to the liver, such as from gastric cancer or leukemia, were withdrawn from the study on the day of death. The cumulative survival rate and cumulative worsened rate of esophageal varices were analyzed using the Kaplan-Meier method and compared with a log rank test. Changes in serum laboratory values were assessed by repeated measures analysis of variance. A value of P < 0.05 was considered significant.

Results

Efficacy and complications

A representative clinical course of B-RTO is shown in Fig. 2. Overall complete obliteration was achieved in 31 of 34 (91%) patients with an acute bleeding episode. In urgent cases, complete obliteration was achieved in 10 of 12 (83%) patients, and in elective cases, complete

obliteration was achieved in 21 of 22 (95%) patients. In one of the remaining patients, there was a technical failure because of difficulty with catheter insertion into a gastrocaval shunt, and the other two had only partial obliteration. The patient with failure of B-RTO obtained spontaneous hemostasis but died of gastric variceal rebleeding 1 year later. The two patients with partial obliteration of B-RTO did not obtain hemostasis. One underwent Hassab's devascularization 9 days after B-RTO and survived, and the other died of liver failure (Fig. 1). Thus, the rate of hemostasis was 94% (31/33). Among 31 patients with complete obliteration, the follow-up gastrointestinal endoscopy showed disappearance of gastric varices in 30 patients (Fig. 2f); the other patient died of pneumonia 1 month after B-RTO.

In the patients with complete obliteration, the average dose of 5% ethanolamine oleate was 23.3 ml. Regarding complications, epigastralgia or low back pain was observed in 26 of 34 patients. Pyrexia (>38°C) was observed in nine of 34 patients. However, no patient experienced rebleeding from gastric varices or was treated for shock during angiography or B-RTO. None of the patients developed acute renal failure, hepatic encephalopathy, or hepatic failure.

Cumulative survival

Table 2 lists the outcomes of 34 patients treated with B-RTO. The median follow-up period for all 34 patients was 33 months (range, 1–107 months). Ten patients (29%) died, and the median period to death was 30 months (range, 1–87 months). The causes of death were hepatocellular carcinoma (n = 3), liver failure (n = 6), and bleeding from gastric varices (n = 1). Among 31 patients with complete obliteration of B-RTO, no patients died of hemorrhage from gastric varices or esophageal varices. The overall cumulative survival rate was 90%, 75%, 68%, and 55% at 1, 3, 5, and 7 years after B-RTO, respectively. At 5 years after B-RTO, the cumulative survival rate of urgent cases and elective cases was 74% and 65%, respectively (Fig. 3).

Aggravation of portal hypertension and hepatic function

We examined the aggravation of portal hypertension and hepatic function among patients with complete obliteration of B-RTO. Newly appeared gastric varices were not observed, while ten patients showed worsening of esophageal varices: appearance of red spots on the esophageal mucosa and F2 or F3 morphology of

 Table 2. Outcome after balloon-occluded retrograde transvenous obliteration

	Urgent cases	Elective cases	P value
Number	12	22	
Complete success	10	21	0.279
Worsening of EV	6	6	0.185
Result (living/died)	9/3	15/7	0.510
Cause of death (HCC/hepatic failure/variceal bleeding)	1/2/0	2/4/1	0.708
Follow-up period (months) ^a	38 (4–97)	32 (1–107)	0.631

EV, esophageal varices; HCC, hepatocellular carcinoma

^aData are mean values (range)

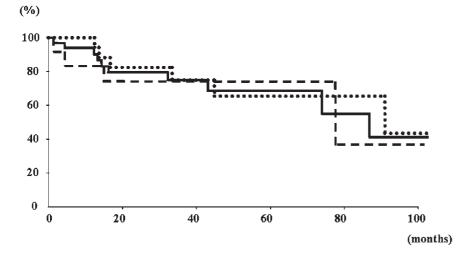


Fig. 3. Cumulative survival after B-RTO. The *solid line* shows overall cases, the *broken line* shows urgent cases, and the *dotted line* shows elective cases

