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ORIGINAL ARTICLE

Balloon-occluded retrograde transvenous obliteration for gastric varices improves hepatic functional reserve in long-term follow-up

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balloon-occluded retrograde transvenous obliteration, gastric varices, hepatic functional reserve, partial splenic embolization, prognosis.

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Author contribution: Nobuo Waguri wrote the manuscript; Akihiko Osaki, Yusuke Watanabe, Tsuyoshi Matsubara, Shun Yamazaki, Hanako Yokoyama, Kiwamu Kimura, Takuya Wakabayashi, Masaki Mito, Shunta Yakubo, Rie Azumi, Junji Kohisa, Kennichi Takaku, and Munehiro Sato collected clinical data; Akihiko Osaki and Yusuke Watanabe played a role in study design and reviewed the paper; Kouichi Furukawa reviewed the paper.

Abstract

Background and Aim: Balloon-occluded retrograde transvenous obliteration (BRTO) has been widely adopted for the management of gastric fundal varices (GVs). There are a few reports that BRTO leads to the improvement of mid-term and long-term hepatic functional reserve (HFR). We retrospectively investigated the long-term effect on HFR and prognosis among patients who had undergone BRTO for GVs.
Methods: This single-center, retrospective study included 57successful patients out of 60 patients who underwent BRTO for GVs from December 2005 to September 2018. We examined the indicators of HFR (e.g., encephalopathy and ascites statuses, serum total bilirubin and albumin levels, % prothrombin time, and Child–Pugh and albumin–bilirubin [ALBI] scores) during 3 years of follow-up after BRTO. We analyzed survival using the Kaplan–Meier method and identified the independent prognostic factors via multivariate analyses.
Results: GVs disappeared in all patients who were successfully treated by BRTO. At 3 years after BRTO, serum albumin levels were significantly elevated (from 3.3 to 4.0 g/dL, $P = 0.008$), while Child–Pugh and ALBI scores were significantly decreased (from 7.0 to 5.7, $P = 0.043$, and from −1.94 to −2.60, $P = 0.006$, respectively). The median survival time among all patients was 2207 days; the survival rates after BRTO were 87.0% at 1 year, 81.8% at 3 years, 67.3% at 5 years, and 44.1% at 10 years. Multivariate analyses revealed that ascites, hepatic encephalopathy, and malignant neoplasms were independently associated with poor prognosis.
Conclusion: BRTO for GVs has a favorable effect on long-term HFR.

Introduction

Rupture of the gastric fundal varices (GVs) is often fatal because the blood flow of the gastrorenal shunt (GRS) which forms GVs is greater than the blood flow of esophageal varices.[1] Balloon-occluded retrograde transvenous obliteration (BRTO), which was invented in Japan,[2] has been widely adopted for the management of GVs.[3–8] BRTO has been reported to improve hepatic encephalopathy and hepatic functional reserve (HFR) by completely obstructing the portosystemic shunt.[9–15] To the best of our knowledge, there have been very few reports confirming that BRTO leads to the improvement of mid-term and long-term prognosis.[13,16–19] We retrospectively investigated the long-term effect on HFR and prognosis among patients who had undergone BRTO for GVs.

Methods

Patients. This single-center, retrospective study included 57successful patients out of 60 patients who underwent BRTO for GVs from December 2005 to September 2018. In this study, the indications of BRTO for GVs[20] were emergent or past ruptured GVs, presence of F2 and red color sign,[21] presence of F3[21] or increased GV size, and presence of hepatic encephalopathy caused by GV-forming portosystemic shunt. Exclusion criteria were one or more of the following: severe hepatic dysfunction (e.g., total bilirubin ≥4.0 mg/dL and/or Child–Pugh score ≥13), severe renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m^2), other serious diseases with poor prognosis, and absence of a portosystemic shunt amenable to a retrograde approach. We also performed partial splenic embolization

(PSE) simultaneously with BRTO in 44 patients with non-strict indications such as splenomegaly and/or thrombocytopenia. Using only 57 cases with successful BRTO, we retrospectively examined the parameters of HFR (e.g., encephalopathy and ascites statuses, total bilirubin and albumin levels, % prothrombin time, and Child–Pugh and albumin–bilirubin (ALBI) scores[22,23]) at 3, 6, 12, 24, and 36 months after BRTO using only cases with successful BRTO. We also analyzed survival of patients with successful BRTO using the Kaplan–Meier method and investigated independent prognostic factors via multivariate analyses.

