The History and Evolution of Balloon-occluded Retrograde Transvenous Obliteration (BRTO): From the United States to Japan and Back

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ABSTRACT

The concept of obliterating varices that complicate portal hypertension dates back to the 1970s, but its minimally invasive clinical utilization was probably lost with the advent of the transjugular intrahepatic portosystemic shunt (TIPS). The conception of retrograde obliteration of a gastroduodenal shunt via the left renal vein was reported by Olson et al from the University of Indiana. However, the definition, development, technical perfection, and clinical implementation of the balloon-occluded retrograde transvenous obliteration (BRTO) occurred in Japan (by Kanagawa et al and others). The BRTO-procedure is currently undergoing a renaissance in the United States particularly for patients who are not TIPS candidates.

KEYWORDS: History, BRTO, transvenous obliteration, varices, TIPS

Objectives: Upon completion of this article, the reader will be able to explain the development of the concept of BRTO, with a comparison with TIPS, and state why each procedure (TIPS vs BRTO) has developed geographically in the West versus the East, respectively.

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Balloon-occluded retrograde transvenous obliteration (BRTO) is a procedure that has become common practice in Japan and has become popular in South Korea for the management of gastric varices.^{1–31} Many erroneously believe that the procedure was conceived in

Japan,^{1–25} as the BRTO procedure has not been popular in the United States.^{1–31}

Here I discuss the conception and evolution of the BRTO procedure and update the status of BRTO in the United States.

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Management of Gastric Varices: Endoscopic, BRTO, and TIPS;

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Semin Intervent Radiol 2011;28:283–287. Copyright © 2011 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI: <http://dx.doi.org/10.1055/s-0031-1284454>.

ISSN 0739-9529.

CONCEPTION AND EVOLUTION OF THE BRTO PROCEDURE

Transvenous obliteration is an old idea that was practiced in the 1970s in the pretransjugular intrahepatic portosystemic shunt (TIPS) era as an interventional radiology procedure for the management of bleeding esophageal and gastroesophageal varices from a percutaneous transhepatic approach.^{32–36} These percutaneous transhepatic obliterations were mostly performed utilizing coils, Gelfoam, and/or sclerosants (such as absolute alcohol and 30–50% glucose solution) without utilizing occlusive balloons to modulate blood flow.^{32–36} These procedures, utilizing current terminology, are now referred to as percutaneous transhepatic obliteration (PTO)^{6,15,24,37,38}, which is a type of balloon-occluded antegrade transvenous obliteration (BATO; please see “Modifications of Transvenous Obliteration: Balloon-occluded Antegrade Transvenous Obliteration (BATO) and Alternative/Adjunctive Routes for BRTO” in this issue). The initial transhepatic obliteration experience in the 1970s was short lived due to relatively poor clinical success^{32–36} and possibly the advent of the TIPS procedure.

BRTO is performed by accessing the portosystemic gastroduodenal shunt via the left renal vein from a transjugular or transfemoral approach.^{1–3,39} Most authors refer to Kanagawa et al (1991–1993) as the originator of the BRTO procedure.¹ However, the first published document of an attempt at balloon-occluded sclerotherapy of the gastroduodenal shunt for the management of gastric varices was authored by Olson et al in 1984.³⁹ This is clearly 5 and 7 years prior to the practice and publications, respectively, of Kanagawa et al (1991–1993, respectively).¹ Olson et al utilized a transfemoral balloon occlusion catheter and absolute alcohol for the successful sclerosis attempt.³⁹ Embolic coils were also placed in the outflow gastroduodenal shunt.³⁹ The term used for the procedure was “transrenal-vein reflux ethanol sclerosis” and not BRTO.³⁹

Subsequently, Kanagawa et al revived the BRTO concept and developed the BRTO procedure in the early 1990s, coining the term “balloon-occluded retrograde transvenous obliteration” (B-RTO).¹ They utilized ethanolamine-oleate, an established upper endoscopic variceal sclerosant, which was unfamiliar to Western (European and American) interventional radiologists. Risks of this agent endovascularly include hemolysis, hemoglobinuria, and potentially hemoglobin-induced renal tubular dysfunction.^{2,3} The antidote of free hemoglobin is haptoglobin, which conjugates with it. Haptoglobin is available in Japan and is not available for human and commercial use in the United States. Consequently, the Japanese developed, refined, and clinically applied this procedure, making it viable and successful.^{1–25}

