Balloon-occluded retrograde transvenous obliteration using foam sclerosants for gastric varices under CT or C-arm CT

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Purpose

Percutaneous transhepatic obliteration (PTO) [1], balloon occluded retrograde transvenous obliteration (B-RTO) [2], and dual balloon occlusion embolotherapy (DBOE) [3] as a combination of them have been shown to be successful techniques for the treatment of gastroduodenal varices or hepatic encephalopathy due to massive portosystemic shunts. However, liquid ethanolamine oleate (EO), the most commonly used sclerosing agent in these cases [2], may, in case of overdose, cause severe complications such as hemolysis [4], allergy, ARDS [5], and others.

Foam sclerotherapy has been used with great enthusiasm by surgeons, phlebologists, or angiologists for any kind of lower extremity varicose veins for more than 50 years [6,7]. Using foam in vivo, the sclerosing agent can be expected to remain along the venous wall for a longer duration than with liquid sclerosants, with substantially lower systemic spillage, provided that the foam has a viscous or creamy consistency [8].

Safe use of this technique requires good visualization of the foam during injection, and this issue has been addressed by introducing echosclerotherapy (ES), which, in combination with the advent of sclerosing foam, has constituted a therapeutic revolution in phlebology [9]. However, to visualize intraabdominal varices or vessels, CT is a theoretically better modality than ultrasound, which is disturbed by gastrointestinal gas. We report here our early clinical experience with B-RTO using foam sclerosants under CT or C-arm CT guidance. To our knowledge, this is the first report of this combined technique in this application.

Methods and Materials

This study was approved by our institutional review board; informed consent for this research, including collecting the clinical data and reporting the results of the study, was obtained.

Seventeen B-RTO procedures were performed between May 2005 and July 2009 in seventeen patients (Table 1 on page 3). The ten woman and seven men had a mean age of 65.2 years (age range, 51-83 years). Multidetector row CT (Fig. 1 on page ) or magnetic resonance (MR) imaging (Fig. 2 on page ) were performed to identify the target varicose veins or portosystemic shunt and to plan the access routes. Prior to the interventions, celiac and superior mesenteric arteriography was performed to evaluate visceral hemodynamics. For the B-RTO procedures, we followed the method of Kanagawa et al [2]. Briefly, a 5.2 or 6 French balloon catheter with an 11- or 20-mm balloon diameter [Terumo-Clinical Supply, Japan] was inserted from the right jugular
or femoral vein and wedged into the left inferior phrenic vein. At first, balloon-occluded transvenous venography (B-RTV, Fig. 3 on page ) was performed with the balloon inflated by air or diluted iodinated contrast medium. Foam EO (Fig. 4 on page ) was made by mixing 10 ml of 10% EO (Oldamin, MOCHIDA Pharmaceutical, Tokyo, Japan) with 10 ml of iodinated contrast medium (5% EOI) and 20 ml of air, and foam polidocanol was made by the mixture of 2 ml of 3% polidocanol (Polidocasklerol, ZERIA Pharmaceutical, Tokyo, Japan) and 8 ml of air; with both EO and polidocanol, the foam was formed by using a pumping method with two syringes on a three-way stopcock. After obtaining opacification of the target varicose veins, foam sclerosants were injected into the target varices until full occupation of the varices by the foam was observed (Fig. 5 on page ). During the balloon occlusion, CT (Fig. 6A on page, 6B on page ) or C-arm CT (AXIOM Artis FD system and DynaCT, Siemens, Erlangen, Germany) was performed to confirm the filling of the target vessels by the sclerosants. After confirming variceal thrombosis (Fig. 7 on page ) the catheter was retrieved and followed by CT (Fig. 8 on page ) and endoscopy. Sclerosing agents used in the foam included ethanolamine (EO) in the first two patients, polidocanol in nine patients, and both in six patients. The net total dose of sclerosing agents required to obliterate the target varicose veins and the dose of contrast media used for B-RTV were documented.