Balloon-occluded retrograde transvenous obliteration. An 8-Fr long shepherd hook-shaped (Asato; Medikit, Tokyo, Japan) sheath introducer was introduced through the right femoral vein. A 6-Fr catheter with a 20-mm-diameter balloon or a 5.2-Fr catheter with a 9-mm-diameter balloon (Selecon MP Catheter; Terumo Clinical Supply Co., Gifu, Japan) was advanced through the sheath introducer into the gastrorenal shunt in a retrograde manner. Balloon-occluded retrograde transvenous venography (BRTV) was performed to identify shunts and their inflowing and outflowing vessels. The stepwise injection method,[24] selective coil embolization[24] of the minor accessory draining veins, and/or the downgrading method[25] was used to downgrade the gastrorenal shunt to a comparatively simple Grade 1 or 2, according to the classification by Hirota *et al*.[26] Under temporary balloon occlusion, a contrast medium was injected through the balloon catheter to confirm stagnation of variceal flow for more than 10 min; it was also used to evaluate the required volume of sclerosing solution. When stagnation of the contrast medium was confirmed, the same volume of 5% ethanolamine oleate with iopamidol (EOI) was injected and maintained in a stagnant state in the vessels with overnight balloon occlusion. The catheter was then removed. To prevent renal

Table 1 Baseline characteristics of patients with GVs treated by BRTO

Parameter	$n = 57$
Age	63.7 ± 9.0
Male/female	34/23
Total bilirubin (mg/dL)	1.4 ± 0.7
Albumin (g/dL)	3.3 ± 0.8
Prothrombin time (%)	72.4 ± 18.6
Platelet count ($\times 10^4/\mu L$)	11.0 ± 4.9
Ascites	10 (17.5%)
Hepatic encephalopathy	10 (17.5%)
Etiology (Alc/HCV/PBC/HBV/NASH/AIH/others)	23/15/5/4/4/2/6
Child-Pugh grade (A/B/C)	25/25/7
mALBI grade (1/2a/2b/3)	11/10/22/14
Ruptured GVs	16 (28.1%)
EVs	26 (45.6%)
With malignant neoplasms (HCC/pancreas/lung/colon)	20 (35.1%) 18/2/1/1
Concomitant PSE	44 (77.2%)

AIH, autoimmune hepatitis; Alc, alcoholic cirrhosis; BRTO, balloon-occluded retrograde transvenous obliteration; EVs, esophageal varices; GVs, gastric varices; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; mALBI, modified albumin–bilirubin; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSE, partial splenic embolization.

