The usefulness of flat panel detector angiographic computed tomography during balloon-occluded retrograde trans venous obliteration.

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Gastroduodenal varices remain a problematic condition due to the threat of rupture and bleeding and to their association with massive portosystemic shunting and potential hepatic encephalopathy. The efficacy of transjugular intrahepatic portosystemic shunts (TIPS) is limited in this indication. Balloon-occluded retrograde transvenous obliteration (BRTO) [1, 2] or dual balloon occlusion embolotherapy (DBOE) [3] have become attractive alternatives that can play an important role in the treatment of gastric varices, in addition to endoscopic, surgical, or other endovascular therapies. To perform BRTO, the left renal vein and gastrorenal shunt are catheterized with a Fogarty-type catheter and balloon-occluded left adrenal venography (BOAV) is obtained, followed by infusion of a sclerosant to occlude the gastric varices. In order to obtain complete thrombosis of the target gastric varices by BRTO, access to the efferent (draining) vein and adequate variceal filling by the sclerosant are essential. Indeed, obliteration of the drainage vein without thrombosis of the upstream gastric varices may instead increase pressure in the varices, which can subsequently rupture. However, it is often difficult to distinguish by conventional venography the efferent vein and vulnerable gastric varices that project into the gastric lumen from the adjacent veins. Therefore, flat panel detector angiographic computed tomography (FACT) during BRTO was introduced to plan and verify access to the efferent vein and to confirm adequate filling of the target gastric varices by contrast media and the subsequent sclerosant.
Methods and Materials

Clinical Setting, Patients and BRTO procedures

This prospective, cohort study was approved by our local institutional review board and included all consecutive patients with gastric varices (Fig. 1A on page ) undergoing BRTO at a single academic hospital. Twenty consecutive patients (Table 1 on page , mean age = 62.4 years, range 31-81, 9 males and 11 females) with gastric varices were included in the study cohort between July 2005 and November 2008. At first the portosystemic collaterals were assessed using multislice (MS) computed tomography (CT) (Sensation Cardiac, Siemens, Erlangen, Germany) (Fig. 1B on page ) or magnetic resonance (MR) imaging (Intera Archieva, Philips, Netherlands) with several postprocessing techniques including multiplanar reconstructions and volume renderings. Prior to BRTO, conventional arteriopportography was performed to evaluate hemodynamics and to exclude specific causes of portal hypertension such as massive arteriportal shunt or portal venous thrombosis [4]. If the efferent vein was not delineated, FACT during arterial portography (FACT-AP) was added [5, 6].

The BRTO procedure was performed according to the method of Kanagawa et al [1]. Briefly, a 5.2 or 6 French balloon catheter (11- or 20-mm balloon diameter (Clinical Supply, Gifu, Japan)) was inserted from the right internal jugular or femoral vein and wedged into the left adrenal vein. First, balloon-occluded left adrenal venography (BOAV, Fig. 1C on page ) was performed with the balloon inflated by air or diluted contrast medium after the administration of effervescent salts to expand the stomach. Then, repeat BOAV during FACT acquisition (Fig.1D-F on page [BOAV-FACT]) was performed to confirm that the contrast medium opacification had reached the target gastric vessels. If not, additional interventions including downgrading and coaxial advancement of a microcatheter were performed and FACT was repeated until full opacification of the target varices was obtained. Downgrading [7] consists of selective occlusion of the venous collaterals using absolute ethanol or coils for patients with varices classified as grade 3 or higher in Hirota’s classification [2]. After obtaining opacification of the target varicose veins, a mixture of 10 mL of 10% ethanolamine oleate (EO) (Oldamin, MOCHIDA Pharmaceutical, Tokyo, Japan) and 10 mL of contrast medium (Iomeron 400, Eisai co., Tokyo, Japan) or a foam made of 2 mL of 3% polidocanol (Polidocasklerol, ZERIA Pharmaceutical, Tokyo, Japan) and 8 mL of air using a pumping method via a three-way stopcock was injected into the target varices (Fig. 1G-H), with confirmation of appropriate location of the sclerosing agent by additional FACT (BRTO-FACT). At least 6 hours later the catheter was retrieved after confirming variceal thrombosis by the absence of blood return on aspiration and by injecting small amount of contrast media under fluoroscopy and observing hemostasis even after balloon deflation. Thereafter, procedure-related complications were recorded during subsequent hospital stay and defined as major if they involved more than standard post-BRTO care and/or
lead to prolonged hospital stay. The patients were followed up by CT (Fig. 1I on page ) and endoscopy (Fig. 1J on page ).

