Journal of Interventional Medicine 5 (2022) 138–142

Contents lists available at ScienceDirect

Journal of Interventional Medicine

journal homepage: www.keaipublishing.com/cn/journals/journal-of-interventional-medicine/

# Balloon-occluded retrograde transvenous obliteration with lauromacrogol sclerosant foam for gastric varices

Zhiyang Wu [a,d,1], Wei Wu [b,1], Cheng Tao [c,1], Qin Liu [a,d], Wenchang Li [a,d], Qinbing Wang [a,d], Wei Huang [a,d], Junwei Gu [a,d], Xiaoyan Fei [a,d], Zhongmin Wang [a,d,**], Xiaoyi Ding [a,d,*]

[a] Department of Interventional Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, China
[b] Department of Gastroenterology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, China
[c] Department of Radiology, University of Pittsburgh School of Medicine, Pittsburgh, 15213, Pennsylvania, USA
[d] Shanghai Clinical Research Center Member for Interventional Medicine, China

ARTICLE INFO

*Keywords:*
Gastric varices
Gastrorenal shunt
Balloon-occluded retrograde transvenous obliteration
Sclerotherapy

ABSTRACT

*Objectives:* To evaluate the safety and efficacy of balloon-occluded retrograde transvenous obliteration (BRTO) using lauromacrogol sclerosant foam for gastric varices (GVs) with gastrorenal venous shunts.
*Methods:* Data of GV patients treated with BRTO using lauromacrogol sclerosant foam in 2016–2020 were retrospectively analyzed along with procedural success rate, complications, and follow-up efficacy.
*Results:* A total of 31 patients were treated with BRTO. The sclerosant foam was prepared by mixing iodinated oil, lauromacrogol, and air at a 1:2:3 ratio. The BRTO procedure was successfully completed in 93.5% of patients. One patient was allergic to the lauromacrogol injection. A mild postoperative fever occurred in three patients. One patient experienced grand mal seizures after the procedure. There was no significant difference in the median Child-Turcotte-Pugh scores before versus after BRTO. Complete GV resolution was observed in 93.1% of patients. One patient underwent endoscopic treatment for the development of high-risk esophageal varices. Another patient underwent transjugular intrahepatic portosystemic shunt placement for the aggravation of ascites.
*Conclusions:* Lauromacrogol sclerosant foam is safe and effective in patients undergoing BRTO for GV.

## 1. Introduction

Gastrointestinal bleeding is a common clinical symptom, among which esophageal and gastric variceal bleeding (EGVB) are the usual causes. Based on the location of the varix in the stomach and its correlation to esophageal varices, esophageal and gastric varices (GVs) are divided into gastroesophageal varices (GEVs) and isolated GVs (IGVs).[1] The risk of bleeding from GVs is relatively low (10%–36% of cases).[2] However, the bleeding is usually significant and the disease is severe. Common prevention and treatment methods for EGVB include non-selective beta-blocker therapy, digestive endoscopy therapy, surgical therapy, liver transplantation, and interventional therapy. Multiple studies have demonstrated that balloon-occluded retrograde transvenous obliteration (BRTO) achieved satisfactory bleeding control rates for IGVs.[3,4] Some reports showed that BRTO is more effective at preventing future variceal rebleeding than transjugular intrahepatic portosystemic shunt (TIPS) in some cases.[5,6]

The American Association for the Study of Liver Disease guidelines recommend secondary prevention of GV bleeding as an alternative to TIPS.[7] Some reports suggest that BRTO be considered a first-line modality for treating GVs with portal hypertension.[8] Although BRTO has been widely conducted abroad for many years, it is not commonly used in China. Ethanolamine oleate is a widely used sclerosant for BRTO sclerosis of varicose veins in Japan; however, it is unavailable in China. The effect of lauromacrogol sclerosant foam in our center as a substitute sclerosant for BRTO is summarized below.