The hemolysis problem with ethanolamine oleate limits the usable sclerosant volume to 40 mL.^{2,3} This led

Japanese operators to resort to one of two strategies. The first strategy was to adopt a staged multisession treatment where the gastric varices and gastroduodenal shunt would be “lavaged” with 5% ethanolamine oleate with a volume limit of 20–30 mL. The patient would then return for a second and possibly a third session if the gastric varices were not completely obliterated.^{9,10,19,22,24} The second strategy was to use an adjunct sclerosant such as 50% glucose solution or absolute alcohol to keep the 5% ethanolamine oleate dose/volume to less than 40 mL.^{4,8,17,19}

Subsequently, American interventionalists introduced a new sclerosant: 3% Sotradecol, to perform the BRTO procedure in 2006–2007. This was due to the lack of the antidote (haptoglobin) for ethanolamine oleate in the United States as well as their unfamiliarity with ethanolamine oleate as an endovascular sclerosant. To the best of my knowledge, John Kaufman (Dotter Interventional Institute, Oregon Health Science Center, Portland, OR) performed the first BRTO with 3% Sotradecol in October 2006 (Personal communication, Dr. John Kaufman, November 29, 2010). The mixture used by the Dotter Institute was 1 part lipiodol, 10 parts 3% Sotradecol, and 2 parts air. Independently, Anondo Stangl (Mount Sinai Hospital, New York, NY) and the combination of Warren Sweet and Alan Matsumoto (University of Virginia, Charlottesville, VA) performed BRTO procedures also using 3% Sotradecol in June 2007 (Mt. Sinai) and August 2007 (University of Virginia) (personal communications with Dr. Aaron Fischman, Mt. Sinai, NY, on March 31, 2011 and Dr. Alan Matsumoto, UVA, Virginia on March 3, 2010). The mixture used by both Mt. Sinai, NY and University of Virginia was 1 part lipiodol, 2 parts 3% Sotradecol, and 3 parts carbon dioxide. Since then, carbon dioxide has been replaced with air with the same mixture fractions. The resultant frothy blend or emulsion enabled the sclerosant to be delivered in larger volumes with smaller doses. In addition, the foam/froth percolates into the gastric varices and maximizes contact of the sclerosant with the endothelial wall (Personal communication, Dr. Alan Matsumoto, September 2010). This has caused some Japanese institutions to reconsider use of their ethanolamine oleate concoctions by mixing them with air to create a frothy consistency to the sclerosant with its desired sclerosant dose reduction (relative to volume) and the frothy percolative effect of the sclerosant.

UPDATE OF THE PRACTICE OF THE BRTO PROCEDURE IN THE UNITED STATES

There are two main hypotheses why BRTO has not been clinically practiced (until recently) in the United States. The first is the unfamiliarity of interventional radiologists in the United States with the well-described (in

Table 1 Status of the BRTO Procedure in the United States as of December 2010

United States Institution*	First BRTO Performed	Sclerosant Utilized	Number of BRTO-Procedures to Date [†]
Stanford University	2000	Gelfoam + EOI	15
Dotter Institute, OHSU	2006	3% STD + Lipiodol + Air	15
Rush University	2006	ETOH + Gelfoam + Coils	15
University of Virginia	2007	3% STD + Lipiodol + Air	35
MIR, Washington University, St. Louis	2008	3% STD + Lipiodol + Air	10

BRTO, Balloon-occluded retrograde transvenous obliteration; EOI, ethanolamine oleate; OHSU, Oregon Health Science University; MIR, Mallinckrodt Institute of Radiology, Washington University, St. Louis, MO. ETOH, Absolute alcohol; STD, Sotradecol.

