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Improved Hepatic Reserve and Fibrosis in a Case of "Portal-Systemic Liver Failure" by Portosystemic Shunt Occlusion

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: Female, 67-year-old
Final Diagnosis: Portal-systemic liver failure
Symptoms: None (second opinion)
Medication: None
Clinical Procedure: Balloon-occluded retrograde transvenous obliteration (BRTO)
Specialty: Radiology

Objective: Unusual or unexpected effect of treatment

Background: This is a case report validating our previous studies showing clinical benefit of balloon-occluded retrograde transvenous obliteration (BRTO) in improving hepatic function and outcomes in patients with a low liver stiffness (LS) and with procedural indication of encephalopathy. Here, we present the case of a woman in her late 60s suffering from hepatitis C virus-related decompensated liver cirrhosis with refractory encephalopathy.

Case Report: The patient presented with a Child-Pugh score of 11, Model for End-Stage Liver Disease-Sodium (MELD-Na) score of 16, and LS of 21.5 kPa. BRTO was expected to improve both the intractable encephalopathy and hepatic function and prolong her vital prognosis. Portosystemic shunt (PSS) occlusion induced drastic changes in the portal-splenic vein hemodynamics, resulting in dramatically improved Child-Pugh and MELD-Na scores. This status was maintained for 1 year postoperatively. However, her LS increased 1 month postoperatively and declined steadily thereafter. The postoperative levels of hepatic fibrosis markers, including Mac-2 binding protein glycosylation isomer, decreased markedly. No ascites, pleural effusion, esophagogastric varices, or relapse of encephalopathy were observed during a 1-year postoperative follow-up period.

Conclusions: Liver failure caused mainly by the advanced development of PSSs (as in our case), rather than hepatic parenchymal cell dysfunction, is considered reversible and controllable via PSS occlusion. We herein propose a novel concept, "portal-systemic liver failure," to describe liver failure with a non-stiff liver and giant PSSs, as in the present case. In patients with "portal-systemic liver failure," BRTO could potentially improve the prognosis in association with improved hepatic reserve and fibrosis.

MeSH Keywords: End Stage Liver Disease • Hepatic Encephalopathy • Hypertension, Portal • Portasystemic Shunt, Surgical • Radiology, Interventional

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Background

Balloon-occluded retrograde transvenous obliteration (BRTO) is used to treat gastric fundal varices and refractory encephalopathy associated with portosystemic shunts (PSSs) [1–3]. Several studies have demonstrated that BRTO, when used for PSS occlusion, reduces collateral venous flow and increases portal venous blood flow, thereby improving the hepatic functional reserve and long-term patient outcomes [4–6]. However, the procedure can result in severe complications, such as ascites and aggravation of esophageal varices, and hepatic function deterioration due to elevated portal venous pressure following major shunt occlusion, leading to worse prognosis postoperatively. In general, BRTO is thought to be a high-risk treatment for patients with decompensated liver cirrhosis, especially those classified as Child-Pugh class C.

In our previous study, we demonstrated that PSS obliteration might reduce both the Child-Pugh and Model for End-Stage Liver Disease-Sodium (MELD-Na) scores to a much greater extent in patients with hepatic encephalopathy than in those with gastric varices. This outcome is attributed to the much more striking changes in portal-splenic vein hemodynamics following shunt occlusion in the former patient group [7]. We additionally reported that a pretreatment liver stiffness (LS) of <21.6 kPa on transient elastography might predict reductions in MELD-Na scores and improvements in vital prognosis after PSS occlusion by BRTO in patients with portal hypertension [8].

In this report, we describe our experience with a woman who presented with hepatitis C virus-related decompensated liver cirrhosis with refractory encephalopathy. She underwent BRTO based on our original evidence.

Table 1. Changes in various test results up to 1 year after balloon-occluded retrograde transvenous obliteration.

