LIVER AND BILIARY TRACT

Predictive Factors of Worsening of Esophageal Varices After Balloon-Occluded Retrograde Transvenous Obliteration in Patients With Gastric Varices

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OBJECTIVES: **Although balloon-occluded retrograde transvenous obliteration (B-RTO) is useful for management of gastric varices, worsening of esophageal varices (EV) is the most important complication of B-RTO. The predictive factors of worsening of EV have not been evaluated in detail. This study was designed to evaluate the role of endoscopic color Doppler ultrasonography (ECDUS) in the detection of possible risk factors for worsening of EV after B-RTO.**

METHODS: **A total of 39 cirrhotic patients with high-risk gastric varices successfully treated by B-RTO were included in this study. All patients underwent ECDUS before B-RTO to measure hemodynamic parameters of gastric varices and regular endoscopic follow-up after B-RTO to detect worsening of EV. The risk factors were analyzed by Cox's proportional hazards regression.**

RESULTS: **Worsening of EV was found in 24 (61.5%) patients. The presence of esophageal varices before B-RTO and a lower degree of liver dysfunction (Child-Pugh class B) were statistically independent risk factors for worsening of EV after B-RTO (hazard ratio, HR, 5.81, 95% confidence interval, CI, 1.71–19.77 and HR 2.92, 95% CI: 1.21–7, respectively). High resistance index (≥0.24), measured by ECDUS, is also an independent risk factor for worsening of EV after B-RTO (HR 4.06, 95% CI: 1.14–14.38) and increase in resistance index is associated with worsening of EV (*P* for trend = 0.028).**

CONCLUSIONS: **The presence of EV, higher Child-Pugh class, and higher resistance index assessed by ECDUS before B-RTO were significant risk factors for worsening of EV after B-RTO.**

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INTRODUCTION

Gastric varices (GV) can be detected at first endoscopy in 20% of patients with all types of portal hypertension, and an additional 10% of patients develop GV within the first 2 years of eradication of esophageal varices (EV) (1). Patients with GV hemorrhage bleed more profusely, require more transfusions, and have a higher risk of rebleeding and mortality than those who bleed from EV (1).

Different lines of treatment are available for GV, including endoscopic injection sclerotherapy, shunt surgery, and transjugular intrahepatic portosystemic shunt. GV with spontaneous gastrorenal shunt (GRS) are usually difficult to treat by endoscopic injection sclerotherapy because the endoscopic approach is difficult, fast intravariceal blood flow to permit injection of sufficient sclerosant (2,3), and it could cause embolism of other organs (4). The mortality rate after elective surgery for GV is

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42–56% and is higher for emergency procedures (5,6). Moreover, the role of shunt surgery in patients with already existing spontaneous GRS is not known (7). The reported rate of efficacy of transjugular intrahepatic portosystemic shunt for GV is 50–63% (8–10). The high rate of shunt dysfunction, leading to recurrence of portal hypertension (11), and new-onset encephalopathy (12,13), is the main limitations of this procedure.

A number of interventional radiological techniques have been developed in Japan for the treatment of GV (7). Balloon-occluded retrograde transvenous obliteration (B-RTO) has been widely performed for GV with GRS (14–17), as the safety and effectiveness of B-RTO were reported by Kanagawa *et al.* (18,19). Both short-term and long-term clinical efficacy of B-RTO have been reported (14,19–22), and it is believed that B-RTO provides lower recurrence and bleeding rates than those of any other treatment, and could become a standard treatment for GV (22). Aggravation of EV is the most important complication of B-RTO (15). Several studies have shown that the rate of worsening of EV is 10–63% (14,15,23). However, the predictive factors of worsening of EV have not been evaluated in detail.

Endoscopic ultrasonography has recently emerged as a less invasive and easily repeatable alternative means of delineation of collaterals around the upper stomach and lower esophagus (24,25), and the usefulness of endoscopic color Doppler ultrasonography (ECDUS) in patients with esophagogastric varices has been reported (26). Several hemodynamic parameters of GV can be assessed by ECDUS. Recently, Sato *et al.* reported that ECDUS is a useful modality for diagnosis of the hemodynamics of GV and may allow the prediction of a high risk for hemorrhage (27). However, we found no reports in literature about the usefulness of ECDUS in assessment the factors that would be associated with worsening of EV after B-RTO. We speculated high velocity and high resistance index of GV measured by ECDUS could be risk factors for worsening of EV after B-RTO. This study was designed to determine the role of ECDUS in detection of possible risk factors for worsening of EV after B-RTO.