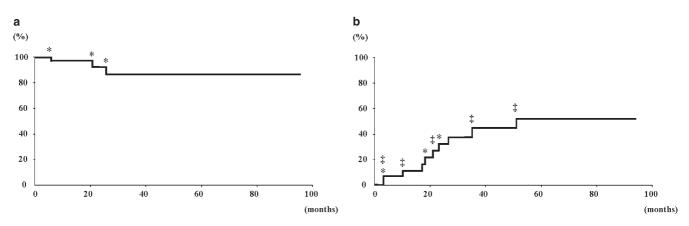


Fig. 4. a Kaplan-Meier analyses of cumulative variceal rebleeding. The *asterisk* shows bleeding from esophageal varices (n = 3). b Overall cumulative worsening rate of esophageal varices after B-RTO: 10 of 31 patients (32%) showed worsening of esophageal varices. The *asterisks* show the times at which patients with bleeding from esophageal varices were treated with endoscopic procedures. The *double daggers* show the times at which patients at risk of hemorrhage from esophageal varices were treated with endoscopic procedures. The remaining patients with worsening esophageal varices without hemorrhage received strict follow-up examinations

esophageal varices. Among these ten patients, three had bleeding esophageal varices and five were in danger of hemorrhage from esophageal varices. They underwent endoscopic procedure (endoscopic injection sclerotherapy, n = 6, and endoscopic variceal ligation, n= 2). The remaining two patients without hemorrhage were given strict follow-up examinations. No patients died of hemorrhage from esophageal varices. Variceal bleeding occurred in three patients from esophageal varices. The rate of rebleeding was 10% (3/31). Rebleeding from gastric varices was not observed after treatment that achieved complete obliteration. The rate of freedom from rebleeding was 97%, 86%, 86%, and 86% at 1, 3, 5, and 7 years after B-RTO, respectively (Fig. 4a). The overall cumulative worsening rate of esophageal varices was 15%, 39%, 52%, and 52% at 1, 3, 5, and 7 years after B-RTO, respectively (Fig. 4b). Portal hypertensive gastropathy is the term used to describe the endoscopic appearance of gastric mucosa with a characteristic mosaic-like pattern with or without red spots. According to McCormack's classification,⁴¹ almost all patients had mild grade portal hypertensive gastropathy and no patient showed a deterioration of grade or bled from portal hypertensive gastropathy. Ectopic varices were not observed at any time during the study period after B-RTO.

There was no significant difference in Child-Pugh score between before and after B-RTO. Among the various parameters of the Child-Pugh score, the serum albumin level was significantly improved $(3.33 \pm 0.65 \text{ vs.} 3.55 \pm 0.52 \text{ g/dl}; P = 0.04$, before and 4 weeks after B-RTO, respectively). The albumin level improved significantly from 1 to 6 months after B-RTO. However, the albumin level did not continue to improve more than 1 year after B-RTO.

Discussion

At first variceal bleeding, pharmacotherapy should ideally be used to achieve hemostasis and protect against rebleeding.⁴² In good responders, drug therapy improves the results in patients with esophageal varices bleeding, although only 30%–40% of patients reduce their portal pressure by >20% from baseline or to levels $\leq 12 \text{ mmHg}$. However, especially with respect to hemorrhage from gastric fundal varices, the outcome after pharmacotherapy is often unsatisfactory at present. In cases of upper gastrointestinal bleeding, an endoscopic examination is necessary to find the bleeding point and to classify the varices. If active bleeding is observed, then hemostatic procedures are required. Some endoscopic treatments may achieve hemostasis in over 90% of cases; however eradication of gastric varices and rebleeding rates are unsatisfactory.43-46 It is difficult to treat huge gastric fundal varices by endoscopic injection sclerotherapy without balloon occlusion of gastrorenal shunts.^{47,48} B-RTO can obliterate gastric varices from draining veins under balloon occlusion, and also obliterate afferent veins in a retrograde manner, even in patients with huge gastric varices. In Japan, B-RTO has been performed in about 3000 patients.⁴⁹ In most cases, the available literature reports prophylactic eradication of high-risk gastric varices. For acute bleeding, B-RTO can be performed after any hemostatic procedure, which is the main limitation of B-RTO. Results of B-RTO in patients with hemorrhage are summarized in Table 3. The success rate was high (95%), which is similar to the prophylactic situation. A low rate of rebleeding was observed after B-RTO. Considering these issues, it is desirable to perform B-RTO after endoscopic hemostatic procedures in patients with bleeding gastric fundal