## 2. Materials and methods

### 2.1. Patients

This retrospective study was performed in accordance with medical

** Corresponding author. Department of Interventional Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, China.
* Corresponding author. Department of Interventional Radiology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, 200025, China.
*E-mail addresses:* wzm0722@hotmail.com (Z. Wang), dxy10456@rjh.com.cn (X. Ding).
[1] Zhiyuan Wu, Wei Wu and Cheng Tao contributed equally to this work.

https://doi.org/10.1016/j.jimed.2022.06.002
Received 30 March 2022; Received in revised form 23 May 2022; Accepted 6 June 2022
Available online 16 June 2022

ethics regulations, and our local institutional review board waived the requirement for informed consent. Written informed consent for the BRTO procedure was obtained from all patients or their families. Between January 2016 and December 2020, 31 consecutive patients with GVs underwent BRTO at our hospital.

The inclusion criteria were as follows[1]: diagnosis of gastrointestinal bleeding due to portal hypertension[2]; underwent preoperative gastroscopy to determine the variceal degree and classification; and[3] underwent portal vein computed tomography (CT) angiography to assess the presence of a gastrorenal venous shunt.

The exclusion criteria were as follows[1]: gastrointestinal bleeding with a non-portal hypertension cause such as peptic ulcers[2]; portal vein thrombosis[3]; uncontrolled esophageal variceal bleeding; and[4] serious impairment of important organs (e.g. heart, lung, kidney, and brain) or blood coagulation.

### 2.2. Preparation of sclerosant foam

The sclerosant foam was prepared by mixing iodinated oil (Yantai Luyin Pharmaceutical Co., Ltd., Shandong, China), lauromacrogol injection (Tianyu Pharmaceutical Co., Ltd., Shaanxi, China), and air at a 1:2:3 ratio, connecting two 50-mL syringes with three-way suction, and repeatedly mixing the solution 15 times.

### 2.3. BRTO procedures

Two interventional radiologists performed all of the BRTO procedures. The patients were placed in the supine position using the right femoral vein approach under local anesthesia. Guided by a 0.035-inch guide wire (Radifocus; Terumo, Tokyo, Japan), a 5F SIM II catheter (Boston Scientific Co., MA, USA) was selectively intubated to the gastrorenal shunt. Then, guided by a 0.035-inch stiff guidewire (Radiofocus; Terumo), a 7F occlusion balloon (Fogarty Thru-lumen embolectomy catheter; Edwards Lifesciences, CA, USA) was inserted into the gastrorenal shunt. For patients with a large inclination angle of the left renal vein toward the feet, an 8F introducer sheath (Flexor Check-Flo Introducer; Cook Medical, IN, USA) was exchanged before the Fogarty catheter was inserted. The gastric and renal shunts were entirely occluded by filling the balloon with a diluted contrast agent (iopamidol injection 370 mg I/mL; Shanghai Bracco Sine Pharmaceutical Co., Ltd., Shanghai, China), and retrograde transvenous venography was performed to evaluate the anatomy of the GVs and portosystemic collateral veins. If there were large draining collateral vessels, such as the inferior phrenic veins or pericardiophrenic veins, superselective catheterization with a microcatheter (Renegade STC-18; Boston Scientific) was performed into the collateral veins and then embolized with a microcoil (Interlock; Boston Scientific).

After the balloon inflation, repeat retrograde venography was performed to calculate the dosage of contrast agent required to reach the portal vein. Subsequently, sclerosant foam was slowly injected through the balloon catheter at the contrast agent dosage used in the previous venography. The filled balloon catheter was inflated overnight to occlude the gastric and renal shunts. The patients went back to the interventional operating room the next day, after which the remaining sclerosant foam was aspirated and the balloon slowly deflated. After manual angiography was performed to confirm complete occlusion of the varicose vein, the balloon catheter and long sheath were withdrawn under fluoroscopic guidance. A local compression dressing was applied at the puncture point of the right femoral vein. The patient's vital signs were monitored during the procedure until the catheter was fully withdrawn.

### 2.4. Follow-up

Enhanced abdominal CT and endoscopy were performed at 1 month, 6 months, and 1 year of follow-up. Varix sclerosis was defined as the absence of residual enhancement within the GVs on follow-up CT or disappearance of the GVs on endoscopy. Clinical success was defined as evidence that the varices did not recur and the absence of proof of rebleeding from the treated varices during follow-up. Complications were also recorded.

### 2.5. Statistical analyses

Descriptive and inferential statistics were used to analyze the data. The Kruskal-Wallis test was used to test the differences in variables before versus after the procedure because the data were not normally distributed. Statistical significance was set at $P < 0.05$. The data were statistically analyzed, and the graphs were generated using GraphPad Prism 8 (GraphPad Software, San Diego, CA).