METHODS

Patients

The patient population included 39 cirrhotic patients with GV treated with B-RTO at Osaka City University Hospital. The patients included 23 men and 16 women, with a mean age of 63.5 years (range: 33–77 years). The causes of liver cirrhosis were hepatitis B ($n=4$), hepatitis C ($n=23$), chronic alcohol ingestion ($n=6$), and others ($n=6$). According to Child-Pugh classification, 27 patients were in class A, 12 patients in class B, and no patients in class C. Concomitant hepatocellular carcinoma measuring less than 5 cm in diameter was present in 12 patients. Of the 39 patients, 23 patients had EV and 4 patients had history of GV bleeding.

All patients met the following criteria: (1) high-risk GV including GV with a diameter greater than 5 mm measured by ECDUS and/or red spots (28), and/or a history of GV bleeding; (2) performance of ECDUS before B-RTO; (3) no portal thrombosis on contrast-enhanced CT; (4) complete obliteration of GV after B-RTO assessed by CE-CT and/or ECDUS performed 2 weeks after B-RTO; and (5) at least 3 months of follow-up after B-RTO.

All patients were hemodynamic stable, and none had severe ascites, hepatic coma, or active variceal bleeding. Written informed consent was obtained from each patient, and the study was approved by the Ethics Committee of our university.

Endoscopic findings

Endoscopic findings of GV and EV were classified according to the criteria proposed by the Japanese Society for Portal Hypertension (29). The form (F) of GV was classified as: straight small-calibered varices (F1), moderately enlarged, beady varices (F2), or markedly enlarged, nodular, or tumor-shaped varices (F3). According to location, GV were classified as: adjacent to the cardiac orifice (Lg-c), distant from the cardiac orifice (Lg-f), or extending from the cardiac orifice to the fornix (Lg-cf). The form of GV was F2 in 26 patients and F3 in 13 patients. The location of GV was Lg-f in 18 patients, Lg-cf in 16 patients, and Lg-c in the remaining 5 patients.

ECDUS procedure

Endoscopic color Doppler ultrasonography was performed with a 120-degree convex scanning echo-endoscope (FG 34UX, Pentax, Tokyo, Japan) and EUB 655 display unit (Hitachi, Medical Corp., Tokyo, Japan). A frequency of 7.5 MHz was used to obtain optimal axial resolution and penetration depth.

Patients were placed in the left lateral position, and the echo-endoscope was inserted into the esophagus and passed to the stomach. After suctioning of air from the stomach, a small volume (100–150 ml) of deaerated water was instilled into the stomach by an automatic water supply source. ECDUS was performed without a balloon attached to the tip of the echo-endoscope. ECDUS provides a color display of blood flow and evaluates the flow pattern using fast Fourier transform (FFT) analysis. Fast Fourier transform analysis can indicate the flow pattern and calculate the velocity of blood flow. We monitored color flow images of GV using color Doppler, with color gain adjusted to eliminate background noise and GV diameter measured along the short axis of the varices. GV hemodynamics were assessed by the pulsed Doppler method, by positioning a sample volume of 1–2 mm in the center of the varices and the insonation angle was adjusted to less than 60°. The patients were asked to stop breathing at the end of inspiration for few seconds to measure the hemodynamic parameters by EDCUS. The peak systolic velocity, end-diastolic velocity, mean velocity, and resistance index were automatically calculated over one cardiac cycle.

Following determination of GV diameter and mean velocity, the GV congestion index, ratio of cross-sectional area to blood flow velocity, was calculated by the equation CI: = (area/mean velocity) × 100 (30). In addition, GV blood flow rate (cm^2/s) was