FACT Technique

The procedures were performed in an interventional radiology suite equipped with a commercially available ceiling-mounted DSA unit (AXIOM Artis FD system and DynaCT, software version VB30E, Siemens, Erlangen, Germany). Several series of 3D rotational flat panel detector angiographic images were obtained during breathhold that covered 200 degrees of circular trajectory for 4 seconds. For FACT-AP, FACT image acquisition was initiated 20 seconds after the injection of iodinated contrast medium (Iomeron 350; Eisai, Tokyo, Japan) at a flow rate of 3-5 mL/sec for 5 seconds. For the other FACT examinations, image acquisitions were obtained immediately after the conventional DSA using manual injection of iodinated contrast during balloon occlusion. Acquired images (240 images; frame rate, 24.8/sec; 0.8 degree of increment for each frame; resolution, 1,024 pixels) were transferred to a workstation (Leonardo, Siemens), where 3D CT-like images were reconstructed in approximately two minutes.

Data Analysis

The visibility of the target gastric varices on BOAV without and with FACT (1; definitely invisible, 2; probably invisible, 3; undetermined, 4; probably visible, 5; definitely visible) was independently recorded by two attending interventional radiologists, each of whom had more than ten years of clinical experience in academic practice (J.K., Y.K.). After independent interpretations, the differences in assessment between both radiologists were resolved by consensus and the diagnostic confidence level regarding whether the target varices were opacified or not (0: undetermined, 1: probable, 2: definite) on BOAV without and with FACT was compared. To evaluate the level of interobserver agreement with regard to the visibility of the target gastric varices, a Kendall W test was performed. Kendall W coefficients between 0.5 and 0.8 were considered to indicate good agreement, and coefficients higher than 0.8 were considered as excellent agreement. To determine statistical differences in the diagnostic confidence level between FACT-BOAV and conventional BOAV, Wilcoxon signed rank test statistics were calculated. Finally, the behavior of the operators was analyzed in consensus with respect to procedural technique during BRTO and the influence of FACT on operators’ strategy/technique was graded in three categories: category 1 if no relevant additional information was gathered, category 2 if more confidence was obtained by performing BOAV-FACT but without leading to technical/strategical modifications during BRTO, and category 3 if FACT provided additional information that influenced the operator’s decision making process enough to modify the steps in the procedural technique.
**Results**

In four (cases 7, 10, 12, 20) of twenty patients in whom conventional arterioportography could not demonstrate the efferent vessels of the varices (Fig. 2B on page), the catheter tip was intentionally displaced from the superior mesenteric artery into the celiac trunk, and a celiac FACT-AP was performed and revealed the gastrorenal shunt and the gastric varices projecting into the gastric lumen (Fig. 2C on page).

BOAV and BOAV-FACT were performed twenty eight times totally (Table2 on page). The results of the Wilcoxon signed rank test revealed that the diagnostic confidence level of BOAV with FACT (1.80 ± 0.07) was significantly higher (p<.0001) than that without FACT (0.87 ± 0.11). The interobserver agreement between the two radiologists in rating the visibility of the target gastric varices was good for BOAV and excellent for BOAV with FACT, with Kendall W values of 0.638 and 0.866, respectively.

In ten patients iodinated contrast that seemed to enter the gastric varices on BOAV (Fig. 3B on page) did not actually reach them on a first BOAV-FACT (Fig. 3C on page); additional contrast agent infusion (Fig. 3D on page) or interventions such as downgrading (for varices with Hirota's grade # 3) and coaxial advancement of a microcatheter allowed full opacification of the target varices on a second BOAV-FACT (Fig. 3E on page) performed thereafter. In one patient BRTO was converted to a percutaneous transhepatic obliteration (PTO) because BOAV-FACT revealed non opacified grade 3 gastric varices. In another patient (Fig. 4 on page) partial splenic embolization (Fig. 4B-C) allowed superselective BRTO (Fig. 4D) confirmed on BOAV-FACT (Fig. 4E), resulting in thrombosed gastric varices (Fig. 4F) without occluding the left adrenal vein (Fig. 4G).

The information provided with FACT was classified as category 1 in one (5%), category 2 in eight (40%), and category 3 in eleven of the twenty patients (55%).

