

ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Management of Gastric Varices Using Retrograde Transvenous Obliteration Procedures



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G&H When should retrograde transvenous obliteration be considered in the management of gastric varices?

EL Gastric varices are the second most common type of varices in patients with end-stage liver disease and develop in approximately 30% of patients with portal hypertension. Medical management should be the first line of treatment for gastric varices. If medical therapy fails, there are 2 interventional options: transjugular intrahepatic portosystemic shunt (TIPS) or retrograde transvenous obliteration (RTO). When and how to decide which procedure to perform should be determined at a multidisciplinary meeting that includes hepatologists, gastroenterologists, hepatic surgeons, and interventional radiologists. The comfort level of the operator should also be taken into account. Even though both TIPS and RTO are considered minimally invasive procedures, operators should not be performing these procedures without proper training. From the clinical assessment perspective, patients who have contraindications to TIPS, mainly a very high Model for End-Stage Liver Disease (MELD) score and uncontrolled hepatic encephalopathy, should not undergo the TIPS procedure. RTO is likely a better option for these patients. Some clinicians may think that TIPS and RTO are interchangeable, but they are not. If anything, they are more complementary than interchangeable. It is important to understand the specific indications for TIPS as well as RTO.

G&H How has RTO evolved over the years?

EL Balloon-occluded retrograde transvenous obliteration (BRTO) was the first RTO procedure developed and was

initially performed mainly in Japan and Korea. A balloon catheter was used to occlude the gastroduodenal shunt (GRS), and a sclerosing agent such as ethanolamine oleate or sodium tetradecyl sulfate was used to treat the gastric varices. As more BRTOs were performed, it was realized that serious complications may be associated with the procedure, such as anaphylactic shock, acute renal failure owing to renal toxicity of the sclerosing agent, irreversible portal vein and renal vein thrombosis, and irreversible pulmonary embolisms. Consequently, it was inevitable that the procedure be improved.

The next RTO procedure developed was plug-assisted retrograde transvenous obliteration (PARTO), which was invented by Dr Dong Il Gwon in Korea. He eliminated the 2 biggest issues with BRTO: the balloon catheter and the sclerosing agent that caused these complications. He used a vascular plug instead of a balloon catheter and a gelfoam slurry instead of a sclerosing agent, and found that PARTO had a very similar clinical efficacy to BRTO without the aforementioned severe complications. In addition, the simplicity of PARTO reduced procedure time, radiation exposure, and likely overall cost.

Thus, PARTO was a needed improvement over BRTO, but even with PARTO, it was realized that there were limitations owing to the plug. The largest plug currently available globally is only 22 mm, which can only occlude a GRS up to 18 mm. Thus, owing to the limited plug size, PARTO cannot be effectively performed in any gastric varices with a shunt larger than 18 mm. Additionally, when performing this procedure, the torturous anatomic course of the inferior vena cava (IVC) to renal vein to GRS can make plug deployment extremely challenging.

As a result, a further improved RTO procedure, coil-assisted retrograde transvenous obliteration (CARTO),

was invented by our group at UCLA Medical Center. This procedure utilizes vascular embolization coils instead of a plug, so there is no size limitation like with PARTO. Also, a microcatheter or small (4 Fr) diagnostic catheter is used to perform CARTO to overcome the anatomic challenges of the IVC, renal vein, and GRS that are encountered during PARTO. Similar to PARTO, CARTO utilizes a gelfoam slurry as a thrombogenic agent instead of a sclerosing agent to improve its safety. Hence, CARTO has clinical efficacy, safety with minimal complications, a faster procedure time, and reduced radiation exposure and cost. Thus, there has been progress from BRTO to PARTO to CARTO over the past 25 years.

G&H What guidance has been provided regarding which of these procedures to perform when managing gastric varices?

EL According to the most recent American Association for the Study of Liver Diseases (AASLD) practice guidance, which was published in January of this year, CARTO and PARTO are recommended over traditional BRTO because of their improved safety profiles as mentioned previously. All 3 procedures have fairly similar clinical and technical efficacy in terms of treating gastric varices, but CARTO and PARTO have fewer complications than traditional BRTO and other forms of modified BRTOs using balloons and sclerosing agents. The AASLD's recommendation is that, at experienced centers, CARTO and PARTO should be considered as alternatives to TIPS to treat gastric varices if TIPS is contraindicated. If the patient can undergo either TIPS or CARTO/PARTO but the patient is experiencing overt hepatic encephalopathy or poor liver function, CARTO/PARTO is preferred. It is important to note that this is the first time the AASLD has included RTO in variceal hemorrhage treatment options in its practice guidance. This information should be read thoroughly and widely disseminated to help the care of patients with gastric varices and liver disease.

Between CARTO and PARTO, there are no randomized controlled trial comparison data to suggest one is better than the other. However, as mentioned, if a patient has a challenging anatomy and has a larger-size shunt, CARTO may be preferred. If the shunt is small and there are no anatomic challenges, either CARTO or PARTO could be performed.

G&H Could you expand on the technical and clinical success of BRTO, PARTO, and CARTO?

EL Technical success is defined as the ability to occlude the GRS, inject a sclerosing or thrombogenic agent such as gelfoam, and obliterate the gastric varices, whereas clinical

success refers to the cessation of active bleeding and obliteration of varices, which do not reoccur within the follow-up period. All 3 procedures have very high technical and clinical success rates. BRTO has a technical success rate of 95% to 97% and a clinical success rate of 95%. CARTO and PARTO have technical success rates of 95% to 98% and clinical success rates around 98% to 100%.