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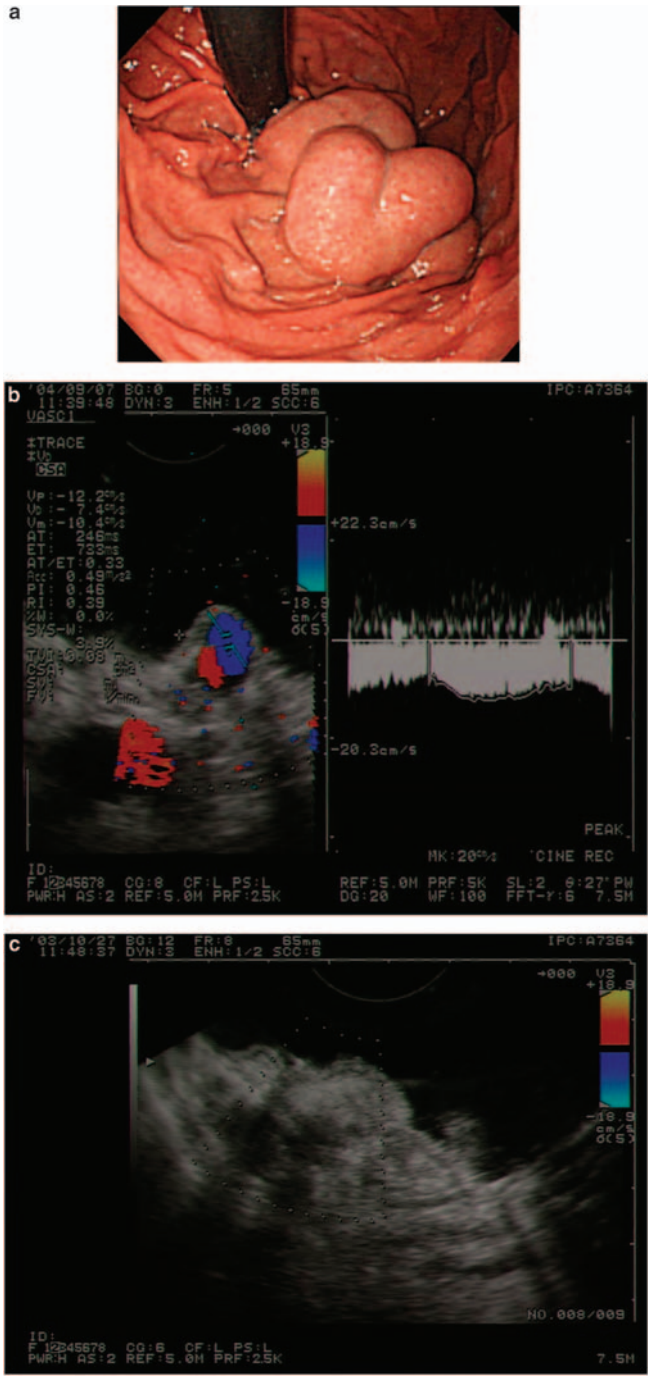

Figure 1. A typical case of gastric varices (GV) included in the present study. (**a**) Endoscopic appearance of GV; Lg-cf, F3, Cw, RC (−). (**b**) Hemodynamic parameters of gastric varices assessed by ECDUS before B-RTO. V_p, peak systolic velocity; V_D, end diastolic velocity; V_m, mean velocity; R_I, resistance index. (**c**) ECDUS revealed no flow, suggesting complete obliteration of GV after B-RTO. B-RTO, balloon-occluded retrograde transvenous obliteration; ECDUS, endoscopic color Doppler ultrasonography.

calculated by the equation; flow rate = "$A \times V$", where A is the cross-sectional area of the vessel (cm^2) and V is the mean velocity of the vessel (cm/s) (31,32). A typical case of GV included in the present study is shown in **Figure 1**.

Measurement of portal vein diameter

Portal vein diameter was measured in mm by CT. The diameter was estimated at a point midway between the main bifurcation of portal vein into the right and left main hepatic branches and portal vein confluence.

B-RTO procedure

Balloon-occluded retrograde transvenous obliteration is technically feasible only in patients with a known GRS, which account for almost 85% of all patients with GV (7). B-RTO was performed as described by Kanagawa *et al.* (2). First, a balloon catheter was inserted into the left renal vein via the femoral vein. The catheter was then advanced into the draining vein of the GV and the balloon was inflated to occlude and control blood flow. At this point, retrograde venography was performed to identify the inflow and outflow vessels of the GV. A 5% ethanolamine oleate mixed with iopamidol was then slowly injected through the catheter until both the GV and inflowing vessels were filled with the solution. After 24-h balloon occlusion, the catheter was removed. To prevent renal dysfunction related to hemolysis as a systemic effect of ethanolamine oleate mixed with iopamidol, 2000–4000 U of heated human haptoglobin was administered to all patients before B-RTO (33).