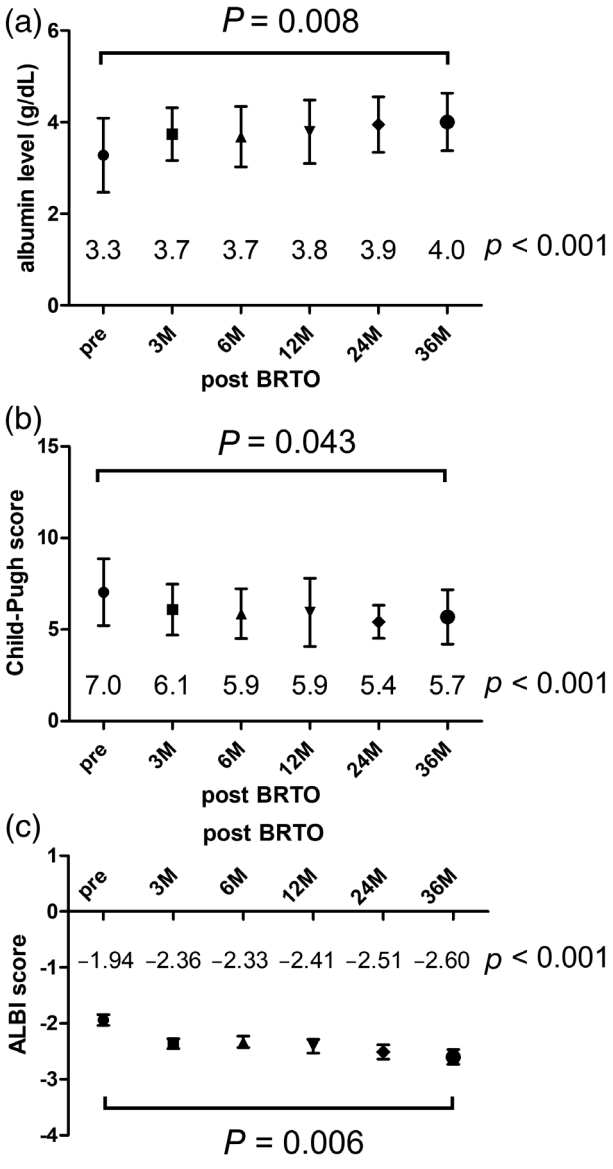

Figure 1 Changes in parameters indicative of hepatic functional reserve before and after balloon-occluded retrograde transvenous obliteration (BRTO). (a) At 3 years after BRTO, serum albumin levels were significantly elevated (from 3.3 to 4 g/dL, $P = 0.008$, paired *t*-test). Serum albumin levels showed a significant increase over the entire 3 years after BRTO ($P < 0.001$, one-way ANOVA). (b) At 3 years after BRTO, Child–Pugh scores significantly decreased (from 7.0 to 5.7, $P = 0.043$, paired *t*-test). The scores showed a significant decrease over the entire 3 years after BRTO ($P < 0.001$, one-way ANOVA test). (c) At 3 years after BRTO, albumin–bilirubin (ALBI) scores significantly decreased (from −1.94 to −2.60, $P = 0.006$, paired *t*-test). ALBI scores showed a significant decrease over the entire 3 years after BRTO ($P < 0.001$, one-way ANOVA test).

dysfunction secondary to hemolysis caused by EOI, human haptoglobin (4000 units) was administered prior to the injection of EOI.[27]

Partial splenic embolization. PSE was performed while checking contrast medium retention in the shunt vessels.[20] A 5-Fr catheter was introduced through the left femoral artery into the splenic or celiac artery. A 2.6-Fr coaxial microcatheter was advanced to the hilum of the spleen or to more peripheral branches. Under fluoroscopic guidance, the splenic arteries were embolized approximately 60–90% of the spleen by means of gelatin sponge pieces cut into approximately 3-mm cubes and immersed in iopamidol.

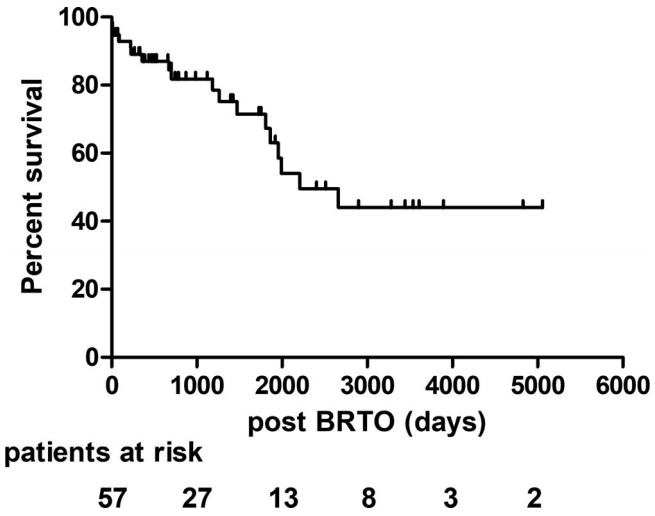

Figure 2 Kaplan–Meier curve showing overall survival after balloon-occluded retrograde transvenous obliteration (BRTO). The median survival time among all patients was 2207 days; the survival rates after BRTO were 87.0% at 1 year, 81.8% at 3 years, 67.3% at 5 years, and 44.1% at 10 years.

Statistical analysis. Clinical index parameters of HFR were compared between pre- and post-procedure periods by paired *t*-tests and one-way ANOVAs using the GraphPad Prism statistical software, version 5 (GraphPad Software, Inc., La Jolla, CA, USA). Data are shown as means ± SDs. Survival curves were estimated using the Kaplan–Meier method; differences between curves were compared using the log-rank test. Univariate and multivariate analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria). In all analyses, $P < 0.05$ was considered statistically significant.

Ethics. All patients provided informed consent for treatment after a physician had explained the advantages and risks of the procedures. This nonrandomized, retrospective clinical study protocol was approved by the Ethics Committee of Niigata City General Hospital. The study protocol conformed to the ethical guidelines of the 2013 revision of the Declaration of Helsinki.