			Hemostasis		
Reference number	Authors	Number of patients	Endoscopic therapy	Other procedure	Eradication of varices
15	Chikamori et al. 1996	6	2	4	6
25	Saeki et al. 1996	2	2	0	2
26	Sonomura et al. 1998	4	0	4	4
27	Kin et al. 1998	6	0	6	6
28	Chikamori et al. 2000	6	5	1	6
29	Fukuda et al. 2001	9	Not described	Not described	9
31	Miyamoto et al. 2003	4	4	0	4
32	Kim et al. 2003	13	Not described	Not described	12
33	Choi et al. 2003	8	Not described	Not described	8
34	Ninoi et al. 2005	35	Not described	Not described	33
35	Sugimori et al. 2005	6	Not described	Not described	6
36	Arai et al. 2005	11	4	0	11
	Our series	34	8	6	31
Total number	of patients	144			138

Table 3. Summary of balloon-occluded retrograde transvenous obliteration results in patients with gastric variceal bleeding

varices. At that time, endoscopic variceal ligation or clipping can be performed. However, patients should be referred to an institution in which B-RTO or injection sclerotherapy using tissue adhesives can be performed immediately after such transient endoscopic hemostatic procedures.

Another problematic long-term sequel of B-RTO is the development or worsening of esophageal varices, which occurs in about 50% of patients.^{23,29,31,34} In the present study, a similar rate of worsening esophageal varices was observed. Those patients were all successfully treated endoscopically. Generally, esophageal varices are managed more easily than gastric varices. Esophageal varices that developed after B-RTO were also easier to treat. Elevation of the portal pressure gradient may be expected owing to obliteration of major shunts, such as gastrorenal shunts. Indeed, development or worsening of esophageal varices after B-RTO indicates aggravation of portal hypertension. However, ectopic varices or severe portal hypertensive gastropathy were not observed after B-RTO in the present study.

Although the long-term outcome after B-RTO has not yet been fully demonstrated, some reports have shown improvement of the Child-Pugh score after B-RTO.^{24,29} In the present study, liver function, especially the serum albumin value, increased significantly from 1 to 6 months after B-RTO. Moreover, some studies demonstrated that portosystemic encephalopathy improved more after B-RTO than after TIPS.^{21,50} An increase in portal blood flow from obliteration of large portosystemic shunts might contribute to improvement in liver function. This was confirmed by Doppler ultrasound before and after B-RTO, and in a hemodynamic study after balloon occlusion of a gastrorenal shunt.^{31,51,52} Liver function improved in patients with Child-Pugh class B or C disease as well as in those with class A disease. However, radiological or surgical occlusion of a portosystemic shunt is sometimes accompanied by liver failure when the portal pressure gradient increases 60% or more from baseline after the procedure.⁵³ Partial splenic arterial embolization can reduce the portal pressure and lead to a good outcome in such cases treated by radiological occlusion of a portal systemic shunt.54,55 At present, it appears that B-RTO is applicable in Child-Pugh class A or B patients, while the benefit remains unclear in Child-Pugh class C patients. With respect to long-term prognosis, the cumulative survival rate was 68% at 5 years after B-RTO in the present study. Our results are consistent with those of other reports, including with regard to B-RTO for prophylaxis.^{23,29,34,56} Considering the factors affecting prognosis, the presence or absence of concomitant hepatocellular carcinoma and the Child-Pugh classification were important factors affecting survival after B-RTO.^{29,34} Among the complications of chronic liver disease. B-RTO can reduce deaths due to gastric varices, which are one of the most difficult variceal sites to treat

