Three benefits of microcatheters for retrograde transvenous obliteration of gastric varices

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Abstract

AIM: To evaluate the usefulness of the microcatheter techniques in balloon-occluded retrograde transvenous obliteration (BRTO) of gastric varices.

METHODS: Fifty-six patients with gastric varices underwent BRTOs using microcatheters. A balloon catheter was inserted into gastrorenal or gastrocaval shunts. A microcatheter was navigated close to the varices, and sclerosant was injected into the varices through the microcatheter during balloon occlusion. The next morning, thrombosis of the varices was evaluated by contrast enhanced computed tomography (CE-CT). In patients with incomplete thrombosis of the varices, a second BRTO was performed the following day. Patients were followed up with CE-CT and endoscopy.

RESULTS: In all 56 patients, sclerosant was selectively injected through the microcatheter close to the varices. In 9 patients, microcoil embolization of collateral veins was performed using a microcatheter. In 12 patients with incomplete thrombosis of the varices, additional injection of sclerosant was performed through the microcatheter that remained inserted overnight. Complete thrombosis of the varices was achieved in 51 of 56 patients, and the remaining 5 patients showed incomplete thrombosis of the varices. No recurrence of the varices was found in the successful 51 patients after a median follow up time of 10.5 mo. We experienced one case of liver necrosis, and the other complications were transient.

CONCLUSION: The microcatheter techniques are very effective methods for achieving a higher success rate of BRTO procedures.

Key words: Balloon-occluded retrograde transvenous obliteration; Gastric varices; Microcatheter; Portal hypertension; Ethanolamine oleate

INTRODUCTION

Balloon-occluded retrograde transvenous obliteration (BRTO) is a treatment for gastric varices that has a high success rate1-9. However, there are three major problems with BRTO procedures such as overdose of the sclerosant,
leakage of the sclerosant into the systemic circulation, and incomplete thrombosis of large gastric varices\[^6-9\]\[^6-9\] We introduced the microcatheter techniques\[^11-14\] in 1999 to solve these problems, and we have been using three major beneficial techniques for BRTO procedures such as selective injection of the sclerosant, microcoil embolization of collateral veins and additional injection of the sclerosant. Since 1999 we have collected a great deal of data and are now able to accurately report on the long-term results of these techniques in a large number of cases.

**MATERIALS AND METHODS**

BRTO using 2.9Fr microcatheters was performed in 56 patients with liver cirrhosis-related gastric varices between August 1999 and December 2008. The subjects consisted of 35 males and 21 females, with a mean age of 65.3 years (range: 33-83 years). Liver cirrhosis was associated with hepatitis B in 3 patients, hepatitis C in 29 patients, alcohol in 15 patients, and unknown factors in 9 patients. According to the Child-Pugh classification, liver function was evaluated as A in 19 patients, B in 31 patients, and C in 6 patients. Prophylactic BRTO was performed in 31 patients with large tumor-like gastric varices or growing varices in danger of rupture. Elective BRTO was performed in 12 patients with a history of hemorrhage related to gastric varices. Emergency BRTO\[^16,19\] was performed in 13 patients within 24 h after hematemesis or tarry stool. Informed consent for BRTO was obtained from all patients.