	Before BRTO	1M post-BRTO	6M post-BRTO	12M post-BRTO
Child-Pugh score	11	7	5	5
MELD-Na score	16	7	8	8
Total bilirubin (mg/dL)	2.1	0.9	0.9	1.0
Albumin (g/dL)	2.7	3.3	3.7	4.1
ALT (U/L)	23	13	15	16
Cholinesterase (U/L)	122	224	224	257
Total cholesterol (mg/dL)	91	105	143	167
Creatinine (mg/dL)	0.59	0.63	0.66	0.70
Sodium (mmol/L)	140	141	140	139
ICG-R15 (%)	55.8	20.9	9.5	9.7
Ammonia (μg/dL)	199	121	29	37
BTR	1.90	3.84	4.86	5.62
PT (%)	36.6	72.7	79.3	82.5
PT-INR	1.80	1.17	1.13	1.11
Antithrombin (%)	55.2	65.0	90.0	102.5
IV COL-7S (ng/mL)	9.1	8.9	7.3	7.2
M2BPGi (C.O.I)	9.89	4.17	1.52	1.08
NOx (mmol/L)	13.8	28.5	45.1	56.2
LS (kPa)	21.5	27.7	20.2	16.0
Portal vein diameter (mm)	6.2	9.1	10.2	10.5
Portal flow volume (mL/min)	No data*	1029.7	980.1	1173.6
Liver volume (cm^3)	434.7	607.8	875.6	879.9

BRTO – balloon-occluded retrograde transvenous obliteration; MELD-Na – Model for End-Stage Liver Disease-Sodium; ALT – alanine aminotransferase; ICG-R15 – indocyanine green retention rate at 15 min; BTR – branched-chain amino acid-to-tyrosine molar ratio; PT – prothrombin time; INR – international normalized ratio; IV COL-7S – 7S domain of type IV collagen; M2BPGi – Mac-2 binding protein glycosylation isomer; NOx – nitrogen oxides; LS – liver stiffness; M – month. * No data indicates an inability to measure the portal flow velocity by Doppler ultrasonography.

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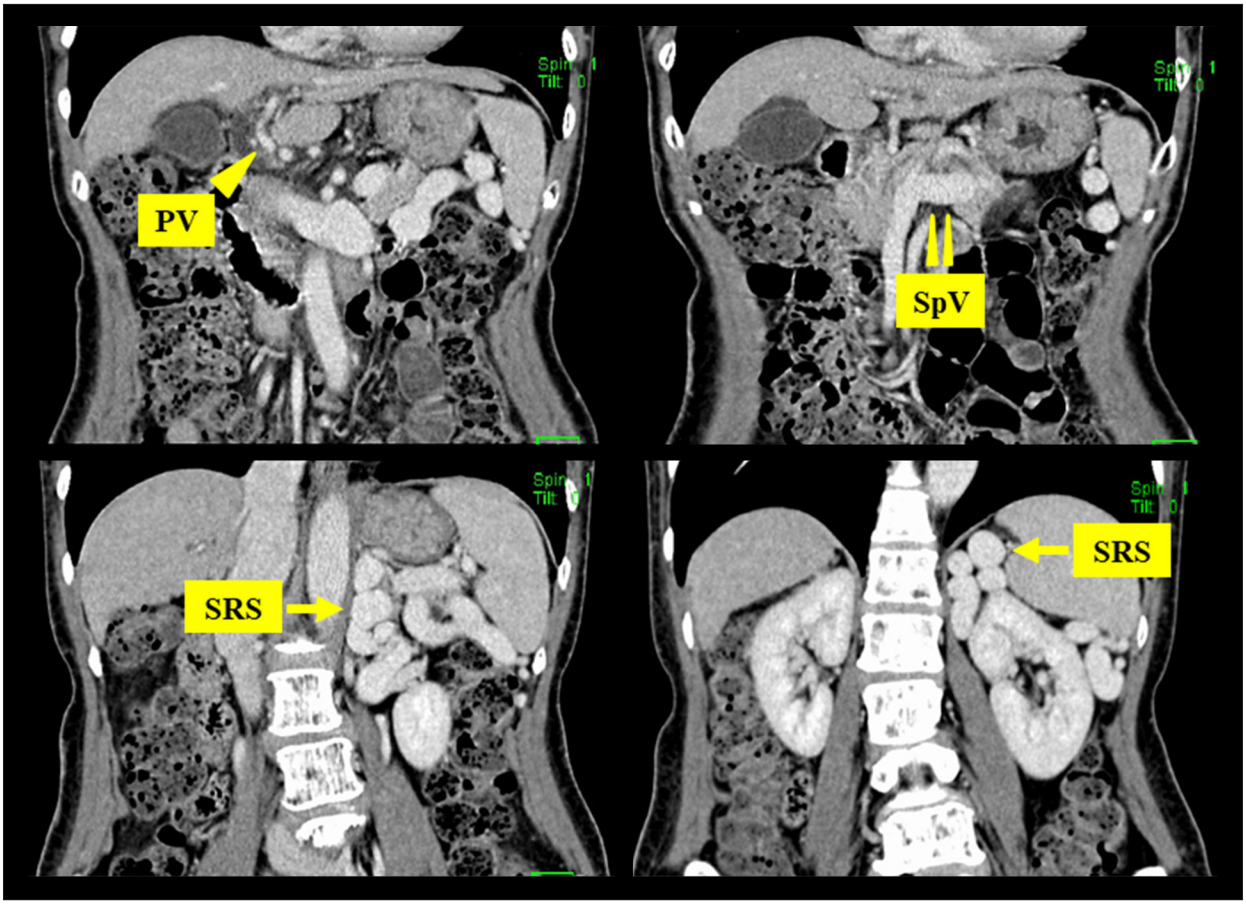