Definition of worsening and follow-up period

Gastrointestinal endoscopy was routinely performed every 3–6 months after B-RTO. In patients with bleeding episodes after B-RTO, gastrointestinal endoscopy was immediately performed to identify the site of bleeding. When endoscopy detected red spots on EV and/or bleeding of EV, the EVs were judged to have worsened, and endoscopic injection sclerotherapy was performed as soon as possible. Appearance of new EV or aggravation of variceal grade after B-RTO was also defined as worsening. The cases in which patients showed feature of worsening of EV after B-RTO were defined as censored. The time to worsening of EV was calculated from the time of B-RTO to the date of endoscopic examination that revealed worsening. If worsening of EV was not found on endoscopic examination, the follow-up period was considered the length of time from B-RTO to the date of the most recent endoscopic examination. Two endoscopists, with more than 5-year experience, were involved in revision of the endoscopic images and grading of varices.

Statistical analysis

The Statistical Package for Social Sciences Version 11.5 for Windows (SPSS 11.5 version) software was used for statistical analysis. Parameters are shown as means±s.d. Continuous data were analyzed by unpaired *t*-test. Paired samples *t*-test was used to compare model for end-stage liver disease (MELD) score before and after B-RTO. Factors seemed to have significant impact on worsening of EV after B-RTO were entered into Cox's proportional hazards model to test for significance. Linear trends in risk associated with resistance index were evaluated by entering ordered categorical variables using the

median value for each category. The cumulative survival free of worsening of EV after B-RTO was estimated. *P* values less than 0.05 were considered significant.

RESULTS

Worsening of EV after B-RTO

Among 39 patients with GV successfully treated with B-RTO, worsening of EV after B-RTO was found in 24 patients (61.5%) during the follow-up period, at a median of 296 days (mean 403 ± 361 (s.d.) days; range: 5–1,472 days). No patient developed hepatic encephalopathy within period 6 weeks after B-RTO. The median period of follow-up in the group with worsening of EV after B-RTO was 221 days (mean 377 ± 403 (s.d.) days; range: 5–1,472 days), although the median period of follow-up in the group without it was 407 days (mean 445 ± 290 (s.d.) days; range: 136–1,031 days). No significant difference was found in the period of follow-up between group with worsening of EV after B-RTO and group without it ($P = 0.575$). Of the 24 patients, 7 patients (29.2%) showed development of new EV, 2 patients (8.3%) showed aggravation of variceal grade, and 15 patients (62.5%) had bleeding and/or red color sign.

Clinical parameters and worsening of EV after B-RTO

The clinical parameters and cumulative survival free of worsening of EV after B-RTO at 500 days were shown in **Table 1**. Given EV before B-RTO, survival free of worsening was better in patients with absence of EV than in patients with presence of EV (**Figure 2a**) and survival free of worsening at 500 days were 65.8% and 37.9%, respectively. Given Child's class, survival free of worsening was better in class A than class B (**Figure 2b**) with 62.9% free of worsening at 500 days in class A and 33.3% in class B. MELD score before and within 4 weeks after B-RTO in the group with worsening was 10.08 ± 2.6 and 9.27 ± 2.1, respectively, and in the group without it 10.13 ± 3.4 and 9.46 ± 4.0, respectively. No significant difference was found in MELD score between the two groups either before or after B-RTO and MELD score in each group showed no significant difference before and after B-RTO.

Table 1. Cumulative survival free of worsening of EV at 500 days regarding clinical parameters

Parameters[a]	Value/category	% of patients
Age	<60/≥60	77.8/40.3
Gender	Male/female	40.9/62.9
MELD score[†]	<10/≥10	61.5/38.4
Child-Pugh class	Child A/Child B	62.9/33.3
Hepatocellular carcinoma	Present/absent	50/55.56
Esophageal varices	Present/absent	37.9/65.8
Bleeding of gastric varices	Positive/negative	25/53.6
Form of gastric varices	F2/F3	48.1/51.3
Location of gastric varices	Lg-c/Lg-cf/Lg-f	40/45.6/56.1

MELD, model for end-stage liver disease; Lg-cf, extending from the cardiac orifice to the fornix; Lg-f, distant from the cardiac orifice.
MELD score[†] divided into two groups according to the median value. Analysis was performed using Kaplan–Meier method.
[a]All parameters were factors or events assessed before B-RTO.