Gastric varices were confirmed by endoscopy. The presence and diameter of gastrorenal shunt or gastrocaval shunt were evaluated by contrast-enhanced computed tomography (CE-CT). An 8Fr sheath (Cobra type; Medikit, Tokyo, Japan) was inserted into the left renal vein or inferior vena cava through the right internal jugular vein or right femoral vein, and a 6Fr balloon catheter (Cobra type; Clinical Supply, Gifu, Japan) was inserted into the gastrorenal shunt or gastrocaval shunt. The balloon diameter was 13 or 20 mm. In patients with a shunt diameter of 13 mm or more, a balloon measuring 20 mm in diameter was used. A 2.9Fr microcatheter was navigated close to the gastric varices. A sclerosant, 5% ethanolamine oleate iopamidol (EOI), was infused slowly and intermittently through a microcatheter during balloon occlusion. 5% EOI was prepared by making a 20 mL solution consisting of 10 mL contrast medium and 10 mL of 10% ethanolamine oleate (Oldamin; Grelan Pharmaceutical, Tokyo, Japan). The infusion of 5% EOI was continued until the entire gastric varices and feeding veins were opacified. The mean volume of sclerosant (5% EOI) was 22.9 mL per one procedure (range: 1.5-47 mL). The balloon occlusion time ranged from 12 to 48 h. To fix the sheath and catheters, sterilized tape (Hogy Medical, Tokyo, Japan) was used. The next morning after the BRTO procedure, thrombosis of gastric varices was evaluated by CE-CT. In patients with incomplete thrombosis after the first BRTO, a second BRTO was performed the following day. After complete thrombosis of gastric varices was confirmed on CE-CT, all catheters were removed. To prevent renal damage due to EOI-induced hemolysis, 4000 units of haptoglobin (Mitsubishi Pharma, Osaka, Japan) was administered intravenously during and after the infusion of EOI in all patients\[^14,19\]. Patients were followed up with endoscopy and CE-CT 1 d, 1 wk and 1, 3, 6 mo after the procedure and every 6 mo thereafter.

**RESULTS**

In all (100%) of 56 patients, the sclerosant was selectively injected through the microcatheter close to the gastric varices (Figures 1 and 2). In 9 (16%) of 56 patients, microcoil embolization of dilated collateral veins was performed using the microcatheter (Figure 3). In 12 (21%) of 56 patients, CE-CT the next day after the first BRTO showed incomplete thrombosis of the varices, and additional injection of the sclerosant was performed in the second BRTO through the microcatheter which remained inserted overnight (Figure 4). Complete thrombosis of the varices was achieved in 51 of 56 patients after all BRTO procedures, and the remaining 5 patients showed incomplete thrombosis of the varices. Endoscopic treatments were performed in 4 of the 5 patients\[^20-24\], and a surgical treatment was performed in the other patient. No cases of recurrence or variceal bleeding of the gastric varices were found in the successful 51 patients after a median follow up time of 10.5 mo (range one day-7 years). Esophageal varices with red color sign appeared in 5 of the 51 patients\[^25-28\]. Red color sign indicates a high risk of variceal bleeding\[^29\]. These patients' varices were treated by endoscopic treatment.

Most complications were transient and minor. These include: hematuria due to the sclerosant (8 of 56 patients), high fever (8 of 56), abdominal pain (5 of 56), elevation of blood pressure during infusion of the sclerosant (3 of 56), pleural effusion (35 of 56), ascites (33 of 56)\[^30\], and extravasation of the sclerosant during the procedure (3 of 56). In the three patients with extravasation, BRTO was continued, and complete thrombosis of the varices was achieved in 2 patients. We experienced one case of liver necrosis after the BRTO procedure\[^31\]. No other major complications such as renal failure, pulmonary embolism, or acute respiratory distress syndrome (ARDS) were experienced.

**DISCUSSION**

Microcatheters have three major benefits in BRTO for gastric varices. The first benefit is a selective injection of the sclerosant through a microcatheter\[^30-31\]. Infusion of the sclerosant with a microcatheter, which is inserted close to the gastric varices, enables a decrease in the dose of the sclerosant, preventing sclerosant-related complications. We consider that the optimal volume of the sclerosant used for one BRTO procedure is 40 mL or less. To decrease the sclerosant volume of 5% EOI, 50% glucose solution may be infused before injection of 5% EOI during BRTO\[^32\].
Figure 1  Selective injection of the sclerosant. A: A microcatheter is navigated close to the gastric varices, and the sclerosant is selectively injected through the microcatheter (arrow); B: The gastric varices and gastrorenal shunt are fully filled with the sclerosant with contrast medium, and the afferent vein (arrow) is opacified; C: Contrast-enhanced computed tomography (CE-CT) before balloon-occluded retrograde transvenous obliteration (BRTO) shows gastric varices (asterisk); D: CE-CT one week after BRTO shows complete thrombosis of the varices (asterisk); E: Endoscopy before BRTO shows tumor-like varices (asterisk) in the fornix of the stomach; F: Endoscopy 3 mo after BRTO shows complete disappearance of the varices.