Figure 1. CE-CT before BRTO. Pre-BRTO CE-CT revealed significant liver atrophy (434.7 cm^3), severe portal vein constriction (6.2 mm), severe splenic vein dilation (14.2 mm), and the development of a giant splenorenal shunt (20.1 mm). CE-CT – contrast-enhanced computed tomography; BRTO – balloon-occluded retrograde transvenous obliteration; PV – portal vein; SpV – splenic vein; SRS – splenorenal shunt.

Case Report

A woman in her late 60s, who had achieved a sustained viral response after the eradication of hepatitis C virus by interferon therapy 10 years ago, had received treatment for liver cirrhosis at another hospital. She had a 4-year history of multiple hospital admissions for hepatic encephalopathy. Her medical regimen to control encephalopathy included maximally tolerated daily lactulose/lactitol and branched chain amino acid drug administration with an add-on of selective intestinal decontamination using rifaximin. She had never taken psychoactive substances that may have induced hepatic encephalopathy such as benzodiazepines, anticholinergics, and opiates. She was referred for liver transplantation but refused this option. Subsequently, she was referred to our department for a second opinion.

Table 1 presents her blood biochemical examination results at admission. Her condition was extremely serious, with a Child-Pugh score of 11, MELD-Na score of 16, and blood ammonia concentration of 199 µg/dL. Contrast-enhanced computed tomography (Figure 1) revealed significant atrophy of the liver (434.7 cm^3), severe constriction of the portal vein (6.2 mm), and severe dilation of the splenic vein (14.2 mm), together with the development of a giant splenorenal shunt (20.1 mm). Her LS was 21.5 kPa, and her condition was not expected to improve with pharmacotherapy. Therefore, after a sufficient explanation of the surgical procedures that included potential postprocedural complications, consent was obtained from the patient and her family, and BRTO was then scheduled with the aim of improving both the intractable encephalopathy and hepatic function and prolonging her vital prognosis.