The technique of B-RTO is complicated and is not yet standardized in Japan. For successful treatment, additional specialized techniques to treat minor collaterals are required.^{15,18,21,23,28,30,39,40} Such techniques result in a decreased use of 5% ethanolamine oleate and may avoid sclerosant-related complications such as hemoglobinemia. In cases with Hirota's grade 3 or 4 in particular,²¹ techniques such as stepwise injection of 5% ethanolamine oleate, use of high concentrated glucose or ethanol, coil embolization of minor collaterals, or double-balloon catheterization are needed. By using these strategies and techniques based on the hemodynamic feature,^{15,18,21,23,28,30,39,40} radiologists worldwide could treat patients with gastric varices with gastrorenal shunts by B-RTO. Indeed, usefulness of B-RTO has recently been reported from outside of Japan,^{32,33} including in the review, guideline, and educational sections of the journals *Gastroenterology*, *Gut*, and *Radiographics*, respectively.^{3,6,18,40}

B-RTO is not feasible in patients without gastrorenal shunts. Ninoi et al.²⁴ demonstrated that antegrade transhepatic obliteration using metallic coils and 5% ethanolamine oleate eradicated gastric varices in patients difficult to treat with B-RTO. While percutaneous transhepatic obliteration only in afferent vessels resulted in transient hemostasis,⁵⁷ antegrade obliteration, including of gastric varices, is reported to be effective as well as B-RTO.²⁴ Similar efficacy was also demonstrated in patients with ectopic varices.58 When hemostasis is performed by TIPS in patients with refractory bleeding, embolization together with TIPS should be performed, as recommended by American Association for the Study of Liver Diseases practice guidelines.¹² At the same time, direct obliteration via the TIPS route would be desirable.^{10,12,13,58} Especially, the use of long-acting occlusion agents such as liquids in addition to metallic coils could obliterate at the peripheral level of the collateral vessels feeding the varices, and lead to a low incidence of rebleeding.^{13,58} These results support the findings that embolization of both esophageal varices and their feeders is essential to lower the recurrence rate after sclerotherapy.⁵⁹ It is desirable to obliterate both varices and the peripheral collateral vessels using 5% ethanolamine oleate, the distribution of which can be monitored, although agent-related complications are sometimes reported. No rebleeding from gastric varices after B-RTO might indicate successful embolization of both gastric varices and afferent veins. Thus, it is important in the treatment of gastric varices with hemorrhage to obliterate varices directly in addition to reducing portal pressure. In bleeding gastric varices, direct obliteration using 5% ethanolamine oleate in a retrograde or antegrade manner is desirable with or without TIPS, and whether the portal pressure gradient is more or less than 12mmHg. When direct obliteration is performed without TIPS, possible ectopic varices or portal hypertensive gastropathy should be considered, although the such aggravation of portal hypertension was not observed in the present study.

In conclusion, B-RTO treatment of bleeding gastric varices achieved high eradication of gastric varices, a low rebleeding rate, and a fairly good prognosis with improved hepatic function.