Figure 2  Selective injection of the sclerosant. A: A balloon catheter is inserted into the gastrocaval shunt. Balloon-occluded venography shows no gastric varices; B: The balloon catheter is advanced further into the shunt, and the sclerosant is selectively injected through the microcatheter which is navigated close to the gastric varices. The varices (asterisk) are opacified sufficiently; C: Contrast-enhanced computed tomography (CE-CT) shows the varices (asterisk) and a large amount of hematomas in the stomach; D: The gastrocaval shunt (arrow) flows into the inferior vena cava; E: CE-CT next day shows complete thrombosis of the gastric varices (asterisk) and the tip of the microcatheter (arrow) close to the varices; F: CE-CT shows the balloon catheter in the shunt (arrow); G: Endoscopy before balloon-occluded retrograde transvenous obliteration (BRTO) shows large gastric varices (asterisk) with a bleeding site (arrow); H: Endoscopy 3 mo after BRTO shows complete disappearance of the varices.
Figure 3  **Microcoil embolization of collateral veins.** A: Pericardiophrenic veins (arrows) develop as collateral draining veins; B: A microcatheter (arrow) is navigated into the pericardiophrenic vein and microcoil embolization is performed; C: The sclerosant is selectively injected through the microcatheter which is withdrawn a little, and the gastric varices are opacified sufficiently. Microcoils (arrow) from embolization and surgical clips from previous operation of gastric cancer (arrowhead) are seen; D: Contrast-enhanced computed tomography (CE-CT) before balloon-occluded retrograde transvenous obliteration (BRTO) shows gastric varices (asterisk); E: CE-CT next day after BRTO shows complete thrombosis of the varices (asterisk) and microcoils close to the varices (arrow).

Figure 4  **Additional injection of the sclerosant.** A: Fluoroscopic image obtained during the first balloon-occluded retrograde transvenous obliteration (BRTO) shows full opacification of the gastric varices and gastrorenal shunt; B: Fluoroscopic image obtained during the second BRTO (next day) shows partial opacification of the varices and shunt, suggesting residual varices (arrow) and thrombosis of the varices and shunt (arrowheads); C: Contrast-enhanced computed tomography (CE-CT) before BRTO shows large varices (asterisk); D: CE-CT after the first BRTO shows residual varices (arrow) in the lateral portion of the stomach. The microcatheter tip (circle) is in the gastrorenal shunt close to the varices; E: CE-CT after the second BRTO shows complete thrombosis of the varices (asterisk). The sclerosant with contrast medium (circle) is detected in the gastrorenal shunt; F: CE-CT 3 mo after BRTO shows complete disappearance of the varices; G: Endoscopy before BRTO shows bulky varices (asterisk); H: Endoscopy 3 mo after BRTO shows complete disappearance of the varices.
The second benefit is a microcoil embolization of dilated collateral veins\cite{33} using a microcatheter\cite{21-28,34-36}. Occlusion of collateral veins prevents renal failure, pulmonary embolism, and ARDS induced by leakage of the sclerosant into the systemic circulation. Haptoglobin was intravenously administered as a counteragent of ethanolamine oleate, which is a sclerosant that damages the endothelial cell of the vessel and induces thrombus formation in the vessel.

The third benefit is an additional injection of the sclerosant through the microcatheter that remained inserted overnight\cite{21-28}. To achieve complete thrombosis of gastric varices, the balloon occlusion time was prolonged from 30 min (original BRTO) to 12 h or more\cite{34-36}. After a complete thrombosis of gastric varices was confirmed on CE-CT done the next morning after the first BRTO, all catheters were removed. When complete thrombosis of gastric varices was not achieved, a second BRTO was performed, and additional sclerosant was injected through the microcatheter. Insertion of a microcatheter close to the gastric varices until the next day allows for an additional injection of the sclerosant into the varices through the microcatheter, even when occlusion of a shunt occurs.

Another minor benefit is that microcatheters can be a safer and more accurate guidance tool for balloon catheters than the 0.035 inch guidewires. The stiff guidewires sometimes induce venous damage. On the other hand, it’s easy to insert a soft microcatheter into the shunts and advance a balloon catheter into the shunts over the microcatheter and microguidewire, because we can check the position of the microcatheter tip by test injection of the contrast material.