Prior to treatment, the balloon occlusion test was applied to estimate the elevation of portal venous pressure following the BRTO procedure. Balloon occlusion induced an increase in the wedged hepatic venous pressure from 15.8 to 22.1 mmHg and an increase in the hepatic venous pressure gradient from 11.4 to 17.3 mmHg. Subsequently, BRTO was performed using 7 mL of 5% ethanolamine oleate with iopamidol. Figure 2 presents

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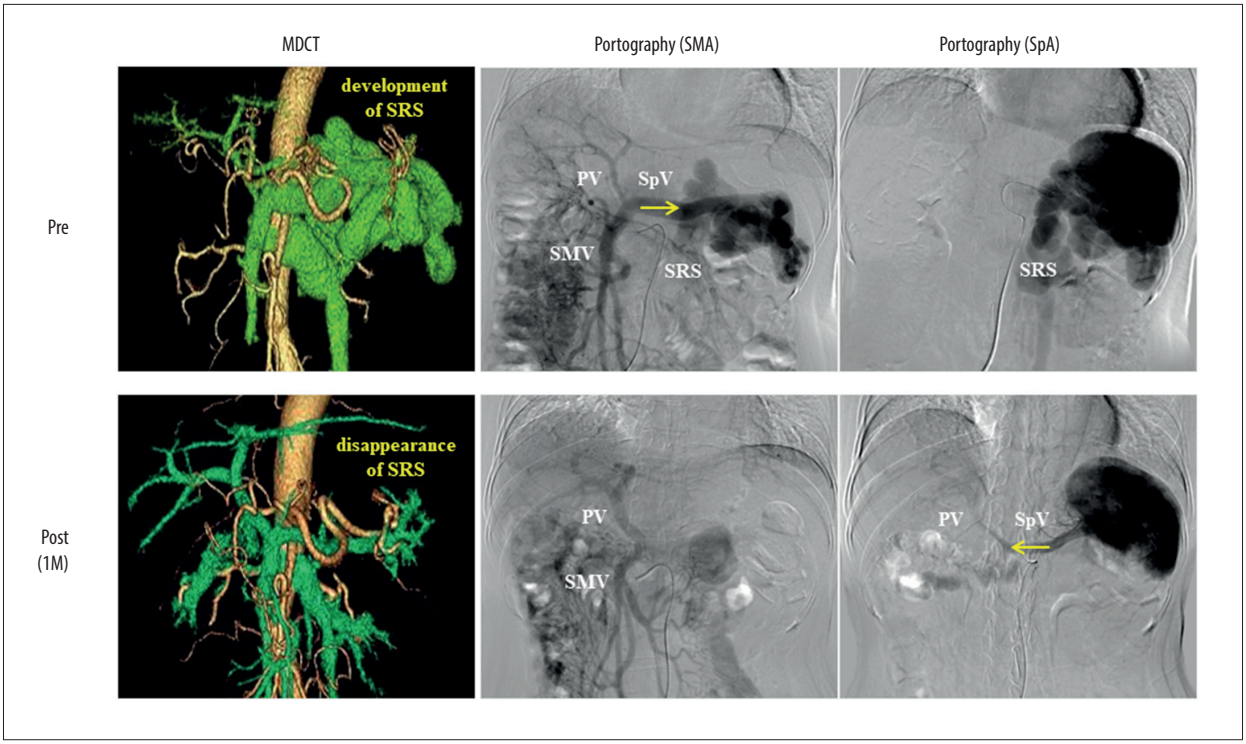

Figure 2. MDCT and indirect portography images obtained through the SMA and SpA before and 1 month after BRTO. MDCT images obtained before (**upper left panel**) and after (**lower left panel**) BRTO demonstrated that the procedure caused the complete disappearance of the SRS. Indirect portography through the SMA during the venous phase of superior mesenteric angiography before BRTO depicted contrast medium in the SMV and PV, which drained hepatofugally toward the SRS via the SpV (**upper middle panel**). Indirect portography through the SMA after BRTO revealed that the SMV flow entered the liver via the PV; consequently, the SpV and SRS were not visible (**lower middle panel**). Indirect portography through the SpA during the venous phase of splenic angiography before BRTO depicted contrast medium in the SpV of the splenic hilum, which communicated with the left renal vein via the SRS (**upper right panel**). Indirect portography through the SpA after BRTO demonstrated that all venous blood in the SpV flowed hepatopetally into the PV; consequently, the SRS was not visible (**lower right panel**). The arrows indicate the direction of the splenic venous flow. MDCT – multi-detector row computed tomography; SMA – superior mesenteric artery; SpA – splenic artery; SRS – splenorenal shunt; PV – portal vein; SMV – superior mesenteric vein; SpV , splenic vein; 1 M – 1 month.

changes in the portal-splenic vein hemodynamics induced by BRTO at 1 month postoperatively. Preoperatively, most of the superior mesenteric venous blood flow drained hepatofugally toward the splenorenal shunt via the splenic vein. After shunt occlusion, however, almost all blood flowed into the liver via the portal vein. Moreover, the splenic venous return, which had flowed into the systemic circulation via the splenorenal shunt pre-BRTO, flowed hepatopetally into the portal vein post-BRTO.