*The data for this table is from personal communications in 2010 with Daniel Sze, M.D., Stanford University, Palo Alto, CA; John Kaufman, M.D., Dotter Institute, OHSU, Portland, OR; Hector Ferral, M.D., Rush University, Chicago, IL; Nael Saad, M.D., Mallinckrodt Institute of Radiology, Washington University, St. Louis, MO.

[†]Approximate number of BRTO procedures.

Japan and Korea) sclerosant, ethanolamine oleate. In addition, the lack of the antidote, haptoglobin (see above), concerned many radiology interventionalists. The second cause of the delayed utilization of BRTO in the United States is the belief that the best management of portal hypertension complications is through decompression and reduction of portal pressure. It is not, as is the case with the BRTO procedure, mere management of a particular complication (in this case potentially bleeding gastric varices) with the added risk of aggravating the portal hypertension and potentially having patients subsequently develop other complications of portal hypertension such as potentially bleeding esophageal varices and/or ascites. Balloon-occluded retrograde transvenous obliteration (BRTO) is known to cause aggravation of esophageal varices and may increase the risk of developing ascites (please see “Transjugular Intrahepatic Portosystemic Shunts (TIPS) versus Balloon-occluded Retrograde Transvenous Obliteration (BRTO) for the Management of Gastric Varices” in this issue). In addition (reinforcing the theory of decompression over sclerosis) the initial experience of transhepatic obliteration of gastroesophageal varices in Europe and the United States did not have a satisfactory technical, hemodynamic, or clinical success.^{32–36} The technical success varied from 54–88% with a rebleed rate of successful cases of 29–86% and an overall intent-to-treat clinical success rate of 25–31% and an image-based variceal recannulation of over 80%.^{32–34} (please compare with the BRTO results in “Balloon-occluded Retrograde Transvenous Obliteration (BRTO): Technical Results and Outcomes” and “Transjugular Intrahepatic Portosystemic Shunts (TIPS) versus Balloon-occluded Retrograde Transvenous Obliteration (BRTO) for the Management of Gastric Varices” in this issue).

To the best of my knowledge, the institution that has purposely pursued the practice of BRTO earliest in the United States was Stanford University. The first BRTO procedure performed at Stanford was in December 1999 and it was performed by Daniel Sze and Michael Dake utilizing a mix of Gelfoam and ethanolamine oleate (Personal communication with Dr. Daniel

Sze, December 17, 2010). In the following 7 years, other academic institutions in the United States started performing the BRTO procedure—probably prioritizing patients who were not TIPS candidates. These institutions included (and probably are not limited to): Rush University, Chicago, IL; Dotter Institute, Portland, OR; and the University of Virginia, Charlottesville, VA. Table 1 shows the five institutions in the United States that have the greatest experience in BRTO. This relatively recent development in the United States is probably because of the publication of favorable data out of Asia regarding BRTO outcomes, which have shown the relative safety and efficacy of the procedure.^{1–31} Furthermore, there is relatively new data accumulating from the United States and Europe regarding candidacy of patients for the TIPS procedure: patients with poor hepatic reserve (MELD >17–19) have been shown to do poorly with the TIPS procedure.^{40–44} This has possibly led to interventionalists managing these patients (non-TIPS candidates with poor hepatic reserve) to offer BRTO as an alternative therapy for gastric varices (please see “Transjugular Intrahepatic Portosystemic Shunts (TIPS) versus Balloon-occluded Retrograde Transvenous Obliteration (BRTO) for the Management of Gastric Varices” in this issue).

CONCLUSION

The concept of obliterating varices that complicate portal hypertension dates back to the 1970s. Its minimally invasive clinical utilization was probably lost with the advent of the transjugular intrahepatic portosystemic shunt (TIPS). The concept of retrograde obliteration of a gastroduodenal shunt via the left renal vein was that of Olson et al from the University of Indiana. However, the definition, development, technical perfection, and clinical implementation of the balloon-occluded retrograde transvenous obliteration (BRTO) procedure was by the Japanese (Kanagawa et al and subsequent others). The BRTO procedure has come full circle and is now gaining popularity in the United States, particularly for patients who are not TIPS candidates.

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