G&H Can these procedures also be used prophylactically?

EL One small retrospective study showed that when RTO was performed prophylactically, it effectively prevented bleeding in a patient over 10 years of follow-up; however, no prospective study has confirmed this finding. As of now, no society such as the AASLD, the American Gastroenterological Association, or the Society of Interventional Radiology has recommended that preventive RTO should be performed. More research is needed to determine whether there is a role for preventive RTO.

G&H What complications have been reported with the RTO procedures?

EL BRTO, which has been studied the most, is associated with the most serious complications. As mentioned, when the sclerosing agent leaks into the portal or systemic circulation, it can cause renal toxicity that can result in acute renal failure as well as irreversible renal vein thrombosis, portal vein thrombosis, and a permanent pulmonary embolism. There have also been reports of anaphylactic shock because of the use of a sclerosing agent.

On the other hand, CARTO and PARTO have a very minimal complication rate, with potential complications including reversible renal vein or portal vein thrombosis with the anticoagulation. Coil or plug migration could also occur but is rare. Those are the few complications that have been reported.

All of these procedures could technically worsen portal hypertension symptoms such as esophageal varices or ascites. These are considered side effects of the procedures, not complications, and are reversible and treatable.

G&H What are the contraindications for these procedures?

EL The main contraindication is complete portal vein thrombosis without any cavernous transformations or other portosystemic shunt. If GRS is the only portosystemic shunt decompressing the patient's portal hypertension and that shunt is embolized, there is no way for portal flow to escape the portal system, which could lead to worsened portal hypertension and associated complications

such as ascites or other varices. Additionally, performing RTO for gastric varices may not be the best option if a patient has very large, high-risk esophageal varices. In those cases, the procedure may make the esophageal varices worse, and the patient may have a severe esophageal variceal bleed. Otherwise, poor liver function such as high MELD or Child-Pugh scores or hepatic encephalopathy are not large concerns or contraindications for RTO.

G&H What should preprocedural evaluation entail?

EL Just like with other hepatic interventions, it is necessary to determine whether the patient's liver function is within reasonable limits, although, as mentioned, poor liver function is not a contraindication for RTO. In fact, several studies have shown that RTO improves liver function. Nonetheless, clinicians should monitor liver function prior to RTO. Also, triple-phase computed tomography (CT) with contrast of the abdomen and pelvis is recommended, which will help identify important anatomic landmarks such as the GRS, varices feeding vessels (short, posterior, or left gastric veins), and other collateral vessels. It is essential that patients be seen by a hepatologist and gastroenterologist to make sure the procedure is appropriate. As mentioned earlier, a multidisciplinary meeting is most often held to determine whether RTO or TIPS is appropriate for each patient.

G&H What postprocedural evaluation and follow-up care are needed?

EL After these procedures, most patients should undergo repeat triple-phase CT before being discharged to confirm that their gastric varices have been completely obliterated. If the varices have not been completely obliterated, a secondary intervention such as antegrade embolization or TIPS may be needed. Postprocedural laboratory evaluation should be performed to confirm that the patient is not bleeding further and that liver function is stable. Otherwise, routine follow-up should take place at 1 month, 3 months, and every 3 months thereafter for 1 year with CT and endoscopic evaluation. Follow-up should involve a hepatologist or gastroenterologist and an interventional radiologist every 3 months.

G&H What are the next steps in research?

EL There is a lack of randomized controlled trials with comparison data between different RTOs, RTO and TIPS, and RTO and other treatment options for gastric varices. Although RTOs have been performed for around

25 years now, there are limited data. A comparison study is needed to determine which of the 3 procedures is the optimal one for patients with gastric varices.

Additionally, one of the most important research needs is long-term clinical follow-up data. With the current data, we may understand what happens 1 or 2 years after RTO, but further research is needed to understand long-term clinical outcomes of these patients 7 or 10 years later. Also, more research is needed to confirm long-term safety of these procedures. One of the biggest concerns has been that RTO makes portal hypertension worse. Theoretically, it could, but we do not have enough data or experience to determine how severe portal hypertension becomes and how patients should be managed. Anecdotally, most of the patients I have been following may experience worsening of their portal hypertension but that resolves within 1 to 3 months after RTO procedures. However, more systematic studies should be performed.

As briefly mentioned, the preventive role of RTO is a crucial research topic. We already know that RTO is very effective at treating bleeding gastric varices. If RTO can effectively prevent gastric varices from bleeding over the long term, it may improve overall patient survival, quality of life, and health care costs.

Lastly, more research is also needed on performing RTO for other conditions, such as hepatic encephalopathy and portal flow enhancement posttransplant. Data suggest that more than 200,000 patients require multiple admissions to the hospital because of hepatic encephalopathy, and there are currently limited treatment options for these patients. Recent studies have shown that using RTO to embolize the spontaneous portosystemic shunt in patients with refractory hepatic encephalopathy can result in significant improvements in their symptoms and survival outcomes. However, most of these studies are retrospective, so further prospective studies should be performed.

Disclosures

Dr Lee has served as a consultant to Gore Medical and Terumo Medical.

Suggested Reading

Lee EW, Eghtesad B, Garcia-Tsao G, et al. AASLD Practice Guidance on the use of TIPS, variceal embolization, and retrograde transvenous obliteration in the management of variceal hemorrhage. *Hepatology*. 2024;79(1):224-250.

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