Results

Baseline characteristics of the 57 patients are presented in Table 1. The mean age was 63.7 years, 59.6% of the patients were men, and alcoholic liver cirrhosis was the most frequent etiology (40.3%). Twenty-five had Child–Pugh grade A,

Table 2 Univariate and multivariate analyses of risk factors for survival after BRTO

	Univariate analyses		Multivariate analyses	
Factor	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)
Age (≥65)	0.714	1.20 (0.46–3.12)		
Male	0.764	1.16 (0.44–3.03)		
Alc	0.483	0.70 (0.26–1.88)		
HCV infection	0.102	2.33 (0.84–6.44)		
T-Bil ≥2 mg/dL	0.798	0.86 (0.26–2.81)		
Alb <3.5 g/dL	0.169	1.96 (0.75–5.09)		
PT <70%	0.288	1.69 (0.64–4.48)		
PLT <100 000/μL	0.661	1.24 (0.47–3.26)		
Ascites	0.058	3.88 (0.96–15.72)	0.020*	4.29 (1.07–13.45)
Hepatic encephalopathy	<0.001***	12.16 (2.95–50.26)	0.021*	3.35 (1.20–9.32)
Child–Pugh grade B & C	0.045*	2.66 (1.02–6.93)	0.891	
mALBI grade 2b &3	0.052	2.65 (0.99–7.08)	0.606	
Ruptured GVs	0.043*	0.35 (0.13–0.97)	0.182	
EVs	0.249	1.78 (0.67–4.72)		
Malignant neoplasms	0.004**	4.36 (1.62–11.74)	0.008**	4.67 (1.50–14.53)
Concomitant PSE	0.780	0.86 (0.29–2.54)		

Statistical significance: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Alb, albumin; Alc, alcoholic cirrhosis; BRTO, balloon-occluded retrograde transvenous obliteration; CI, confidence interval; EVs, esophageal varices; GVs, gastric varices; HCV, hepatitis C virus; HR, hazard ratio; mALBI, modified albumin–bilirubin; PLT, platelet count; PSE, partial splenic embolization; PT, prothrombin time; T-Bil, total bilirubin.

25 grade B, and 7 grade C liver disease. Similarly, 11, 10, 22, and 14 patients had modified ALBI grades[23] 1, 2a, 2b, and 3 liver disease, respectively. Sixteen patients (28.1%) underwent emergent or elective treatment because of ruptured GVs; the remaining patients underwent prophylactic treatment. In patients with active bleeding due to ruptured GVs, BRTO was performed after obtaining primary hemostasis by endoscopic band variceal ligation, endoscopic clipping, or a Sengstaken–Blakemore tube.