Overall, in all but one patient who underwent conversion to PTO, complete thrombosis was confirmed on postcontrast CT one week after the BRTO procedure. No major procedure-related complications occurred.
Conclusion

Rupture of esophagogastric varices is one of the most severe complications for patients with portal hypertension (approximately 30% prevalence) [8-10], with rupture of gastric varices resulting in a 45%-55% mortality rate [8-11]. Therefore, in addition to urgent and elective treatment, prophylactic obliteration of high-risk large fundic varices has been recommended [12]. However, the optimal method for treatment of gastric varices has not yet been determined and remains controversial, while endoscopic variceal ligation (EVL) [13] and endoscopic injection sclerotherapy (EIS) [14], which have become the treatments of choice for management of esophageal varices, are widely performed.

Because gastric varices are almost always associated with large gastrorenal shunting and the blood flow in these collateral veins is fast and abundant [8], it is difficult to control bleeding from gastric varices by endoscopic procedures such as EVL or EIS [8-10]. Endoscopic features and location allow distinguishing three types of gastric varices [15]: Lg-c varices are located at or around the cardia, Lg-cf varices span from the cardia to the fornix, and Lg-f varices involve exclusively the level of the fornix. Bleeding rates for gastric varices has been reported to be 78% for Lg-f, 63% for Lg-cf, and 43% for Lg-c by Obara and Kusukawa [16], and 78% for Lg-cf and 55% for Lg-c by Sarin et al. [9, 10]. Sarin et al. also reported that the rebleeding rate after elective gastric variceal sclerotherapy was 19% for patients with Lg-c and 55% for those with Lg-f [9, 10]. Hence, location of the varices in the stomach is crucial as both spontaneous bleedings and post-treatment rebleedings are more likely in the fornical region than along the cardia.

Many alternatives other than EVL and EIS have been suggested for the management of gastric varices, such as transjugular intrahepatic obliteration via an existing TIPS [17], percutaneous transhepatic obliteration (PTO) [18], and transileocecal obliteration (TIO) [18] with [19] or without cyanoacrylate. TIPS creation, first reported by Rösch et al. in 1987 [20], involves percutaneous decompression of portal hypertension and is now often performed for intractable ascites or refractory esophageal variceal bleeding in the United States and Europe [21-24]. However, gastric varices in the fundus frequently fail to disappear after being treated by TIPS creation, and the reported success rate is only 50%-63%. In addition, patients with severe hepatic encephalopathy are not always good candidates for a TIPS procedure because of possible worsening of their encephalopathy [21-24]. Surgical portosystemic shunt creation is used to reduce high portal pressure and decompress the esophageal and gastric varices. However, this treatment is limited to patients with impaired liver function and the mortality rate after surgery is 42%-56% for elective surgery and even higher for emergency treatment [25].

Since BRTO was first introduced by Kanagawa et al. to embolize gastric varices through the gastrorenal shunt, satisfactory results have been reported for patients with gastric varices and hepatic encephalopathy [1, 2], and BRTO has been extensively applied during the past decade for the management of fundic gastric varices in several
specialized centers. Because BRTO is less invasive than surgical treatment, it can be performed on patients with poor hepatic function reserve or hemorrhagic diathesis [1, 2]. In addition, it can be used for emergency treatment to control bleeding from gastric varices. The efficacy of BRTO for the treatment of gastric varices and hepatic encephalopathy has been reported to be in the 87%-100% range and the relapse rate is 0%-10% [1, 2].

To select the appropriate technique for BRTO, it is necessary to determine the supply of the 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 results obtained with BOAV and reported that 22 of 50 (44%) patients needed second or third procedures to obliterate the gastric varices completely. Nevertheless, repeat BRTO is a burden for patients and results in additional radiation exposure, iodinated contrast load and longer hospitalization. To obliterate gastric varices completely at the first procedure, it is necessary to decrease the blood flow of the feeding vein(s) and to obliterate the collateral veins more effectively. To reduce blood flow in the feeding vein(s), partial splenic embolization (PSE) or temporary occlusion of the splenic artery or coronary vein with a balloon catheter can be used. However, although PSE can decrease flow in the feeding veins such as the short or posterior gastric veins, the procedure requires longer hospitalization because of resultant high fever or abdominal pain. The other method to successfully obliterate gastric varices is to completely occlude the collateral veins by using metallic coils, absolute ethanol and EO after selective catheterization. However, the injected dose of absolute ethanol should be determined carefully because of possible severe, acute alcohol intoxication or a highly destructive effect on endothelial cells. Moreover, EO may cause several complications such as intravascular hemolysis leading to renal dysfunction [26], allergic reaction including cardiogenic shock [27], pulmonary glue embolization resulting in pulmonary infarction [28] or acute respiratory distress syndrome (ARDS) with alveolar wall lesions, edema and lung congestion [29]. Because some of these complications are correlated with the amount of infused EO [30], total dosage should be minimized. Hence superselective venous embolization after advancing the balloon catheter using a coaxial system has also been reported [31].