Determination of GV hemodynamics by ECDUS

Given resistance index of GV, survival free of worsening of EV after B-RTO was better in patients with lower resistance index (tertile 1, 0.10–0.15) than in patients with higher resistance index (tertile 3, 0.24–0.41; **Figure 2c**) with 72.5% free of worsening at 500 days in tertile 1 and 29.1% in tertile 3. Cumulative survival free of worsening of EV after B-RTO regarding hemodynamic parameters at 500 days was shown in **Table 2**.

Evaluation of risk factors for worsening of EV after B-RTO

To identify potential risk factors for worsening of EV after B-RTO, we used Cox's proportional hazard regression model. First, we screened the possible clinical, endoscopic, and hemodynamic variables by univariate analysis and examined whether or not each individual variable was a risk factor at $P < 0.05$. The presence of EV before B-RTO and lower degree of liver dysfunction (Child-Pugh class B) were significant risk factors for worsening of EV after B-RTO by univariate analysis (HR 2.93, 95% CI: 1.41–7.49 and HR 2.5, 95% CI: 1.09–5.72, respectively; **Table 3**). Other variables including age, gender, previous bleeding of GV, concomitant hepatocellular carcinoma, form, and location of GV were not significant factors by univariate analysis. Among hemodynamic parameters of GV assessed by ECDUS, higher resistance index (≥0.24) was a significant risk factor for worsening of EV after B-RTO in univariate analysis (HR 3.71, 95% CI: 1.11–12.38). Peak systolic, end diastolic, and mean velocities were not significant risk factors for worsening of EV after B-RTO in univariate analysis (HR 1.038, 95% CI 0.967–1.114; HR 1.003, 95% CI 0.903–1.114; HR 1.04, 95% CI: 0.925–1.136, respectively, and HR is reported per 1 cm/s change). Portal vein diameter and GV diameter, flow rate, congestion index were not significant risk factors for worsening of EV (HR 0.729, 95% CI: 0.393–1.352; HR 0.954, 95% CI: 0.791–1.152; HR 0.998, 95% CI: 0.930–1.071; HR 0.885, 95% CI: 0.691–1.33, respectively. HR is reported per 1 mm change in diameters and per cm^2/s for flow rate).

Subsequently, the significant variables detected by univariate analysis including presence of EV, lower degree of liver dysfunction (Child-Pugh class B), and higher resistance index were examined by multivariate analysis to detect the independent significant factors. Cox's proportional hazard model using multivariate analysis showed that presence of EV, lower degree of liver dysfunction (Child-Pugh class B), and higher resistance index were independent significant risk factors for worsening of EV after B-RTO (HR 5.81, 95% CI: 1.71–19.77 and HR 2.92, 95% CI: 1.21–7 and HR 4.06, 95% CI: 1.14–14.38, respectively, with *P* for trend = 0.028; **Table 3**).