References

- 1. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992;16:1343–9.
- Kim T, Shijo H, Kokawa H, Tokumitsu H, Kubara K, Ota K, et al. Risk factors for hemorrhage from gastric fundal varices. Hepatology 1997;25:307–12.
- Ryan BM, Stockbrugger RW, Ryan JM. A pathophysiologic, gastroenterologic, and radiologic approach to the management of gastric varices. Gastroenterology 2004;126:1175–89.
- Rossle M, Haag K, Ochs A, Sellinger M, Noldge G, Perarnau JM, et al. The transjugular intrahepatic portosystemic stent-shunt procedure for variceal bleeding. N Engl J Med 1994;330:165–71.
- Sanyal AJ, Freedman AM, Luketic VA, Purdum PP 3rd, Shiffman ML, DeMeo J, et al. The natural history of portal hypertension after transjugular intrahepatic portosystemic shunts. Gastroenterology 1997;112:889–98.
- Jalan R, Hayes PC. UK guidelines on the management of variceal haemorrhage in cirrhotic patients. British Society of Gastroenterology. Gut 2000;46:1–15.
- Rossle M, Siegerstetter V, Olschewski M, Ochs A, Berger E, Haag K. How much reduction in portal pressure is necessary to prevent variceal rebleeding? A longitudinal study in 225 patients with transjugular intrahepatic portosystemic shunts. Am J Gastroenterol 2001;96:3379–83.
- 8. Tripathi D, Therapondos G, Jackson E, Redhead DN, Hayes PC. The role of the transjugular intrahepatic portosystemic stent shunt (TIPSS) in the management of bleeding gastric varices: clinical and haemodynamic correlations. Gut 2002;51:270–4.
- Zhuang ZW, Teng GJ, Jeffery RF, Gemery JM, Janne d'Othee B, Bettmann MA. Long-term results and quality of life in patients treated with transjugular intrahepatic portosystemic shunts. AJR Am J Roentgenol 2002;179:1597–603.
- Boyer TD. Transjugular intrahepatic portosystemic shunt: current status. Gastroenterology 2003;124:1700–10.
- Tripathi D, Helmy A, Macbeth K, Balata S, Lui HF, Stanley AJ, et al. Ten years' follow-up of 472 patients following transjugular intrahepatic portosystemic stent-shunt insertion at a single centre. Eur J Gastroenterol Hepatol 2004;16:9–18.
- 12. Boyer TD, Haskal ZJ; American Association for the Study of Liver Diseases. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension. Hepatology 2005;41:386–400.
- Tesdal IK, Filser T, Weiss C, Holm E, Dueber C, Jaschke W. Transjugular intrahepatic portosystemic shunts: adjunctive embolotherapy of gastroesophageal collateral vessels in the prevention of variceal rebleeding. Radiology 2005;236:360–7.
- Kanagawa H, Mima S, Kouyama H, Gotoh K, Uchida T, Okuda K. Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol 1996;11: 51–8.
- Chikamori F, Shibuya S, Takase Y, Ozaki A, Fukao K. Transjugular retrograde obliteration for gastric varices. Abdom Imaging 1996;21:299–303.
- Koito K, Namieno T, Nagakawa T, Morita K. Balloon-occluded retrograde transvenous obliteration for gastric varices with gastrorenal or gastrocaval collaterals. AJR Am J Roentgenol 1996;167:1317–20.
- Matsumoto A, Kitamoto M, Imamura M, Nakanishi T, Ono C, Ito K, et al. Three-dimensional portography using multislice helical CT is clinically useful for management of gastric fundic varices. AJR Am J Roentgenol 2001;176:899–905.
- Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y. Transcatheter obliteration of gastric varices. Part 1. Anatomic classification. Radiographics 2003;23:911–20.
- Ryan BM, Stockbrugger RW, Ryan JM. TIPS for gastric varices. Gut 2003;52:772.