Images for this section:
**Fig. 1:** Table 1. Characteristics of patients. The gastric varices (GV) were classified based on gastroendoscopic criteria according to the system adopted in Japan; Lg-c: adjacent to the cardiac ring, Lg-f: separated from the cardiac ring, Lg-cf: extending from the cardiac ring to the gastric fundus. EV; esophageal varices, Tx.; treatments, LC; liver cirrhosis, C: type C virus, Alc; alcoholic, B; type B virus, ca. carcinoma, HCC; hepatocellular carcinoma, CCC; cholangiocellular carcinoma. PDL; polidocanol, EO; ethanolamine oleate, EOI; EO with iodine contrast media.
Fig. 2: Fig. 4. Foam ethanolamine oleate (EO) by pumping method. A. Foam EO is made by the mixture of 10mL of 10% EO (Oldamin, MOCHIDA Pharmaceutical, Tokyo, Japan) with 10mL of iodine contrast media (5%EOI) and 20mL of air. B. Foam EO on fluoroscopy.
Results

In all patients (Case 1; Fig. 1, 2, 3, 4, 5, 6, 7, 8, Case 3; Fig. 9 on page 10 on page 11 on page 12 on page 13 on page 14 on page 6, 15 on page 16 on page 17 on page 18 on page Case 8; Fig. 19 on page 20 on page 21 on page 22 on page 23 on page 9, 24 on page 25 on page 26 on page Case 13; Fig. 27 on page 28 on page 7, 29 on page 8, 30 on page 10), air mixed with the sclerosant remained contained in the target vessels on CT or C-arm CT during the procedures. Full thrombosis was confirmed on postcontrast CT one week after B-RTO except one (Case 12; Fig. 31 on page 32 on page 33 on page 34 on page 35 on page 36 on page ) recanalization (success rate 94.1%). In one patient (Case 16; Fig. 37 on page 38 on page 39 on page 40 on page ) air migrated into liver during B-RTO, but it was spontaneously absorbed without any hepatic infarction on postcontrast CT one week later. The doses of sclerosants used for B-RTO (6.3±1.1mL) were significantly (Fig. 41 on page p<0.01) smaller than the doses of contrast media used for B-RTV (22.9±3.5mL).

Images for this section:
Fig. 1: Fig. 14. B-RTO using `foam` polidocanol. The foam is identified as a negative contrast media into the iodine contrast media used B-RTV. 4mL of polidocanol mixed with 16mL of air was used.
Fig. 2: Fig. 28. B-RTV to B-RTO using double sclerosants. First B-RTV (A) does not opacify the gastric varices. After downgrading by coils (B; arrows) and small amount of ethanolamine oleate from a deeply advanced balloon catheter (C), the target gastric varices (D, E; GV) appear and foam polidocanol was injected (F).
Fig. 3: Fig. 29. C-arm CT during B-RTV (A-C) and B-RTO using double sclerosants (D-F). A, D; coronal, B, E; sagittal, C, F; axial reformations. Dorsal portion of the gastric varices (red arrows) and GR shunt are opacified by heavy ethanolamine oleate iodine contrast, while ventral portion of the varices are filled by light air bubbles (orange arrows). Note ethiodized accumulation (circle) into hepatocellular carcinoma after the previous transcatheter arterial chemoembolization.
**Fig. 4:** Fig. 23. Volume renderings from C-arm CT during B-RTV. A. frontal, B. right anterior oblique views. The target gastric varices (GV) is well visualized.
Fig. 5: Fig. 30. Postcontrast CT before (A) and one week after (B) B-RTO. The gastric varices (GV) are completely thrombosed. Note ethiodized accumulation (arrow) into hepatocellular carcinoma after the previous transcatheter arterial chemoembolization.
Conclusion