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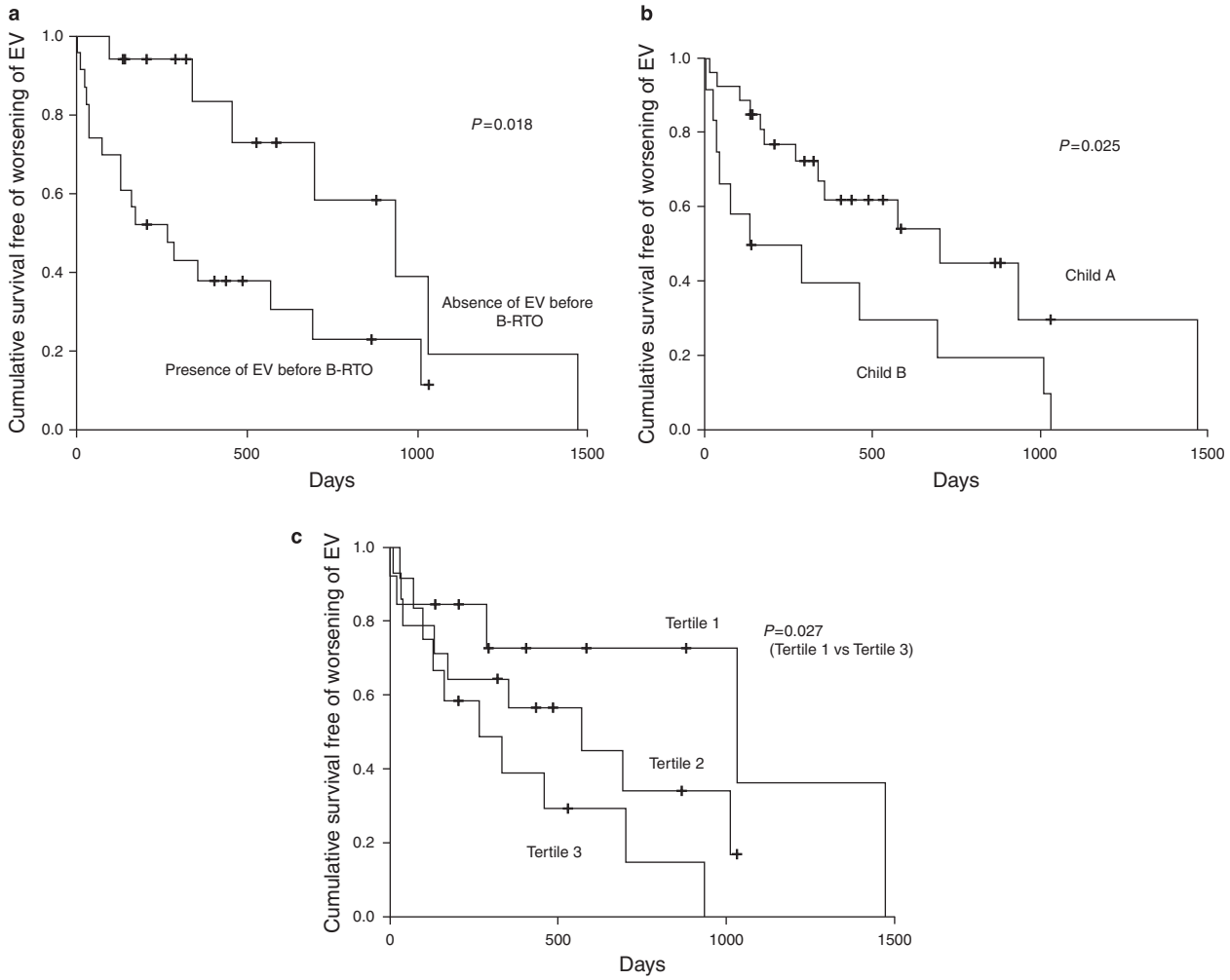

Figure 2. Cumulative survival free of worsening of esophageal varices after B-RTO in relation to the presence of EV (**a**), Child-Pugh class (**b**), and resistance index (**c**).

The cumulative probability of patients free from the worsening of EV after B-RTO in relation to the presence of EV, Child-Pugh classification, and resistance index are shown in **Figure 2**.

DISCUSSION

Worsening of EV is common after B-RTO, and detection of risk factors and possible mechanisms of worsening is required to improve the management of GV. In the present study, the rate of worsening of EV was 61.5%, and the presence of EV before B-RTO, lower degree of liver dysfunction, and higher resistance index measured by ECDUS were significantly associated with worsening of EV after B-RTO. The reader could suggest that the number of endoscopies would be higher in patients with more advanced liver disease or in patients with worsening of EV and thus EV were more likely to be found and classified as worsened, However, the numbers of performed endoscopies during follow-up period in group with worsening, group without, patients with Child A, and Child B were 68, 69, 109, and 28, respectively, suggesting that number of endoscopies in patients with more advanced liver disease did not affect the present data.

Several studies have shown that the rate of worsening of EV is 10–63% (14,15,23). This wide range could be because of variation in patient population, causes and severity of liver cirrhosis, or duration of follow-up. It could also be because of differences in the definition of worsening. In one report, EV were judged to have worsened when red spots on EV and/or bleeding of EV was detected (22), although in another report EV were considered worsened when varices became enlarged, tortuous, or large and coil-shaped, or when a red spot was observed (23). Our relatively high rate of worsening of EV after B-RTO might have been because of the definition of worsening of EV we used, which included red spots on EV, bleeding of EV, appearance of new EV, and aggravation of variceal grade.