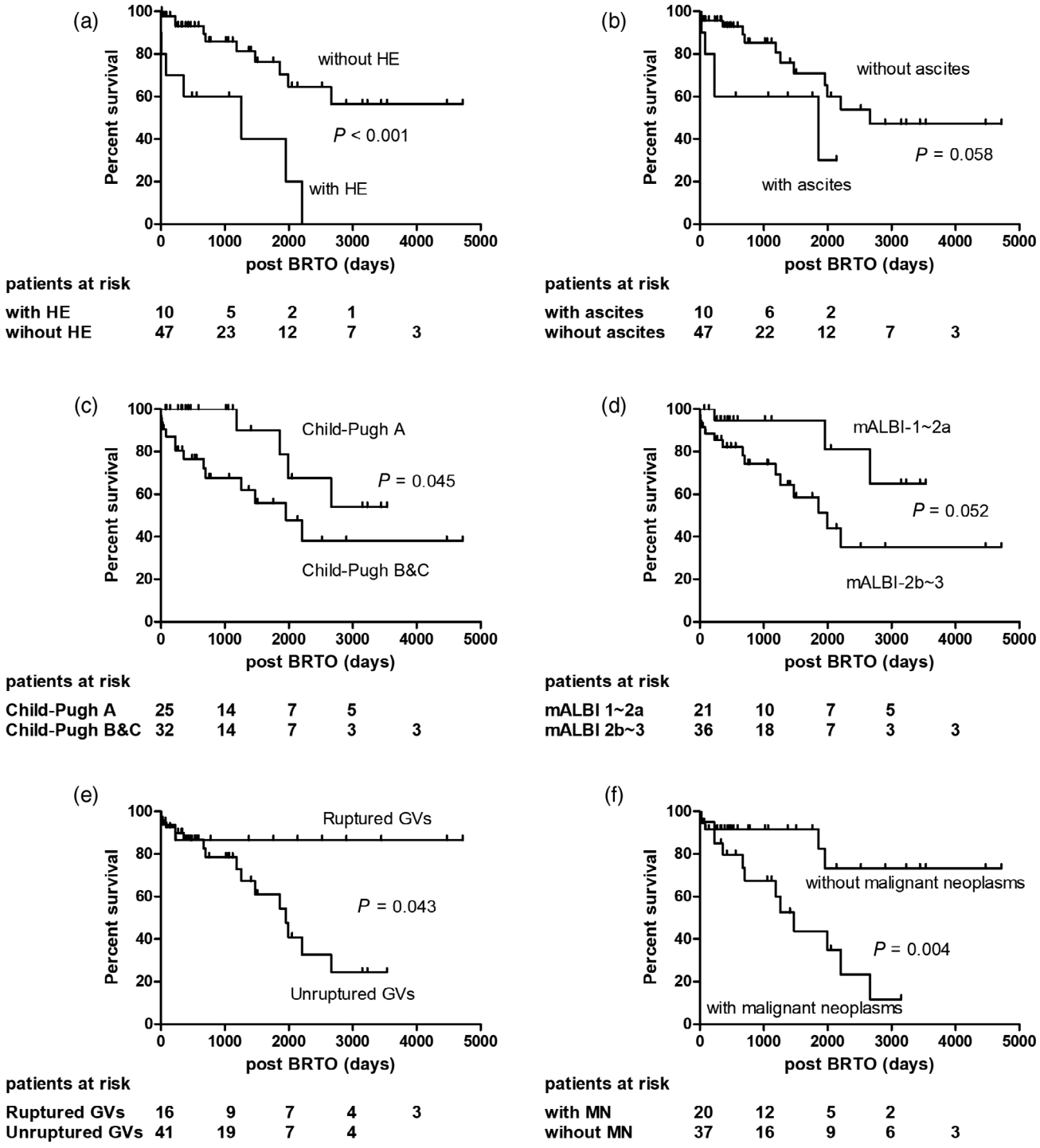

Figure 3 Kaplan–Meier survival curves after balloon-occluded retrograde transvenous obliteration (BRTO), compared between groups according to individual factors. Hepatic encephalopathy status (a), ascites status (b), Child–Pugh grades A and B–C (c), modified albumin–bilirubin (mALBI) grades 1–2a and 2b–3 (d), gastric varices (GVs) status (ruptured and unruptured/prophylactically treated) (e), and malignant neoplasm status (f).

Table 3 Summary of previous reports referring to the prognosis of patients who underwent BRTO for GVs

Author	References	*n*	BRTO success rate (%)	% Survival			Prognostic factors
				1-year	3-year	5-year	
Kumamoto M	[16]	20	100	100	100	85.0	
Naeshiro N	[18]	100	97.0			50	Child–Pugh grade, HCC development
Imai Y	[19]	154	95.4	91	76	72	Child–Pugh score, HCC
Hiraga N	[31]	34	91.1	90	75	68	
Akahoshi T	[32]	68	92.6		96.5	81.7	HCC
Katoh K	[33]	47	78.7	92	90	73	
Waguri N	This study	57	95.0	87.0	81.8	67.3	Ascites, HE, malignant neoplasms

BRTO, balloon-occluded retrograde transvenous obliteration; GVs, gastric varices; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy.

Twenty-six patients (45.6%) had esophageal varices. Twenty patients (35.1%) had advanced malignant neoplasms (18 hepatocellular carcinoma, 2 pancreatic cancer, 1 lung cancer, and 1 colon cancer; there was duplication).

BRTO was successful in 57 out of 60 patients, that is, the success rate of the procedure was 95.0%. GVs disappeared in all patients who were successfully treated by BRTO. After BRTO, bleeding or recurrence of GVs was not observed during the observation period. Of the three patients with unsuccessful BRTO, one patient in which only PSE was performed is being followed up, with a slight reduction in GVs. Another was treated with Hassab's operation, and yet another with percutaneous transhepatic portal obliteration.

Post-procedural complications were splenic abscess in 2 (3.5%), portal vein and/or splenic vein thrombosis in 3 (5.3%), and moderate pleural effusion and/or ascites retention in 10 patients (17.5%). Exacerbation of esophageal varices within 2 years after BRTO was seen in 14 patients (24.6%). As previously reported,[20] the frequency of exacerbation of esophageal varices after BRTO was significantly reduced by combining PSE with BRTO.