Table 1 lists the changes in various test results up to 1 year after BRTO. The patient's Child-Pugh and MELD-Na scores decreased dramatically at 1 month postoperatively, and this status was maintained for 1 year postoperatively. The various parameters indicate improvements in the overall hepatic synthesis and metabolism capacity and marked reductions in the levels of hepatic fibrosis markers. Moreover, her portal venous blood flow and liver volume increased significantly. Although her LS had increased at 1-month post-BRTO, this parameter declined steadily thereafter. During a 1-year postoperative follow-up, we observed no ascites, pleural effusion, or esophagogastric varices, and no relapse of hepatic encephalopathy. During this time, we reduced her medication use from 8 drugs taken preoperatively to 3. Her postoperative progress was uneventful and good.

Finally, we compared the pre-BRTO clinical characteristics and laboratory data (Table 2) and the post-BRTO Child-Pugh and MELD-Na scores over time (Figure 3) of the present patient, a low-LS case, and another high-LS case with a Child-Pugh score of 11, MELD-Na score of 16, and LS of 46.4 kPa pre-BRTO. The patients differed only in their magnitude of preoperative LS, cause of cirrhosis and procedural indication. In contrast to the high-LS case, the present patient with low pre-BRTO LS exhibited marked improvements in both scores at 1, 6, and 12 months post-BRTO.

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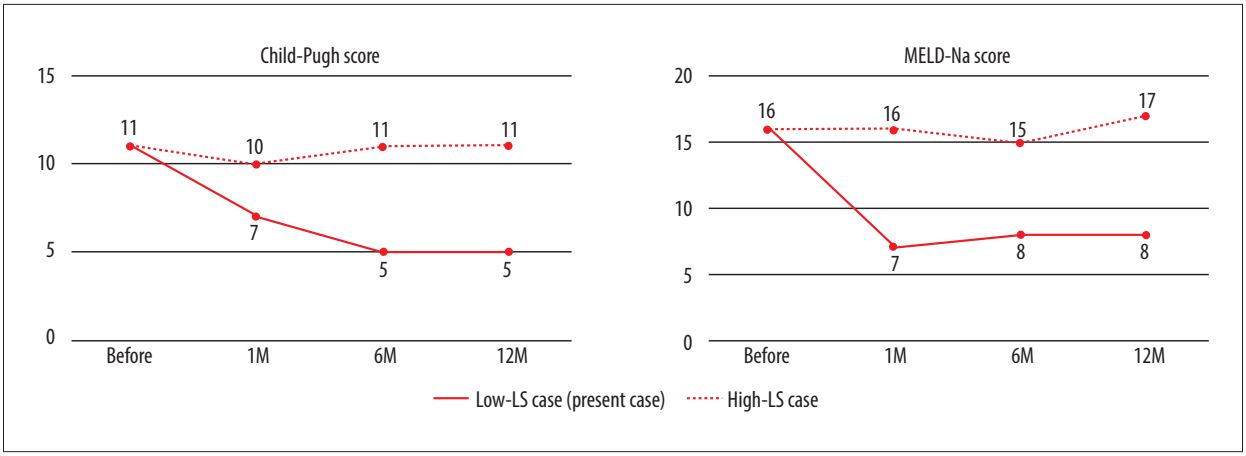

Figure 3. Comparison of changes in the Child-Pugh and MELD-Na scores over time after BRTO in the present patient with low pre-BRTO LS and in another patient with high pre-BRTO LS. The present patient with low LS exhibited marked improvements in both the Child-Pugh and MELD-Na scores at 1, 6, and 12 months after BRTO, in contrast to the patient with high LS. MELD-Na – Model for End-Stage Liver Disease-Sodium; BRTO – balloon-occluded retrograde transvenous obliteration; LS – liver stiffness; M – month.