## 3. Results

### 3.1. Demographic data

Thirty-one patients (22 men, nine women; age range, 39–75 years) were enrolled. Liver cirrhosis was caused by hepatitis B virus (58.1%). The patients' demographic data are presented in Table 1.

### 3.2. Varicose vein classification

GEV and IGV cases were classified according to preoperative gastroscopy and abdominal contrast-enhanced CT findings. Two patients (6.5%) were classified as GEV1, four (12.9%) as GEV2, six (19.4%) as GEV3, and 19 (61.3%) as IGV. All abdominal CT scans showed variable-sized GVs with a gastrorenal shunt.

### 3.3. Procedural success rate

The BRTO procedure was successfully completed in 29 (93.5%) patients (Fig. 1). Among the two unsuccessful cases, one was due to too many collateral vessels, and the other was due to the excessively large gastrorenal shunt and no suitable balloon catheter. Both patients underwent TIPS successfully. Collateral vessels were embolized in 11 patients (35.5%) with microcoils before the injection of the lauromacrogol sclerosant foam. The dosage of the lauromacrogol sclerosant foam was 15–50 mL (mean, 36.8 ± 10.8 mL).

### 3.4. Complications

One patient was allergic to lauromacrogol injection as evidenced by an intraprocedural decreased heart rate and blood pressure, which recovered after epinephrine treatment. The procedure was successfully

**Table 1**
Patient characteristics.

| | | |
|---|---|---|
| Age | Median | 61.5 years |
| | Range | 39–75 years |
| Gender | Male | 22 (71.0%) |
| | Female | 9 (29.0%) |
| Etiology | Alcohol related | 3 (9.7%) |
| | HBV related | 18 (58.1%) |
| | HCV related | 1 (3.2%) |
| | Primary biliary cirrhosis | 3 (9.7%) |
| | Schistosomiasis cirrhosis | 1 (3.2%) |
| | HBV and HCV related | 1 (3.2%) |
| | Alcohol and HCV related | 1 (3.2%) |
| | Cryptogenic cirrhosis | 3 (9.7%) |
| CTP score | A (5–6) | 19 (61.3%) |
| | B (7–9) | 11 (35.5%) |
| | C (10–15) | 1 (3.2%) |
| MELD score | ≤14 | 28 (90.3%) |
| | 15–18 | 2 (6.5%) |
| | >18 | 1 (3.2%) |

CTP score: Child-Turcotte-Pugh score. MELD score: Model for End-Stage Liver Disease score.