Since B-RTO was first introduced by Kanagawa et al [2] to embolize gastric varices through a gastrorenal shunt, satisfactory results have been reported for patients with gastric varices and hepatic encephalopathy [2, 10]. To date, B-RTO has been extensively applied in the past decade for the management of fundic gastric varices in several specialized centers. Because B-RTO is less invasive than surgical treatment, it can be performed on patients with poor hepatic function reserve or hemorrhagic diathesis [2, 10]. In addition, it can be used for emergency treatment to control bleeding from gastric varices. The efficacy of B-RTO for the treatment of gastric varices and hepatic encephalopathy has been reported in the 87% - 100% range and the relapse rate is as low as 0% - 10% [2, 10]. To select the appropriate technique for B-RTO, it is necessary to determine the volume of gastric varices and collateral veins. Hirota et al. [2] classified the degree of the gastric varices and collateral veins into five grades, according to the venographic findings obtained from B-RTV and reported that 22 of 50 (44%) patients needed second or third procedures to obliterate gastric varices completely. Nevertheless, repeated B-RTO is considered to be a burden for patients and results in longer hospitalization. In the present series, none of the patients required more than one procedure to achieve variceal thrombosis except for one (success rate 94.1%). To obliterate gastric varices completely at the first procedure, it is necessary (1) to reduce the blood flow of the feeding vein and/or (2) to obliterate the collateral veins more effectively. To achieve the former, partial splenic embolization or balloon occlusion of the splenic artery and coronary vein with a balloon catheter can be used. However, although partial splenic embolization can reduce the flow of the feeding veins, such as the short or posterior gastric vein, the procedure requires long hospitalization because of resultant high fever or abdominal pain. For the latter, collaterals can be occluded with use of metallic coils, absolute ethanol and stepwise injection of EO after selective catheterization [11]. However, the injected dose should be determined carefully because of possible severe and acute alcohol intoxication or a highly destructive effect on endothelial cells. Moreover, EO may cause several complications such as intravascular hemolysis [4] leading to renal dysfunction [12], allergic reaction possibly leading to cardiogenic shock [13], pulmonary embolization resulting in pulmonary infarction [14] or ARDS [5] following alveolar wall edema and lung congestion, etc. Because some of these complications are correlated with the amount of infused EO [15], total dosage should be minimized. Consequently, more effective and safe sclerosing agents or methods need to be developed.

Foam sclerotherapy has a long track record of success and safety for any kind of lower extremity varicose veins for more than 50 years [6-8]. As compared to the older, non-foamed, liquid sclerotherapy, foam offers the advantage of decreasing the injected dose as only the surface of the bubbles carries the active drug. This dose decrease has been associated with increased safety thanks to the lower dose of sclerosing agent that may spill into the central veins and systemic circulation [9]. Using foam, we could reduce the
amount of the sclerosants given to less than a third of the volume of contrast media used in B-RTV. That is, if we had used liquid EOI as in the traditional sclerotherapy technique, we would have injected a volume of liquid EOI equal (half net EO) to the volume of contrast media needed to fill the target varices. Moreover, when performing B-RTO, foam sclerosants tend to ascend immediately into the non-dependent target gastric varices which are located more ventral than the gastro-renal shunt, as opposed to heavy liquid sclerosants which remain in dependent location (i.e., dorsal in a supine patient). This may occasionally be very helpful in difficult B-RTO cases where vessels are too tortuous and the target gastric varices cannot be quite reached by the catheter: the foam can ascend from the more dorsal gastro-renal shunt into more ventral gastric varices and remain trapped in them as 'air-pocket', eventually leading to their thrombosis.

For sclerosing agents, we used initially a solution of EO and iodinated contrast foamed with an equal amount of air, and lately polidocanol and air at a 1:4 ratio; as the latter mixture is widely used for treatment of lower extremity varicose veins thanks to its lesser allergenic potential compared to EO and because its injection is painless [6-8]. In addition, replacement of blood by foamed polidocanol may minimize hemolysis, a classical complication of EO. Because intravenous administration of haptoglobin (a preventive measure against EO-induced hemolysis routinely adopted by Japanese authors) is not FDA-approved, the choice of polidocanol appears more appropriate in the USA. The drawback of using polidocanol highly diluted in air (and not mixed with iodinated contrast) is its poor visibility under fluoroscopy. Our only complication in this series can be retrospectively explained by this fact. During B-RTO, the gastric coronary vein was located more ventrally than the target gastric varices, hence facilitating migration of sclerosing foam into the portal vein beyond 'air-pocket' like gastric varices. Thus, excessive amount of foam should be avoided. Although the foam could be easily identified as a negative contrast agent after iodinated contrast had been given during previous B-RTV, CT may allow us optimal filling of foam sclerosants into the gastric varices during B-RTO. C-arm CT was deemed to provide sufficient visualization of air distribution, even despite its lower contrast and time resolutions than conventional CT.

In conclusion, B-RTO using foam sclerosants is feasible to treat gastric varices, allowed to reduce the amount of injected sclerosants with theoretically improved safety profile, and achieved a satisfactory technical success (variceal thrombosis) rate in a single procedure. CT or C-arm CT during the procedures is reliable to confirm the filling of the target vessels by foam sclerosants. Future research should be performed to confirm whether the decreased sclerosant dose provided by foam sclerotherapy results indeed in less hemolysis.

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Images for this section:
Fig. 1: Fig. 41. The volume comparison between the contrast media used for B-RTV and the net sclerosants used for B-RTO. The doses of sclerosants used for B-RTO (6.3±1.1mL) were significantly (p
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