In the Kanagawa et al\cite{21-28} on use of BRTO without the microcatheter technique, complete eradication of gastric varices was not achieved after a single BRTO procedure in 7 (22%) of 32 patients. This is compatible with our results that show 21% of patients with incomplete thrombosis of the varices and 16% of patients having microcoil embolization.

BRTO procedures for gastric varices may be difficult to conduct when varices lack a gastrorenal shunt\cite{21-28,34-36}. However, gastric varices without the gastrorenal shunt are rare.

We experienced one case of liver necrosis. It is supposed that the liver necrosis was due to leakage of the sclerosant into the portal vein through afferent veins. So we must be careful in order to prevent leakage of the sclerosant into the portal vein.

Esophageal varices with red color sign appeared in 5 patients\cite{21-28,34-36}. Occlusion of a gastrorenal shunt and/or gastrocaval shunt may have induced esophageal varices as another collateral route. Esophageal varices can be readily treated by endoscopic treatment. Therefore, the status of esophageal varices should be endoscopically checked at 6-month intervals after BRTO.

Three major beneficial techniques of microcatheters for BRTO of gastric varices are selective injection of the sclerosant, microcoil embolization of collateral veins and additional injection of the sclerosant. Microcatheters are useful for achieving a higher success rate of BRTO procedures.

**REFERENCES**

1. Kanagawa H, Mima S, Kouyama H, Gotoh K, Uchida T, Okuda K. Treatment of gastric fundal varices by balloon-occluded retrograde transvenous obliteration. *J Gastroenterol Hepatol* 1996; 11: 51-58
2. Koito K, Namieno T, Nagakawa T, Morita K. Balloon-occluded retrograde transvenous obliteration for gastric varices with gastrorenal or gastrocaval collaterals. *AJR Am J Roentgenol* 1996; 167: 1317-1320
3. Akahane T, Iwasaki T, Kobayashi N, Tanabe N, Takahashi N, Gama H, Isihii M, Toyota T. Changes in liver function parameters after occlusion of gastrorenal shunts with balloon-occluded retrograde transvenous obliteration. *Am J Gastroenterol* 1997; 92: 1026-1030
4. Sonomura T, Sato M, Kishi K, Terada M, Shioyama Y, Kimura M, Suzuki K, Kutsukake Y, Ushimi T, Tanaka J, Hayashi S, Tanaka S. Balloon-occluded retrograde transvenous obliteration for gastric varices: a feasibility study. *Cardiovasc Intervent Radiol* 1998; 21: 27-30
5. Hirota S, Matsumoto S, Tomita M, Sako M, Kono M. Retrograde transvenous obliteration of gastric varices. *Radiology* 1999; 211: 349-356
6. Nakai M, Sato M, Kawai N, Minamiguchi H, Tanihata H, Terada M, Takeuchi T, Masuda M, Yamada K, Iwamoto T, Horihata K. A case report of adult respiratory distress syndrome (ARDS) after balloon-occluded retrograde transvenous obliteration (BRTO) for gastric varices. *Jpn J Intervent Radiol* 1999; 14: 380-384
7. Kiyosue H, Matsumoto S, Onishi R, Okahara M, Hori Y, Yamada Y, Dono S, Mori H. Balloon-occluded retrograde transvenous obliteration (B-RTO) for gastric varices: therapeutic results and problems. *Nihon Igaku Hoshasen Gakkai Zasshi* 1999; 59: 12-19
8. Hwang SS, Kim HH, Park SH, Kim SE, Jung JI, Ahn BY, Kim SH, Chung SK, Park YH, Choi KH. N-butyl-2-cyanoacrylate pulmonary embolism after endoscopic injection sclerothera-
Sonoura T et al. Benefits of microcatheters for BRT0

py for gastric variceal bleeding. J Comput Assist Tomogr 2001; 25: 16-22

9 Shimoda R, Horiiuchi K, Hagiwara S, Suzuki H, Yamazaki Y, Kosone T, Ichikawa T, Arai H, Yamada T, Abe T, Takagi H, Mori M. Short-term complications of retrograde transvenous obliteration of gastric varices in patients with portal hypertension: effects of obliteration of major portosystemic shunts. Abdom Imaging 2005; 30: 306-313