At 3 years after BRTO, serum albumin levels were significantly elevated (from 3.3 to 4.0 g/dL, $P = 0.008$) (Fig. 1a), while Child–Pugh and ALBI scores were significantly decreased (from 7.0 to 5.7, $P = 0.043$, and from -1.94 to -2.60, $P = 0.006$, respectively) (Fig. 1b,c). Total bilirubin levels in serum did not change (from 1.38 to 1.14 mg/dL) significantly ($P = 0.313$); however, % prothrombin time was slightly but significantly improved (from 72.4 to 86.8%, $P = 0.008$).

During the observation period, 17 patients died for the following causes: 8 due to hepatocellular carcinoma, 2 due to chronic liver failure, 2 due to pancreatic cancer, 1 due to lung cancer, 1 due to interstitial pneumonia, 1 due to splenic abscess, and 1 due to multiple organ failure at the first visit following ruptured GVs. The median survival time among all patients was 2207 days; the survival rates after BRTO were 87.0% at 1 year, 81.8% at 3 years, 67.3% at 5 years, and 44.1% at 10 years (Fig. 2). Univariate analyses were used to compare the cumulative survival rates between the two groups, according to individual factors (Table 2). The survival rate was significantly lower in patients with hepatic encephalopathy before BRTO compared to those who did not have hepatic encephalopathy ($P < 0.001$, Fig. 3a). Patients with ascites tended to have a low survival rate compared to those who did not have ascites, but this difference was not statistically significant ($P = 0.058$, Fig. 3b). The cumulative survival rate was significantly lower among patients with Child–Pugh grades B and C liver disease than among those with Child–Pugh grade A liver disease ($P = 0.045$, Fig. 3c). Similarly, the survival rate tended to be lower among patients with ALBI grades 2b and 3 liver disease than among those with mALBI grades 1 and 2a, but this difference was not statistically significant ($P = 0.052$, Fig. 3d). Surprisingly, the survival rate was significantly higher among patients with ruptured GVs than among patients with non-ruptured GVs ($P = 0.043$, Fig. 3e). The survival rate was significantly lower in patients with malignant neoplasms than in patients without malignant neoplasms ($P = 0.004$, Fig. 3f). However, the addition of PSE did not significantly improve the patient survival rate. Multivariate analyses revealed that ascites, hepatic encephalopathy, and malignant neoplasms were independently associated with poor prognosis (Table 2).

Discussion

The hemodynamics of GVs associated with GRS cause reduced portal venous pressure, which is harmful for the liver.[28] Various toxins derived from the intestinal tract (e.g., ammonia) must be detoxified by the liver; these toxins reach the systemic circulation through the hepatofugal portosystemic shunt flow, which causes hepatic encephalopathy. Shunt obstruction by BRTO reportedly leads to rapid correction of the blood ammonia level and improvement of hepatic encephalopathy.[9–15] Decreased hepatopetal portal venous flow reduces the transport of various nutrients from the intestinal tract to hepatocytes. In our study of 57 cases of GVs, we observed a long-term improvement in HFR after BRTO; however, the main observation was an increase in the albumin level, which is a representative index of protein synthesis ability. Thus, the improvement of HFR is largely related to the liver-associated nutritional improvement effect following the increase in hepatopetal portal venous flow. PSE reportedly can improve HFR.[29,30] In a previous short-term study,[20] we found that HFR was significantly improved in the BRTO + PSE group compared to the BRTO monotherapy group. Increased portal venous flow after BRTO is mainly caused by increased splenic venous blood flow without substantial enhancement of hepatopetal mesenteric venous blood flow. We speculate that hepatopetal mesenteric venous blood flow increases after PSE causes decreased splenic venous blood flow, thus improving

HFR. The combination of PSE with BRTO resulted in a short-term improvement in HFR; however, survival was not significantly prolonged. Addition of PSE aims to alleviate the rapid increase in portal pressure caused by BRTO and contributes to the improvement of short-term hepatic reserve and the prevention of early exacerbation of esophageal varices. The effect of PSE is not long-lasting, and the long-term improvement of HFR is considered to be mainly due to BRTO as a shunt occlusion. In this study also, the effect of concomitant PSE on the life prognosis was not significant.

Table 3 summarizes previous reports regarding the prognoses of patients who underwent BRTO for gastric varices.[16,18,19,31–33] Notably, poor hepatic reserve according to the Child–Pugh classification and hepatocellular carcinoma were factors associated with poor prognosis.[18,19,32] The results of this study were similar to those of previous studies. In our multivariate analysis, we found that ascites, hepatic encephalopathy, and malignant neoplasms were independently associated with poor prognosis. After BRTO, gastric varices disappear, HFR improves, and the prognosis is generally good in patients with no concomitant malignant neoplasms.