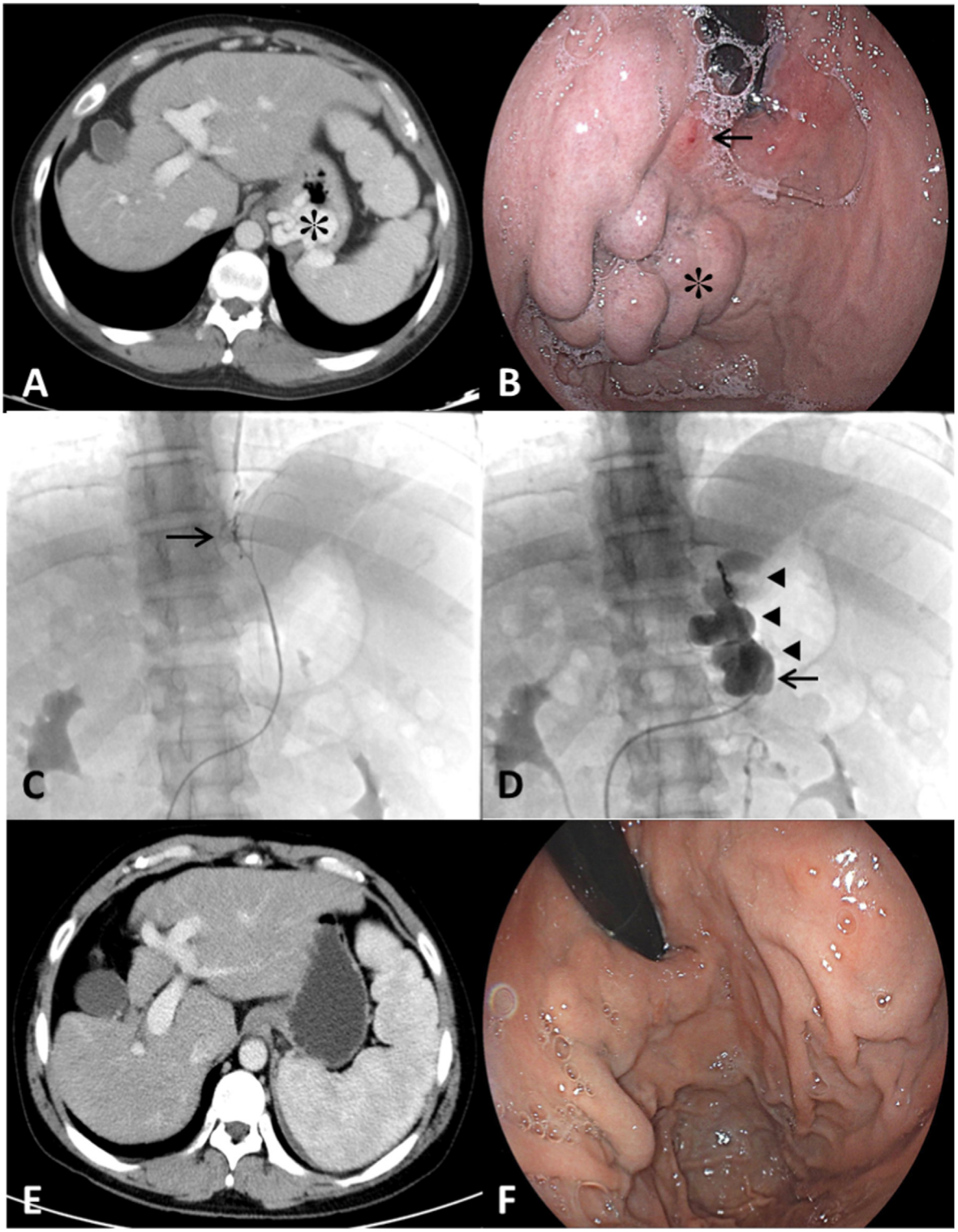


**Fig. 1.** A 40-year-old man presented with hepatitis B cirrhosis and upper gastrointestinal bleeding. A. Enhanced abdominal computed tomography (CT) performed prior to balloon-occluded retrograde transvenous obliteration (BRTO) demonstrated isolated gastric varices in the stomach fundus (black star). B. Endoscopy performed before BRTO showed large isolated gastric varices at the fundus (black star). Red whale signs (black arrow) were visible on the varices, indicating a high risk of bleeding. C. The collateral vessels were embolized with microcoils (black arrow). D. Fluoroscopic image showing that the gastrorenal shunt was occluded by a Fogarty balloon catheter (black arrow) and the varices filled with sclerosant foam (black arrowheads). E. Enhanced CT performed 1 year after BRTO showing complete variceal regression. F. Endoscopy performed 2 years after BRTO showing nearly complete variceal regression with a few small emerging collaterals.

completed. A mild postoperative fever occurred in three patients. After symptomatic treatment with antipyretics, the body temperature normalized the next day. One patient had a grand mal seizure 5 h after the procedure, and the symptoms disappeared after medication. Reexamination of the liver function 1–3 days post-procedure showed no changes. No procedure-related deaths occurred.

### 3.5. Postoperative follow-up

Hepatic functional reserve was assessed using the Child-Turcotte-Pugh score, and no significant differences before versus 6 months after the procedure were noted ($p = 0.54$) (Fig. 2).

By December 31, 2021, all patients were followed up for more than 1 year, with an average follow-up time of 508 days. Among the 29 patients who underwent successful BRTO, no rebleeding occurred in the treated varices during follow-up. CT portovenography or upper gastrointestinal endoscopy demonstrated complete resolution of the GVs in 27 patients (93.1%) (Fig. 1). One patient underwent endoscopic treatment for the development of high-risk esophageal varices. No further clinical episodes of upper gastrointestinal bleeding were noted. The other patient underwent TIPS for the aggravation of ascites.

## 4. Discussion

BRTO is a common treatment method for GVs with gastrorenal shunts. Here we performed BRTO with materials available in China with a high success rate and a low rebleeding rate.