To perform selective BRTO, precise identification of the target varicose veins is essential. Multislice CT [32], MR imaging [33], or curved linear array (CLA) echoendoscopy [34] have been used to demonstrate portosystemic collaterals and to determine appropriate procedures. Based on the mapping images, the possibility of transvenous access to the gastric varices, the appropriate route (transjugular or transfemoral), and the correct size of the balloon to use (10 or 20 mm of diameter) could be determined in most of our cases. However, we recognize that it is sometimes difficult to identify accurately the efferent vein due to the complexity of the surrounding vascular anatomy as seen by these imaging techniques. Moreover, CT requires high doses of contrast media. MR imaging has some advantages over CT with no need for iodinated contrast (although with the risk of nephrogenic systemic sclerosis in patients with renal failure), and without any irradiation risk. However, the use of MR imaging is limited in patients with pacemakers or
comorbidities that require aggressive life support, and it is difficult to perform MR imaging for patients with ruptured gastric varices.

CTAP (celiac or splenic CT arterial portography) prior to venous approach treatment such as BRTO has been reported to be useful to reveal the efferent vessels from complex duodenal varices into the systemic vein(s) [5, 6], and our experience using FACT-AP in four of our cases supports this assertion. For this purpose, unified CT and angiography systems [35] are desirable. These systems, however, have not been widely used because of their higher investment cost for equipment and the amount of space necessary for installation. Since Feldkamp et al [36] reported the practical algorithm for cone-beam CT reconstruction intensity, 3D rotational angiography has been used in interventional neuroradiology and in coronary, renal and uterine angiography with varying success. In addition to 3D rotational angiography, the combination with flat panel detectors enabled users to create soft tissue images named FACT [37], cone beam CT [38], or c-arm CT [39]. There are several reports describing its efficacy in transcatheter arterial chemoembolization of liver tumors [40], adrenal venous sampling [39], partial splenic embolization [41], etc. In the experience reported here, two successive sessions of BOAV-FACT were required in ten of our twenty patients to confirm that the contrast medium had reached and filled properly the target gastric varices. To our knowledge there is no prior report of applying FACT during BRTO for this purpose.

Using FACT during BOAV, the three-dimensional vascular anatomy including the gastrorenal shunt, gastric varices, and other collaterals can be clearly visualized and it influenced our decision making process enough to modify the interventional technique in 55% of patients in this study. Although the contrast resolution of FACT is lower (10 Hounsfield units) and the time for scanning and reconstruction for FACT is longer than conventional CT, its true isotropic spatial resolution is higher than that of 16-slice spiral CT [42]. In our study, the low contrast resolution of FACT could be compensated by the use of effervescent salts to produce air to expand the stomach and delineate the target gastric varices opacified by dense iodinated contrast media from BOAV without additional contrast load. The smaller field of view (9 inches) was also large enough for the demonstration of the target gastric varices with efferent and afferent vessels, hence resulting in a lesser irradiated volume than when scanning of the entire liver during TACE [38]. Additionally, FACT does not require moving the patient between CT and angiography units. This advantage helps avoiding both time-consuming procedures and the occurrence of catheter tip retraction or movement during transfer to the CT scanner or upon return to the angiography suite. The additional radiation exposure from FACT can be attenuated because the use of FACT may avoid multiple DSA projections and shorten the total fluoroscopy and procedure times. Hence further comparative study is required to assess the true magnitude of this additional irradiation.

Another inherent caveat of using FACT is its limited capability to describe flow directionality in real time, as compared to angiography. Venographic classifications based on the afferent or draining veins have suggested the possibly large complexity of flow patterns and circuits in BRTO candidates [43]. A more comprehensive assessment
combining three-dimensional imaging of this complex vascular anatomy (e.g., by FACT or MRI) with assessment of directionality in these tortuous flow circuits (e.g., by phase-contrast MRI or duplex ultrasonography) is a goal for the future that may perhaps enhance our understanding in selected cases. However, it remains to be proven whether adding complexity to the anatomical description of variceal circuits would actually improve procedural and patients' outcomes. We did not find this need for complexity to be clinically relevant in the experience reported here.

In conclusion, BRTO under FACT guidance seems to be a reliable method to obtain successful thrombosis of gastric varices. In contrast to conventional venography, the capability of FACT-BOAV to provide three-dimensional anatomical imaging appears helpful for procedure planning, choice of catheter positioning and technical strategy during BRTO, and immediate assessment of treatment efficacy / technical success at completion of the procedure.
References


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