In this study, BRTO improved hepatic encephalopathy. Nevertheless, the results of multivariate analysis that hepatic encephalopathy is a factor in poor prognosis seem contradictory. Improvement of hepatic encephalopathy and increase of serum albumin level are the two pillars of improvement of HFR by BRTO. Patients undergoing BRTO already have a GRS, a large portosystemic shunt. That is, it seems that there are differences in hepatocyte function and hepatic fibrosis between patients with and without hepatic encephalopathy before BRTO treatment. Even though BRTO improves hepatic encephalopathy, the presence or absence of encephalopathy before treatment may be reflected in the difference in life prognosis.

Serum albumin levels increased significantly in each case compared to before and after BRTO. However, there was no significant difference in survival between cases with high and low albumin levels before BRTO.This result also seems contradictory, but it is a real phenomenon. Serum albumin levels were not only elevated in patients with hypoalbuminemia prior to BRTO. However, we speculate that the increase in albumin levels by BRTO may have brought the prognosis of patients with hypoalbuminemia closer to that of patients without hypoalbuminemia. However, it is still speculative and needs to be clarified in future studies.

Surprisingly, patients with ruptured GVs had significantly better survival than patients who received prophylactic treatment. Most patients with ruptured GVs were new patients, and the frequency of alcohol polydipsia was high among patients with ruptured GVs. Because there were many confounding factors (e.g., hepatic encephalopathy) in preventive treatment cases, the presence of a ruptured GVs was not an independent prognostic factor.

In conclusion, BRTO for GVs had a favorable long-term effect on HFR. However, this study was limited by its small number of cases, as well as by its retrospective and non-randomized design. Although randomized controlled trials for GVs are difficult, further multicenter studies with additional patients and propensity score matching are needed to confirm the findings.

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References

1 Watanabe K, Kimura K, Matsutani S, Ohto M, Okuda K. Portal hemodynamics in patients with gastric varices. A study in 230 patients with esophageal and/or gastric varices using portal vein catheterization. *Gastroenterology*. 1988; **95**: 434–40.
2 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.
3 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.
4 Ninoi T, Nishida N, Kaminou T *et al*. Balloon-occluded retrograde tranvenous obliteration of gastric varices with gastrorenal shunt: long-term follow-up in 78 patients. *Am. J. Roentgenol.* 2005; **184**: 1340–6.
5 Takuma Y, Nouso K, Makino Y, Saito S, Shiratori Y. Prophylactic balloon-occluded retrograde transvenous obliteration for gastric varices in compensated cirrhosis. *Clin. Gastroenterol. Hepatol.* 2005; **3**: 1245–52.
6 Sabri SS, Swee W, Turba UC *et al*. Bleeding gastric varices obliteration with balloon-occluded retrograde transvenous obliteration using sodium tetradecyl sulfate foam. *J. Vasc. Interv. Radiol.* 2011; **22**: 309–16.
7 Patel A, Fischman AM, Saad WE. Balloon-occluded retrograde transvenous obliteration of gastric varices. *Am. J. Roentgenol.* 2012; **199**: 721–9.
8 Saad WE, Simon PO, Rose SC. Balloon-occluded retrograde transvenous obliteration of gastric varices. *Cardiovasc. Intervent. Radiol.* 2014; **37**: 299–315.
9 Fukuda T, Hirota S, Sugimura K. Long-term results of balloon-occluded retrograde transvenous obliteration for the treatment of gastric varices and hepatic encephalopathy. *J. Vasc. Interv. Radiol.* 2001; **12**: 327–36.
10 Kato T, Uematsu T, Nishigaki Y, Sugihara J, Tomita E, Moriwaki H. Therapeutic effect of balloon-occluded retrograde transvenous obliteration. *Intern. Med.* 2001; **40**: 688–91.
11 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.
12 Waguri N, Hayashi M, Yokoo T *et al*. Simultaneous combined balloon-occluded retrograde transvenous obliteration and partial splenic embolization for portosystemic shunts. *J. Vasc. Interv. Radiol.* 2012; **23**: 650–7.
13 Inoue H, Emori K, Toyonaga A *et al*. Long-term results of balloon-occluded retrograde transvenous obliteration for portosystemic shunt encephalopathy in patients with liver cirrhosis and portal hypertension. *Kurume Med. J.* 2014; **61**: 1–8.
14 Choudhary NS, Baijal SS, Saigal S *et al*. Results of portosystemic shunt embolization in selected patients with cirrhosis and recurrent hepatic encephalopathy. *J. Clin. Exp. Hepatol.* 2017; **7**: 300–4.
15 Ishikawa T, Sasaki R, Nishimura T *et al*. Comparison of patients with hepatic encephalopathy and those with gastric varices before and after balloon-occluded retrograde transvenous obliteration. *Hepatol. Res.* 2018; **48**: 1020–30.
16 Kumamoto M, Toyonaga A, Inoue H *et al*. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric fundal varices: hepatic deterioration links to portosystemic shunt syndrome. *J. Gastroenterol. Hepatol.* 2010; **25**: 1129–35.