- Akahane T, Iwasaki T, Kobayashi N, Tanabe N, Takahashi N, Gama H, et al. Changes in liver function parameters after occlusion of gastrorenal shunts with balloon-occluded retrograde transvenous obliteration. Am J Gastroenterol 1997;92:1026– 30.
- Hirota S, Matsumoto S, Tomita M, Sako M, Kono M. Retrograde transvenous obliteration of gastric varices. Radiology 1999;211: 349–56.
- Matsumoto A, Hamamoto N, Nomura T, Hongou Y, Arisaka Y, Morikawa H, et al. Balloon-occluded retrograde transvenous obliteration of high risk gastric fundal varices. Am J Gastroenterol 1999;94:643–9.
- 23. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y. Eight years of experience with transjugular retrograde obliteration for gastric varices with gastrorenal shunts. Surgery 2001;129:414–20.
- Ninoi T, Nakamura K, Kaminou T, Nishida N, Sakai Y, Kitayama T, et al. TIPS versus transcatheter sclerotherapy for gastric varices. AJR Am J Roentgenol 2004;183:369–76.
- 25. Saeki H, Hashizume M, Ohta M, Kishihara F, Kawanaka H, Sugimachi K. The treatment of gastric varices by a balloonoccluded retrograde transvenous obliteration; a transjugular venous approach. Hepatogastroenterology 1996;43:571–4.
- Sonomura T, Sato M, Kishi K, Terada M, Shioyama Y, Kimura M, et al. Balloon-occluded retrograde transvenous obliteration for gastric varices: a feasibility study. Cardiovasc Intervent Radiol 1998;21:27–30.
- 27. Kin H, Kubota Y, Tsuji K, Takeuchi Y, Takaoka M, Ogura M, et al. MR imaging in the evaluation of the therapeutic effect of B-RTO for gastric varices. Hepatogastroenterology 1998;45: 677–83.
- Chikamori F, Kuniyoshi N, Shibuya S, Takase Y. Urgent transjugular retrograde obliteration for prophylaxis of rebleeding from gastric varices in patients with a spontaneous portosplenorenal shunt. Dig Surg 2000;17:23–8.
- Fukuda T, Hirota S, Sugimura K. Long-term results of balloonoccluded retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy. J Vasc Interv Radiol 2001;12:327–36.
- Kitamoto M, Imamura M, Kamada K, Aikata H, Kawakami Y, Matsumoto A, et al. Balloon-occluded retrograde transvenous obliteration of gastric fundal varices with hemorrhage. AJR Am J Roentgenol 2002;178:1167–74.
- Miyamoto Y, Oho K, Kumamoto M, Toyonaga A, Sata M. Balloon-occluded retrograde transvenous obliteration improves liver function in patients with cirrhosis and portal hypertension. J Gastroenterol Hepatol 2003;18:934–42.
- 32. Kim ES, Park SY, Kwon KT, Lee DS, Park MJ, Chung IK, et al. The clinical usefulness of balloon occluded retrograde transvenous obliteration in gastric variceal bleeding. Taehan Kan Hakhoe Chi 2003;9:315–23.
- 33. Choi YH, Yoon CJ, Park JH, Chung JW, Kwon JW, Choi GM. Balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding: its feasibility compared with transjugular intrahepatic portosystemic shunt. Korean J Radiol 2003;4: 109–16.
- 34. Ninoi T, Nishida N, Kaminou T, Sakai Y, Kitayama T, Hamuro M, et al. Balloon-occluded retrograde transvenous obliteration of gastric varices with gastrorenal shunt: long-term follow-up in 78 patients. AJR Am J Roentgenol 2005;184:1340–6.
- 35. Sugimori K, Morimoto M, Shirato K, Kokawa A, Tomita N, Numata K, et al. Retrograde transvenous obliteration of gastric varices associated with large collateral veins or a large gastrorenal shunt. J Vasc Interv Radiol 2005;16:113–8
- Arai H, Abe T, Shimoda R, Takagi H, Yamada T, Mori M. Emergency balloon-occluded retrograde transvenous obliteration for gastric varices. J Gastroenterol 2005;40:964–71.
- The Japan Society for Portal Hypertension. The general rules for study of portal hypertension. 2nd ed. Tokyo: Kanehara; 2004. p. 51–9.