10 Takaji R, Kiyosue H, Matsumoto S, Okahara M, Tanoue S, Kondo Y, Mori H. Partial thrombosis of gastric varices after balloon-occluded retrograde transvenous obliteration: CT findings and endoscopic correlation. AJR Am J Roentgenol 2011; 196: 686-691

11 Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y, Transcatheter obliteration of gastric varices: Part 2. Strategy and techniques based on hemodynamic features. Radiographics 2003; 23: 921-937; discussion 937

12 Takahashi K, Yamada T, Hyodo H, Yoshikawa T, Katada R, Nagasawa K, Absuno T. Selective balloon-occluded retrograde sclerosis of gastric varices using a coaxial microcatheter system. AJR Am J Roentgenol 2001; 177: 1091-1093

13 Sonomura T, Horihata K, Yamahara K, Dozai K, Toyonaga T, Hirota T, Sato M. Ruptured duodenal varices successfully treated with balloon-occluded retrograde transvenous obliteration: usefulness of microcatheters. AJR Am J Roentgenol 2003; 181: 725-727

14 Yoneda M, Inamori M, Iwasaki T, Akiyama T, Fujita K, Takahashi H, Abe Y, Kubota K, Ueno N, Shiba M, Abe A, Nagashima T, Inoue M, Nakajima A. Balloon-occluded retrograde transvenous obliteration for gastric varices with plural draining veins: effectiveness of coil embolization for collateral vessels. Digestion 2007; 75: 100

15 Sonomura T, Sahara S, Ono W, Sato M, Kawai N, Minamiguchi H, Nakai M, Kishi K. Usefulness of microcatheters inserted overnight for additional injection of sclerosant after initial balloon-occluded retrograde transvenous obliteration of gastric varices. Case Rep Gastroenterol 2011; 5: 534-539

16 Kitamoto M, Inamura M, Kamada K, Aikata H, Kawakami Y, Matsumoto A, Kuribara Y, Kono H, Shirakawa H, Nakashiki T, Itó K, Chayama K. Balloon-occluded retrograde transvenous obliteration of gastric fundal varices with hemmorhage. AJR Am J Roentgenol 2002; 178: 1167-1174

17 Arai H, Abe T, Shimoda R, Takagi H, Yamada T, Mori M. Emergency balloon-occluded retrograde transvenous obliteration for gastric varices. J Gastroenterol 2005; 40: 964-971

18 Hashizume M, Kitano S, Yamaga H, Sugimachi K. Haptoglobin to protect against renal damage from ethanolamine oleate sclerosant. Lanecat 1988; 2: 340-341

19 Miyoshi H, Ohshiba S, Matsumoto A, Takada K, Umegaki E, Hirata I. Haptoglobin prevents renal dysfunction associated with intravascular infusion of ethanolamine oleate. Am J Gastroenterol 1991; 86: 1638-1641

20 Oho K, Iwai T, Sumino M, Toyonaga A, Tanikawa K. Ethanolamine oleate versus butyl cyanocrylate for bleeding gastric varices: a nonrandomized study. Endoscopy 1995; 27: 349-354

21 Miyazaki S, Yoshida T, Harada T, Shigemitsu T, Takeo Y, Okita K. Injection sclerotherapy for gastric varices using N-butyl-2-cyanocrylate and ethanolamine oleate. Hepato-gastroenterology 1998; 45: 1135-1158

22 Ogawa K, Ishikawa S, Naritaka Y, Shimakawa T, Wagatsuma Y, Katsube A, Kajiwara T. Clinical evaluation of endoscopic injection sclerotherapy using n-butyl-2-cyanocrylate for gastric variceal bleeding. J Gastroenterol Hepatol 1999; 14: 245-250

23 Lo GH, Lai KH, Cheng JS, Chen MH, Chiang HT. A prospective, randomized trial of butyl cyanocrylate injection versus band ligation in the management of bleeding gastric varices. Hepatology 2001; 33: 1060-1064