BRTO was first reported in 1984 by Olsen et al.[9] and is the first-line treatment for GVs with a gastrorenal shunt in Japan.[2] Indications include GVs with a left gastrorenal shunt and refractory hepatic encephalopathy.[10] Contraindications included severe coagulation disorders, regional portal hypertension due to splenic venous embolism, portal thrombosis, and uncontrolled esophageal venous bleeding.

Simmons II balloon catheters, cobra-shaped balloon catheters, and micro-balloon catheters are commonly used.[3,11] Ethanolamine oleate and sodium tetradecyl sulfate are widely used sclerosants. However, these products are not readily available in China. Lauromacrogol injection, with the molecular formula $C_{12}H_{25}$ ($OCH_2CH_2$) nOH ($\bar{n} = 9$), was used in this study. It is often used to treat sclerosis in cases of vascular malformation. Its main side effects include fever, chest pain, decreased heart rate, stomach discomfort, and allergic reactions. In this study, lauromacrogol injection was mixed with iodized oil and air using the Tessari method[12] to form a sclerosant foam. Sclerosant foams have many advantages. First, the total sclerosant dosage was reduced. In this study, the average dosage of the lauromacrogol sclerosant foam was 36.8 mL. The sclerosant foam was prepared by mixing iodinated oil, lauromacrogol, and air at a 1:2:3 ratio. Even in patients with the highest foam dosage (50 mL), only 16.7 mL of lauromacrogol was injected. In addition, before balloon catheter removal, as much of the residual sclerosant as possible was withdrawn to avoid large amounts of embolism from entering the blood circulation.[13] Second, it is more effective to contact the vascular endothelium by increasing the surface area. Third, the foam could diffuse completely in varicose veins with better flowability. The results showed that the varicose veins were sclerotic in 93.1% of the cases during follow-up.

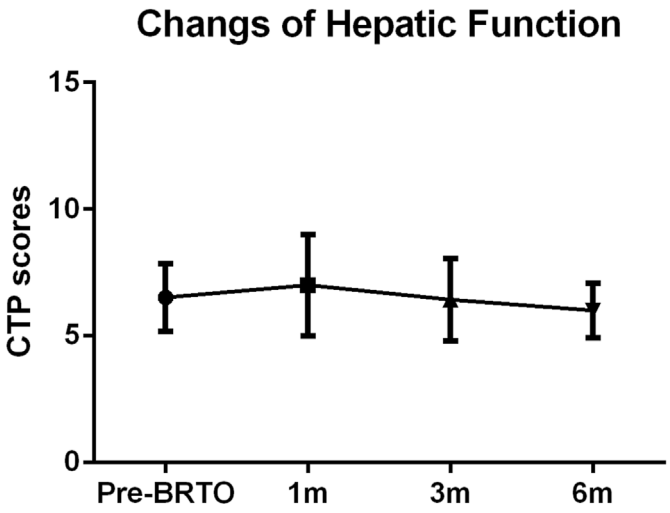


**Fig. 2.** Changes in hepatic function. Child-Turcotte-Pugh scores before and 1, 3, and 6 months after BRTO were 6.5 ± 1.3, 7.0 ± 2.0, 6.4 ± 1.6, and 6.0 ± 1.1, respectively. The change was insignificant ($p = 0.54$).

The success rate of BRTO is higher in patients with clearly defined gastrorenal shunts. In this study, 93.5% of the patients completed the BRTO procedure. Collateral vessels require embolization[14] or "downgrading".[15] In our study, large collateral vessels were embolized using microcoils. No sclerosant leakage into the systemic circulation was observed. Balloon catheters of an appropriate diameter should be selected to avoid sclerosant backflow. Since only the Fogarty balloon catheter could be used in our hospital, occlusion failed in one patient with an excessively large gastrorenal shunt despite maximum balloon inflation. Of course, other methods such as coils could be used for the occlusion. The patient ultimately chose TIPS.