Table 2. Comparison of pretreatment clinical characteristics and laboratory data between the low-liver stiffness case and high-liver stiffness case.

	Low-LS case	High-LS case
LS (kPa)	21.5	46.4
Age (years)	67	62
Sex	Female	Female
Cause of cirrhosis	HCV (post-SVR)	NASH
Procedural indication	Encephalopathy	Gastric varices
Child-Pugh score	11	11
MELD-Na score	16	16
Total bilirubin (mg/dL)	2.1	2.6
Albumin (g/dL)	2.7	2.7
Creatinine (mg/dL)	0.59	0.44
Sodium (mmol/L)	140	141
PT (%)	36.6	37.2
PT-INR	1.80	1.84

LS – liver stiffness; HCV – hepatitis C virus; SVR – sustained viral response; NASH – non-alcoholic steatohepatitis; MELD-Na – Model for End-Stage Liver Disease-Sodium; PT – prothrombin time; INR – international normalized ratio.

Discussion

The term "portosystemic shunt syndrome," which was coined by Kumamoto et al., refers to a gradual decline in liver function due to the presence of large spontaneous PSSs. This syndrome is reflected by progressive changes in the Child-Pugh score. Kumamoto and colleagues stated that PSS occlusion could inhibit this decline in the hepatic functional reserve and improve the long-term vital prognoses, thus indicating a functional protective role for BRTO [4]. Saad et al. elaborated this concept further by describing a complete syndrome that comprised clinical and imaging findings indicative of hepatic encephalopathy, hepatic function, hepatic atrophy, vanishing portal branches, and portal vein thrombosis [9].

Our previous study demonstrated that patients with encephalopathy showed more dramatic hemodynamic changes in the portal-splenic venous system following shunt occlusion compared with those with gastric varices, leading to more significant reductions in both the Child-Pugh and MELD-Na scores in the former patient group [7]. In addition, we previously reported that transient elastography provides a useful measure of LS that can predict improvements in the MELD-Na score post-BRTO [8]. Accordingly, we encourage the use of preprocedural LS to predict the postprocedural hepatic function and long-term outcomes of portal hypertension patients undergoing BRTO. In reference to other similar studies, we previously stated that an LS value of approximately 21–23 kPa might represent a "point of no return" in relation to the post-procedural recovery of hepatic function and extension of vital prognosis in patients with advanced chronic liver disease [10,11]. In other words, liver failure can be considered a reversible pathology controllable by PSS occlusion in cases mainly attributable to the advanced development of PSSs, as in our case with a low LS, rather than hepatic parenchymal cell dysfunction. This is supported by the intact hepatocyte theory [12,13]. Importantly, in this case, Child-Pugh classification was converted from C to A

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by PSS occlusion only. There were no severe complications due to elevated portal venous pressure following BRTO during the follow-up period and her medication use was reduced from 8 drugs to 3 with uneventful postoperative progress during this time. Overall, this case indicates the clinical benefit of BRTO, not only on patients' clinical outcomes, but also on economy of medical supplies. Consistent with the concept of "portal-systemic encephalopathy" as proposed by Sherlock et al. [14], we herein propose a novel concept, "portal-systemic liver failure," to describe liver failure with a non-stiff liver and giant PSSs, as seen in the present case. As shown in Table 2 and Figure 3, the post-PSS occlusion clinical courses of patients with a low and high LS differed significantly, despite the application of technically similar BRTO procedures for functionally similar decompensated cirrhosis and anatomically similar shunt formations. This observation indicates that liver failure was reversible in the former case but irreversible in the latter case.