- Idezuki Y. General rules for recording endoscopic findings of esophagogastric varices (1991). Japanese Society for Portal Hypertension. World J Surg 1995;19:420–2.
- 39. Takahashi K, Yamada T, Hyodoh H, Yoshikawa T, Katada R, Nagasawa K, et al. Selective balloon-occluded retrograde sclerosis of gastric varices using a coaxial microcatheter system. AJR Am J Roentgenol 2001;177:1091–3.
- Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y. Transcatheter obliteration of gastric varices: part 2. Strategy and techniques based on hemodynamic features. Radiographics 2003;23:921–37.
- McCormack TT, Sims J, Eyre-Brook I, Kennedy H, Goepel J, Johnson AG, et al. Gastric lesions in portal hypertension: inflammatory gastritis or congestive gastropathy? Gut 1985;26: 1226–32.
- Bosch J, Abraldes JG, Groszmann R. Current management of portal hypertension. J Hepatol 2003;38:S54–68.
- Trudeau W, Prindiville T. Endoscopic injection sclerosis in bleeding gastric varices. Gastrointest Endosc 1986;32:264–8.
- 44. Oho K, Iwao T, Sumino M, Toyonaga A, Tanikawa K. Ethanolamine oleate versus butyl cyanoacrylate for bleeding gastric varices: a nonrandomized study. Endoscopy 1995;27:349–54.
- 45. Huang YH, Yeh HZ, Chen GH, Chang CS, Wu CY, Poon SK, et al. Endoscopic treatment of bleeding gastric varices by *N*-butyl-2-cyanoacrylate (Histoacryl) injection: long-term efficacy and safety. Gastrointest Endosc 2000;52:160–7.
- 46. Akahoshi T, Hashizume M, Shimabukuro R, Tanoue K, Tomikawa M, Okita K, et al. Long-term results of endoscopic Histoacryl injection sclerotherapy for gastric variceal bleeding: a 10-year experience. Surgery 2002;131:S176–81.
- 47. Matsumoto A, Hamamoto N, Kayazawa M. Balloon endoscopic sclerotherapy, a novel treatment for high-risk gastric fundal varices: a pilot study. Gastroenterology 1999;117:515–6.
- 48. Shiba M, Higuchi K, Nakamura K, Itani A, Kuga T, Okazaki H, et al. 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 2002;56:522–8.
- Kokubu S, Ono K, Oho K, Murashima N, Miyoshi H, Watanabe N, et al. Management of gastric varices in Japan: the first questionnaire of B-RTO. Jpn J Portal Hypertens 2004;10:72–8.
- Kawanaka H, Ohta M, Hashizume M, Tomikawa M, Higashi H, Kishihara F, et al. Portosystemic encephalopathy treated with balloon-occluded retrograde transvenous obliteration. Am J Gastroenterol 1995;90:508–10.
- 51. Akahane T, Iwasaki T, Kobayashi N, Tanabe N, Takahashi N, Gama H, et al. Changes in liver function parameters after occlusion of gastrorenal shunts with balloon-occluded retrograde transvenous obliteration. Am J Gastroenterol 1997;92:1026–30.
- 52. Yamagami T, Kato T, Iida S, Tanaka O, Nishimura T. Change in the hemodynamics of the portal venous system after retrograde transvenous balloon occlusion of a gastrorenal shunt. AJR Am J Roentgenol 2003;181:1011–5.
- Futagawa S. Surgical therapy of portal hypertension. In: Osuga T, Monna T, Takebe T, edited. ShinShoukakibyougaku, vol. 2. Tokyo: Igaku shoin; 1987. p. 191–5 (in Japanese).
- Chikamori F, Kuniyoshi N, Kawashima T, Shibuya S, Takase Y. Combination treatment of partial splenic embolization, endoscopic embolization and transjugular retrograde obliteration for complicated gastroesophageal varices. Hepatogastroenterology 2004;51:1506–9.
- 55. Yoshida H, Mamada Y, Taniai N, Yamamoto K, Kaneko M, Kawano Y, et al. Long-term results of partial splenic artery embolization as supplemental treatment for portal-systemic encephalopathy. Am J Gastroenterol 2005;100:43–7.
- 56. Oho K, Kumamoto M, Morita Y, Emori K, Tsuruta O, Toyonaga A, et al. long-term results of balloon-occluded retrograde transvenous obliteration (B-RTO) for fundal varices and encephalopathy. Gut 2005;54:A11.

- L'Hermine C, Chastanet P, Delemazure O, Bonniere PL, Durieu JP, Paris JC. Percutaneous transhepatic embolization of gastroesophageal varices: results in 400 patients. AJR Am J Roentgenol 1989;152:755–60.
- Vangeli M, Patch D, Terreni N, Tibballs J, Watkinson A, Davies N, et al. Bleeding ectopic varices—treatment with transjugular

intrahepatic porto-systemic shunt (TIPS) and embolisation. J Hepatol 2004;41:560-6.

 Takase Y, Shibuya S, Chikamori F, Orii K, Iwasaki Y. Recurrence factors studied by percutaneous transhepatic portography before and after endoscopic sclerotherapy for esophageal varices. Hepatology 1990;11:348–52.