The complications of BRTO are primarily temporary and self-limited and mainly include upper abdominal and back pain, increased portal pressure, ascites, pleural effusion, pulmonary embolism, nausea, elevated blood pressure, and abnormal liver and kidney function.[13] BRTO had minimal effects on the liver function in this group of patients. Increased portal vein pressure after BRTO is likely to exacerbate esophageal varices, which requires attention. In the group of cases reported by Watanabe et al. esophageal varices worsened in 21.2% of patients.[16] Imai et al. reported that the cumulative exacerbation rates of esophageal varices at 1, 3, and 5 years were 13%, 20%, and 27%, respectively.[17] Elevation of the hepatic venous pressure gradient and spleen stiffness after BRTO might be useful for predicting the exacerbation of esophageal varices.[18] In this study, the postoperative esophageal varices of one patient progressed significantly and required endoscopic treatment.

BRTO was more effective than endoscopic cyanoacrylate injection in a randomized controlled trial to prevent GV rebleeding with similar complications and mortality rates.[19] BRTO has a favorable effect on long-term hepatic functional reserve.[20] Comparisons between BRTO and TIPS have always been controversial. A retrospective study by Lee et al. showed that cumulative rebleeding rates after BRTO (8.6% at 1 year; 22.7% at 3 years) were significantly lower than those after TIPS (19.8% at 1 year; 48.2% at 3 years; $p = 0.006$).[21] A meta-analysis by Wang et al. showed that BRTO provided more benefits to patients with a higher overall survival rate and lower rebleeding rate.[5] In another retrospective study, BRTO appeared to be an effective method of treating isolated GVs with outcomes and complication rates similar to those of TIPS with a covered stent but with a lower hepatic encephalopathy rate.[22] In the present study, BRTO showed a sound clinical effect. Complete GV resolution was demonstrated in 93.1% of patients, and no further clinical episodes of upper gastrointestinal bleeding occurred. However, one patient underwent TIPS for ascites aggravation. However, owing to the lack of extensive sample data from prospective randomized controlled trials, the long-term efficacies of BRTO and TIPS require further data accumulation.

Another advantage of BRTO is that it is less expensive than TIPS. However, if too many collateral vessels require embolization, this advantage may not be obvious. In our study, the BRTO procedure failed in one patient because of the large number of collateral vessels. According to angiographic images, more than 20 controllable microcoils were needed to completely embolize all collateral vessels, which would lead to a high cost. Therefore, we discontinued the BRTO procedure and switched to TIPS treatment, which is relatively inexpensive.

The shortcomings of this study are that it was not a prospective

controlled study, its sample size was small, and some patients were lost to regular follow-up during the coronavirus disease 2019 crisis. More cases are needed to accumulate data, especially when comparing BRTO and TIPS.

In conclusion, the current literature and our study suggest that BRTO is especially suitable for GVs with a gastrorenal shunt using lauromacrogol sclerosant foam. With fewer complications, satisfactory variceal sclerosis rates, a low rebleeding rate, and a relatively low cost, BRTO is worthy of application and promotion.

## Funding

This work was funded by the National Natural Science Foundation of China (62173223), Shanghai Municipal Key Clinical Specialty (grant number shslczdzk06002), and Shanghai Clinical Research Center for Interventional Medicine (19MC1910300).

## Declarations

This retrospective study was performed in accordance with the medical ethics regulations. Written informed consent was obtained from all participants. The ethics committee approved all experimental protocols of the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine.

## Each author's degrees

Zhiyuan Wu, Wei Wu, Cheng Tao, Qin Liu, Wenchang Li, Qinbing Wang, Wei Huang, Junwei Gu, Xiaoyan Fei, Zhongmin Wang, Xiaoyi Ding.

## Declaration of competing interest

The authors declare that they have no competing interests.