We further note that an increased LS at 1 month postoperatively may reflect an enlarged liver due to an increased portal flow volume after BRTO. In our case, however, this value began to decrease after 1 month postoperatively, although the portal venous blood flow and liver volume leveled out. The concurrent marked reductions in various fibrosis markers, including the 7S domain of type IV collagen and Mac-2 binding protein glycosylation isomer, suggests that the BRTO-mediated correction of the portal-splenic vein hemodynamics also improved the hepatic fibrosis. Based on previous reports [15,16], we speculate that the shear stress-induced release of nitric oxides into hepatic circulation, a consequence of increased portal flow volume after BRTO, might not only contribute to a reduction in hepatic fibrosis but might also induce liver regeneration.

This case study verifies findings from our previous studies demonstrating clinical benefit of BRTO in improving hepatic function and outcomes in patients with a low LS measured by transient elastography and with procedural indication of encephalopathy. To the best of our knowledge, this is the first report specifically to evaluate the effectiveness of PSS occlusion on hepatic fibrosis in addition to hepatic functional reserve in patients with decompensated liver cirrhosis undergoing BRTO. However, the study's limitation of data being derived from only one case should be considered when interpreting the results. In our future work, we aim to clarify this mechanism during the post-treatment clinical course. Finally, in addition to the present case, much larger and longer prospective cohort studies are necessary to validate our previous retrospective studies.

Conclusions

BRTO could potentially prolong the prognosis of patients with "portal-systemic liver failure" by improving the hepatic reserve and fibrosis. Thus, this technique may serve as a bridging therapy prior to liver transplantation or as an alternative to transplantation for cases of liver failure with low LS and refractory encephalopathy, similar to the present case.

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Department and institution where work was done

This clinical work was done at the Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine.

Conflicts of interest

None.

References:

1. Kanagawa H, Mima S, Kouyama H et al: Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol, 1996; 11: 51–58
2. Hirota S, Matsumoto S, Tomita M et al: Retrograde transvenous obliteration of gastric varices. Radiology, 1999; 211: 349–56
3. 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
4. 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
5. 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
6. Imai Y, Nakazawa M, Ando S et al: Long-term outcome of 154 patients receiving balloon-occluded retrograde transvenous obliteration for gastric fundal varices. J Gastroenterol Hepatol, 2016; 31: 1844–50
7. 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
8. Ishikawa T, Sasaki R, Nishimura T et al: Liver stiffness measured by transient elastography as predictor of prognoses following portosystemic shunt occlusion. J Gastroenterol Hepatol, 2019; 34: 215–23
9. Saad WE: Portosystemic shunt syndrome and endovascular management of hepatic encephalopathy. Semin Intervent Radiol, 2014; 31: 262–65
10. Yamamoto A, Nishida N, Morikawa H et al: Prediction for improvement of liver function after balloon-occluded retrograde transvenous obliteration for gastric varices to manage portosystemic shunt syndrome. J Vasc Interv Radiol, 2016; 27: 1160–67

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11. Rajakannu M, Cherqui D, Ciacio O et al: Liver stiffness measurement by transient elastography predicts late posthepatectomy outcomes in patients undergoing resection for hepatocellular carcinoma. Surgery, 2017; 162: 766–74
12. Wood AJ, Villeneuve JP, Branch RA et al: Intact hepatocyte theory of impaired drug metabolism in experimental cirrhosis in the rat. Gastroenterology, 1979; 76: 1358–62
13. Kawasaki S, Imamura H, Bandai Y et al: Direct evidence for the intact hepatocyte theory in patients with liver cirrhosis. Gastroenterology, 1992; 102: 1351–55
14. Sherlock S, Summerskill WH, White LP, Phear EA: Portal-systemic encephalopathy; Neurological complications of liver disease. Lancet, 1954; 267: 454–57
15. Langer DA, Das A, Semela D et al: Nitric oxide promotes caspase-independent hepatic stellate cell apoptosis through the generation of reactive oxygen species. Hepatology, 2008; 47: 1983–93
16. Schoen JM, Wang HH, Minuk GY, Lautt WW: Shear stress-induced nitric oxide release triggers the liver regeneration cascade. Nitric Oxide, 2001; 5: 453–64

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]