The mechanisms of worsening of EV after B-RTO are unknown and several factors correlate with occurrence and

Table 2. Cumulative survival free of worsening of EV after B-RTO at 500 days regarding hemodynamic parameters of GV assessed by ECDUS

Parameters[a]	Value	% of patients
Mean velocity[b]	<17.8/≥17.8	55/52.6
Peak systolic velocity[b]	<20.5/≥20.5	52.3/55.5
End diastolic velocity[b]	<15.6/≥15.6	55/52.63
Diameter in mm	<7.2/≥7.2	40.4/56.7
Flow rate in cm^2/s	<6.47/≥6.47	50/48.4
Congestion index	<1.95/≥1.95	38.1/60.2
Diameter of PV[c]	<10.25/≥10.25	33.3/36.3
Resistance index		
Tertile 1	0.10–0.15	72.5
Tertile 2	0.16–0.23	56.2
Tertile 3	0.24–0.41	29.1

PV, portal vein.
Analysis was performed using Kaplan-Meier method.
[a]Parameters were divided into two groups according to the median value. [b]velocity was measured in cm/s. [c]PV in mm was measured by computed tomography.

Table 3. Univariate and multivariate analysis of predictive factors affecting worsening of esophageal varices after B-RTO in all patients

Parameters[a]	Cases	Crude HR (95% CI)	Multiple-adjusted HR (95% CI)
Age[b]	39	1.00 (0.956–1.058)	
Gender			
Female	16	1	
Male	23	2.6 (0.922–7.333)	
Child-Pugh class			
Child A	27	1	1
Child B	12	2.5 (1.09–5.72)	2.92 (1.21–7.00)
Bleeding of GV			
Negative	35	1	
Positive	4	1.30 (0.374–4.529)	
HCC			
Negative	27	1	
Positive	12	1.30 (0.487–3.486)	
Esophageal varices			
Absent	16	1	1
Present	23	2.93 (1.14–7.49)	5.81 (1.71–19.77)
Form of GV			
F2	26	1	
F3	13	0.83 (0.313–2.232)	
Location of GV			
Lg-c	5	1	
Lg-f	18	0.97 (0.257–3.680)	
Lg-cf	16	0.57 (0.150–2.241)	
Resistance index			
Tertile 1 (0.10–0.15)	13	1	1
Tertile 2 (0.16–0.23)	14	2.08 (0.63–6.81)	0.62 (0.15–2.58)
Tertile 3 (0.24–0.41)	12	3.71 (1.11–12.38)*	4.06 (1.14–14.38)*
MELD score[c]	39	0.97 (0.835–1.126)	

CI, confidence interval; GV, gastric varices; HCC, hepatocellular carcinoma; HR, hazard ratio; Lg-c, adjacent to the cardiac orifice; Lg-cf, extending from the cardiac orifice to the fornix; Lg-f, distant from the cardiac orifice; MELD, model for end-stage liver disease.
*P for trend = 0.028.
[a]All parameters were factors or events assessed before B-RTO. Cox's proportional hazards model was used for univariate and multivariate analyses. [b]HR is reported per 1 year change in age. [c]HR is reported per 1 point change in MELD score.

recurrence of EV in patients with portal hypertension (34,35). The left gastric vein, which drains both the anterior and posterior surfaces of the stomach, is the major feeding vein for EV in portal hypertension, whereas the short gastric vein, which drains the gastric fundus, less frequently feeds EV. As B-RTO leads to obliteration of GRS, a sequence of hemodynamic changes that increase the pressure and blood flow velocity in the left gastric vein and/or short gastric vein may contribute to worsening of EV after B-RTO. This is supported by the finding that the presence of EV is significantly associated with worsening of EV after B-RTO. In addition, increase in portal blood flow and portal pressure after B-RTO might subsequently be decompressed by the development of alternate collaterals.

In the present study, lower degree of liver dysfunction (Child B) was independent risk factor for worsening of EV after B-RTO. Portal pressure has been shown to be closely correlated with the severity of liver cirrhosis, as assessed by liver biopsy (36,37) or Child-Pugh classification (38), and the portal pressure gradient is expected to increase after B-RTO (16). The expected increase in portal pressure gradient after B-RTO in the group with worsening would be greater than that in the group without it, and may contribute to the development of new collaterals and worsening of EV.