## References

1. Sarin SK. Long-term follow-up of gastric variceal sclerotherapy: an eleven-year experience. *Gastrointest Endosc*. 1997;46:8–14.
2. Kiyosue H, Mori H, Matsumoto S, et al. Transcatheter obliteration of gastric varices. Part 1. Anatomic classification. *Radiographics*. 2003;23:911–920.
3. Saad WE, Kitanosono T, Koizumi J, et al. The conventional balloon-occluded retrograde transvenous obliteration procedure: indications, contraindications, and technical applications. *Tech Vasc Intervent Radiol*. 2013;16:101–151.
4. de Franchis R, VI Faculty Baveno. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. *J Hepatol*. 2015;63:743–752.
5. Wang ZW, Liu JC, Zhao F, et al. Comparison of the effects of TIPS versus BRTO on bleeding gastric varices: a meta-analysis. *Can J Gastroenterol Hepatol*. 2020;2020, 5143013.
6. Yu Q, Liu C, Raissi D. Balloon-occluded retrograde transvenous obliteration versus transjugular intrahepatic portosystemic shunt for gastric varices: a meta-analysis. *J Clin Gastroenterol*. 2021;55:147–158.
7. Clements W, Barrett R, Roberts SK, et al. Balloon-occluded retrograde transvenous obliteration (BRTO) of gastric varices using foam sclerosant and a reduced balloon inflation time: feasibility and efficacy. *J Med Imaging Radiat Oncol*. 2020;64:490–495.
8. Paleti S, Nutalapati V, Fathallah J, et al. Balloon-occluded retrograde transvenous obliteration (BRTO) versus transjugular intrahepatic portosystemic shunt (TIPS) for treatment of gastric varices because of portal hypertension: a systematic review and meta-analysis. *J Clin Gastroenterol*. 2020;54:655–660.
9. Olson E, Yune HY, Klatte EC. Transrenal-vein reflux ethanol sclerosis of gastroesophageal varices. *AJR Am J Roentgenol*. 1984;143:627–628.
10. Takakusagi S, Shimizu M, Yokoyama Y, et al. Hepatitis C virus-associated decompensated liver cirrhosis with refractory hepatic encephalopathy successfully treated by balloon-occluded retrograde transvenous obliteration after sofosbuvir/velpatasvir. *Clin J Gastroenterol*. 2020;13:1303–1309.
11. Tanaka K, Osuga K, Higashihara H, et al. Triaxial micro-balloon system for balloon-occluded retrograde transvenous obliteration of gastric varices. *Cardiovasc Intervent Radiol*. 2021;44:1284–1285.
12. Saad WE, Nicholson D, Koizumi J. Inventory used for balloon-occluded retrograde (BRTO) and antegrade (BATO) transvenous obliteration: sclerosants and balloon occlusion devices. *Tech Vasc Interv Radiol*. 2012;15:226–240.
13. Hirota S, Matsumoto S, Tomita M, et al. Retrograde transvenous obliteration of gastric varices. *Radiology*. 1999;211:349–356.
14. Patel A, Fischman AM, Saad WE. Balloon-occluded retrograde transvenous obliteration of gastric varices. *AJR Am J Roentgenol*. 2012;199:721–729.
15. Fukuda T, Hirota S, Sugimoto K, et al. Downgrading" of gastric varices with multiple collateral veins in balloon-occluded retrograde transvenous obliteration. *J Vasc Interv Radiol*. 2005;16:1379–1383.
16. Watanabe M, Shiozawa K, Ikehara T, et al. Short-term effects and early complications of balloon-occluded retrograde transvenous obliteration for gastric varices. *ISRN Gastroenterol*. 2012;2012, 919371.
17. 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;31:1844–1850.
18. Takuma Y, Morimoto Y, Takabatake H, et al. Changes in liver and spleen stiffness by virtual touch quantification technique after balloon-occluded retrograde transvenous obliteration of gastric varices and exacerbation of esophageal varices: a preliminary study. *Ultraschall Med*. 2020;41:157–166.
19. Luo X, Xiang T, Wu J, et al. Endoscopic cyanoacrylate injection versus balloon-occluded retrograde transvenous obliteration for prevention of gastric variceal bleeding: a randomized controlled trial. *Hepatology*. 2021;74:2074–2084.
20. Waguri N, Osaki A, Watanabe Y, et al. Balloon-occluded retrograde transvenous obliteration for gastric varices improves hepatic functional reserve in long-term follow-up. *JGH Open*. 2021;5:1328–1334.
21. Lee SJ, Kim SU, Kim MD, et al. Comparison of treatment outcomes between balloon-occluded retrograde transvenous obliteration and transjugular intrahepatic portosystemic shunt for gastric variceal bleeding hemostasis. *J Gastroenterol Hepatol*. 2017;32:1487–1494.
22. Kim SK, Lee KA, Sauk S, et al. Comparison of transjugular intrahepatic portosystemic shunt with covered stent and balloon-occluded retrograde transvenous obliteration in managing isolated gastric varices. *Korean J Radiol*. 2017;18:345–354.