17 Kamezaki H, Maruyama H, Shimada T, Takahashi M, Okugawa H, Yokosuka O. Short- and long-term clinical outcome after balloon-occluded retrograde transvenous obliteration: is pretreatment portal flow direction a predictive factor? *Hepatol Int.* 2013; **7**: 241–7.
18 Naeshiro N, Aikata H, Kakizawa H *et al*. Long-term outcome of patients with gastric varices treated by balloon-occluded retrograde transvenous obliteration. *J. Gastroenterol. Hepatol.* 2014; **29**: 1035–42.
19 Imai Y, Nakazawa M, Ando S, Sugawara K, Mochida S. Long-term outcome of 154 patients receiving balloon-occluded retrograde transvenous obliteration for gastric fundal varices. *J. Gastroenterol. Hepatol.* 2016; **31**: 1844–50.
20 Waguri N, Osaki H, Ikarashi S *et al*. Simultaneous combined balloon-occluded retrograde transvenous obliteration and partial splenic embolization for gastric fundal varices. *United Eur. Gastroenterol. J.* 2016; **4**: 62–9.
21 Tajiri T, Yoshida H, Obara K *et al*. General rules for recording endoscopic findings of esophagogastric varices (2nd edition). *Dig. Endosc.* 2010; **22**: 1–9.
22 Johnson PJ, Berhane S, Kagebayashi C *et al*. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. *J. Clin. Oncol.* 2015; **33**: 550–8.
23 Hiraoka A, Kumada T, Tsuji K *et al*. Validation of modified ALBI grade formore detailed assessment of hepatic function in hepatocellular carcinoma patients: a multicenter analysis. *Liver Cancer.* 2019; **8**: 121–9.
24 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.
25 Fukuda T, Hirota S, Sugimoto K, Matsumoto S, Zamora CA, Sugimura K. "Downgrading" of gastric varices with multiple collateral veins in balloon-occluded retrograde transvenous obliteration. *J. Vasc. Interv. Radiol.* 2005; **16**: 1379–83.
26 Hirota S, Matsumoto S, Tomita M, Sako M, Kono M. Retrograde transvenous obliteration of gastric varices. *Radiology*. 1999; **211**: 349–56.
27 Hashizume M, Kitano S, Yamaga H, Sugimachi K. Haptoglobin to protect against renal damage from ethanolamine oleate sclerosant. *Lancet.* 1988; **2**: 340–1.
28 Nakano R, Iwao T, Oho K, Toyonaga A, Tanikawa K. Splanchnic hemodynamic pattern and liver function in patients with cirrhosis and esophageal or gastric varices. *Am. J. Gastroenterol.* 1997; **92**: 2085–9.
29 Murata K, Shiraki K, Takase K, Nakano T, Tameda Y. Long term follow-up for patients with liver cirrhosis after partial splenic embolization. *Hepatogastroenterology*. 1996; **43**: 1212–7.
30 Smith M, Ray CE. Splenic artery embolization as an adjunctive procedure for portal hypertension. *Semin Intervent Radiol.* 2012; **29**: 135–9.
31 Hiraga N, Aikata H, Takaki S *et al*. The long-term outcome of patients with bleeding gastric varices after balloon-occluded retrograde transvenous obliteration. *J. Gastroenterol.* 2007; **42**: 663–72.
32 Akahoshi T, Hashizume M, Tomikawa M *et al*. Long-term results of balloon-occluded retrograde transvenous obliteration for gastric variceal bleeding and risky gastric varices: a 10-year experience. *J. Gastroenterol. Hepatol.* 2008; **23**: 1702–9.
33 Katoh K, Sone M, Hirose A, Inoue Y, Fujino Y, Onodera M. Balloon-occluded retrograde transvenous obliteration for gastric varices: the relationship between the clinical outcome and gastrorenal shunt occlusion. *BMC Med. Imaging*. 2010; **10**: 2.