Hemodynamic evaluation of portal hypertension reveals that hepatofugal flow in the collateral veins and hyperdynamic state at the lower esophagus and cardiac area are involved in the formation of EV. Hepatofugal blood flow velocity of the left gastric vein is significantly correlated with the size of EV (39) and high flow velocity in the left gastric vein was strongly associated with variceal bleeding (40). In addition, patients with a dominant anterior branching pattern of the left gastric vein

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assessed by ECDUS tend to have larger EV than those with a posterior branching pattern, and have significantly less response to endoscopic treatment (41). ECDUS is a useful modality for the evaluation of the hemodynamics of EV and ECDUS examinations using ultrasound echo-enhancing agent showed that arterial flow is involved in the formation of EV (42). Moreover, contrast enhanced ECDUS can improve the diagnostic quality of the hemodynamics of recurrent EV after endoscopic therapy and the perforating veins can be detected at a high rate (43). We speculate that examination of the left gastric veins and other collaterals with contrast enhanced ECDUS should be considered to evaluate worsening of EV after B-RTO.

ECDUS is useful for evaluating GV hemodynamic parameters. In the present study, Cox's proportional hazards model using univariate and multivariate analysis showed that resistance index was an independent significant risk factor for worsening of EV after B-RTO. Higher resistance index, assessed by ECDUS, could be an important hemodynamic parameter to predict worsening of EV after B-RTO. The resistance index is considered to reflect vascular resistance peripheral to the location of measurement, and resistance refers to opposition to blood flow created by the amount of friction the blood encounters as it passes through the vessels and is related to blood viscosity (h), the length of blood vessels (l), and vessel radius (r) (44). The resistance index can vary from 0 to 1, with higher values indicating greater vascular resistance. Several studies have indicated that measurement of resistance index is clinically useful in a variety of vascular beds (45–47). However, resistance index of GV has not been previously determined. All patients were hemodynamically stable and GV diameter was not significant risk factor for worsening. Therefore, we suggested that the significance of resistance index, as risk factor for worsening, indicates presence of paragastric and/or paraesophageal collaterals that are responsible for increasing vascular resistance and may contribute to worsening of EV after B-RTO.

The present study has some limitations. There were no significant differences in many clinical, endoscopic, and hemodynamic variables examined for detection of risk factors for worsening of EV after B-RTO. This could be because of the small sample size in this study. On the basis of the expected multifactor mechanism of worsening of EV after B-RTO, we evaluated several parameters in spite the limited number of patients in our study. We did not measure hemodynamics of other collateral veins, in particular the left gastric vein. The hemodynamic changes in these collateral veins also need to be evaluated.

In conclusion, the presence of EV, higher Child-Pugh class, and higher resistance index of GV measured by ECDUS are significant risk factors for worsening of EV after B-RTO. ECDUS has an important role in predicting worsening of EV after B-RTO.

CONFLICT OF INTEREST

Guarantor of the article: Yasuhiro Fujiwara, MD, PhD.

Specific author contributions: Development of the protocol and the study, collection of data, statistical calculations, and writing of the paper: Mahmoud Kamal Elsamman; supervision of the protocol, statistical calculations, and paper revision: Yasuhiro Fujiwara; revising of ECDUS and endoscopic images and performance of endoscopy during follow-up period: Natuhiko Kameda and Hirotoshi Okazaki; revision of the paper: Tetsuya Tanigawa and Nobuhide Oshitani; statistical calculations and revision of the paper: Masatsugu Shiba; patients' enrollment and follow-up: Kazunari Tominaga and Toshio Watanabe; supervision of the protocol: Usama A Arafa and Adel A El-Sayed; revision of the B-RTO procedure in the paper: Kenji Nakamura; final approval of the paper: Tetsuo Arakawa.

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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Worsening of esophageal varices (EV) after balloon-occluded retrograde transvenous obliteration (B-RTO) is common.
- ✓ Predictive factors for worsening of EV are unknown.

WHAT IS NEW HERE

- ✓ Presence of EV before B-RTO, higher Child-Pugh class, and higher resistance index of gastric varices were risk factors for worsening of EV after B-RTO.
- ✓ Endoscopic color Doppler ultrasonography could predict worsening of EV after B-RTO.

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