24 Hong CH, Kim HJ, Park JH, Park DJ, Cho YK, Sohn CI, Jeon WK, Kim BI, Hong HP, Shin JH. Treatment of patients with gastric variceal hemorrhage: endoscopic N-butyl-2-cyanocrylate injection versus balloon-occluded retrograde transvenous obliteration. J Gastroenterol Hepatol 2009; 24: 372-378

25 Matsumoto A, Hamamoto N, Nomura T, Hongyu Y, Arisaka Y, Morikawa H, Hiraia L, Katsu K. Balloon-occluded retrograde transvenous obliteration of high risk gastric fundal varices. Am J Gastroenterol 1999; 94: 643-649

26 Choi YS, Lee JH, Shin DH, Song YB, Gwak GY, Choi MS, Koh KC, Paik SW, Yoo BC. Effect of balloon-occluded retrograde transvenous obliteration on the natural history of coexisting esophageal varices. J Clin Gastroenterol 2008; 42: 974-979

27 Tanigata H, Minamiguchi H, Sato M, Kawai N, Sonomura T, Takasaka I, Nakai M, Sahara S, Nakata K, Shirai S. Changes in portal systemic pressure gradient after balloon-occluded retrograde transvenous obliteration of gastric varices and aggravation of esophageal varices. Cardiovasc Intervent Radiol 2008; 32: 1209-1216

28 Elsamman MK, Fujiwara Y, Kameda N, Okazaki H, Tanigawa T, Shiba M, Tominaga K, Watanabe T, Oshibani N, Arafa UA, El-Sayed AA, Nakamura K, Arakawa K. Predictive factors of worsening of esophageal varices after balloon-occluded retrograde transvenous obliteration in patients with gastric varices. Am J Gastroenterol 2009; 104: 2214-2221

29 Idezuki Y. General rules for recording endoscopic findings of esophagogastric varices. (1991). Japanese Society for Portal Hypertension. World J Surg 1995; 19: 420-423; discussion 423

30 Cho SK, Shin SW, Yoo EY, Do YS, Park KB, Choo SW, Han H, Choo IW. The short-term effects of balloon-occluded retrograde transvenous obliteration, for treating gastric variceal bleeding, on portal hypertensive changes: a CT evaluation. Korean J Radiol 2007; 8: 520-530

31 Cho SK, Shin SW, Do YS, Park KB, Choo SW, Kim SS, Choo IW. Development of thrombus in the major systemic and portal veins after balloon-occluded retrograde transvenous obliteration for treating gastric variceal bleeding: its frequency and outcome evaluation with C.T. J Vasc Interv Radiol 2008; 19: 520-538

32 Yamagami T, Kato T, Hirota T, Yoshimatsu R, Matsumoto T, Nishimura T. Infusion of 50% glucose solution before injection of ethanolamine oleate during balloon-occluded retrograde transvenous obliteration. Australas Radiol 2007; 51: 334-338

33 Kiyosue H, Mori H, Matsumoto S, Yamada Y, Hori Y, Okino Y. Transcatheter obliteration of gastric varices. Part 1. Anatomic classification. Radiographics 2003; 23: 911-920

34 Ibukuro K, Mori K, Tsukiyama T, Inoue Y, Iwamoto Y, Tagawa K. Balloon-occluded retrograde transvenous obliteration of gastric varix draining via the left inferior phrenic vein into the left hepatic vein. Cardiovasc Intervent Radiol 1999; 22: 415-417

35 Kameda N, Higuchi K, Shiba M, Kadouchi K, Machida H, Okazaki H, Tanigawa T, Watanabe T, Tominaga K, Fujitaya Y, Nakamura K, Arakawa T. Management of gastric fundal varices without gastro-renal shunt in 15 patients. World J Gastroenterol 2008; 14: 448-453

36 Matsumoto T, Yamagami T, Nakamura N, Kato T, Hirota T, Yoshimatsu R, Nishimura T. Balloon-occluded retrograde transvenous obliteration of a gastric varix via the left inferior phrenic vein. Br J Radiol 2008; 81: e246-e248

37 Araki T, Hori M, Motosugi U, Sano K, Ishigame K, Nakajima H, Okada H, Araki T. Can balloon-occluded retrograde transvenous obliteration be performed for gastric varices without gastrorenal shunts? J Vasc Interv Radiol 2010; 21: 663-670

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