Successful retrograde transvenous obliteration for splenorenal shunts after liver transplantation: Midterm results

Hao Wang, Haijun Gao, Guang Chen, Zhengjia Yi

Department of Radiology, Tianjin First Center Hospital, Tianjin, China

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ABSTRACT

Background/Aims: *The objective of this study was to evaluate the use of Amplatzer-assisted retrograde transvenous obliteration (RTO) in patients with splenorenal shunts (SRSs) after orthotopic liver transplantation (OLT).*

Materials and Methods: *From August 2015 to March 2017, 5 patients received RTO at our center because of SRSs after OLT. The clinical features of the patients with SRSs included demographics, donor type, new-onset symptoms, liver function tests, imaging examinations, interventional examinations and treatments, and outcomes. The patients who received RTO were regularly monitored, and data were gathered before and after the procedures and compared using the paired-sample t test.*

Results: *Percutaneous interventional management was successfully undertaken in all patients, and 5 Amplatzers and 2 stents were also implanted successfully in patients owing to portal vein (PV) stenosis. There were no procedure-related complications in these patients. In all 5 patients with SRSs, 2 weeks after the interventional therapy, the computed tomography findings showed that the splenic renal shunt vein was completely blocked. The mean blood pressure in the donor lateral PV and the mean blood flow velocity of the donor lateral PV after RTO were all improved significantly ($p<0.05$). It also suggested that all 5 patients with SRSs survived, with the primary graft functioning normally at the final follow-up.*

Conclusion: *Amplatzer-assisted RTO is a safe and effective treatment for SRSs after OLT. Considering the complexity of the diagnosis and treatment of SRSs in liver transplantation, this complication should be taken seriously.*

Keywords: *Orthotopic liver transplantation, portal vein stenosis, retrograde transvenous obliteration, splenorenal shunts*

INTRODUCTION

Orthotopic liver transplantation (OLT) is currently the only effective means of treatment for end-stage liver disease. Although vascular complications after OLT seldomly occur, they are the most feared complications with a high incidence of both graft loss and mortality, because they compromise the blood flow of the transplant (either inflow or outflow). The true incidence of portal vein (PV) stenosis (PVS) after liver transplantation (LT) is not really known, and the only data reported in the literature concerning the incidence of venous complications indicated the incidence of <3% (1). These complications are associated with high morbidity and graft loss (2, 3). Another important fact to mention is that PVCs are more common with split liver and living donor LT and also in pediatric transplantation (1, 4). The main reason for insufficient venous blood flow is PVS, but recent clinical observations showed that residual spleen and kidney shunts after OLT can also lead to insufficient blood flow in the PV.

Retrograde transvenous obliteration (RTO) includes balloon-occluded RTO, coil-assisted RTO, or plug-assisted RTO, which is a procedure to occlude a spontaneous portosystemic shunt, minimizing the shunting of portal blood to the systemic circulation (5). RTO is usually used to manage gastric varices, and little is known about its potential to treat patients with splenorenal shunts (SRSs) after OLT. In this study, we retrospectively analyzed the clinical data of 5 patients with residual SRSs after OLT and further discussed the application of intravenous retrograde intervention in these cases.

MATERIALS AND METHODS

Patient Population

This retrospective single-center study was approved by our institutional review board (approval number: 4678123). The requirement for informed consent was waived owing to the study's retrospective nature. Executed prisoners' organs were not used in this study. This study included 5 male patients who developed SRSs and accepted Amplatzer-assisted RTO (AMPLATZER™ Vasculat Plug II, AGA Medical Corporation, Plymouth, MN, USA) between August 2015 and March 2017 after adult

Corresponding Author: **Guang Chen; guangchen2018@aliyun.com**

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LT. PV reconstruction was performed with a standard end-to-end anastomosis between donor and recipient, and all patients underwent classic OLT. Before interventional therapy, blood pressure and blood flow velocity of the donor lateral PV were measured by Doppler ultrasonography (SonoSite Inc, Bothell, WA, USA).

Technique

Before angiography, all patients underwent computed tomography (CT) to evaluate the vascular anatomy, and 1 case presented with intrahepatic PV slender branch.

Angiography of patients was conducted using an FD20 digital angiographer, after local anesthesia, the right axillary midline approach was chosen, and a 21G cannula needle (Angiotech Pharmaceuticals, Inc., Vancouver, British Columbia, Canada) was used to penetrate the skin and liver to reach the right branch of the PV under the guidance of X-ray fluoroscopy. Immediately, after the successful puncture, a 0.018-inch guidewire was placed in the main PV. Then, an expanding sheath was used to change to a 0.035 inch guidewire, and a 7- to 8-Fr vascular sheath (Cordis Corporation, Miami Lakes, FL, USA) was placed along the larger guidewire into the PV. The catheter (Cordis Corporation, Miami Lakes, FL, USA) was placed in the superior mesenteric vein and the splenic vein for PV angiography to determine the stenosis position and length and the normal diameter of the main PV near the donor side of the stenosis along with the pressure gradient on both sides of the narrow section. Based on the abovementioned measurements, appropriate balloon catheters and balloon-expandable stents (Scuba, Invatec SpA, Italy) were selected to perform blood vessel angioplasty at the stenosis section. The diameter of the balloon should be the same as the extrahepatic PV, the stent should be 10% to 15% wider than the extrahepatic PV, and the length of stent should exceed the stenosis. Angiography was then performed once again, and the pressure gradient at the stenosis was measured.

If the SRS was still in a severe varicose state and affected PV perfusion, RTO was required. Briefly, after the puncture of the common femoral vein, an 8-Fr vascular sheath (Cordis Corporation, Miami Lakes, FL, USA) was inserted. A 20-mm-diameter balloon catheter was first used to occlude the left renal vein. Next, the catheter was placed in the splenic vein for PV angiography to visualize its blood flow. If the blood flow was significantly improved, after inserting a 0.035-inch and 150-cm-long hydrophilic guidewire (Terumo, Tokyo, Japan) and a 4-Fr angled-tip catheter (Cobra; Cordis Corporation, Miami Lakes, FL, USA) into the left renal vein, a 0.038-inch and 260-cm-long stiff wire (Terumo, Tokyo, Japan) was moved into the SRS to exchange the catheter. The 9- to 10-Fr long sheath (Flexor Check-Flo; Cook Medical, Bloomington, IN, USA) was then inserted into the SRS. The stiff wire and catheter were subsequently removed and the Amplatzer (HeartR™ ASD) was deployed. The size of the selected Amplatzer depended on the narrowest diameter of the SRS measured by the CT scan near the left renal vein, and it was 20% larger than the targeted SRS to prevent migration. The Amplatzer was then deployed to the narrowest SRS in an additional effort to prevent migration.

Follow-Up

All patients were followed up until December 2017, with an average follow-up of 23.8 months (range: 9–31 months). Within 1 week of Amplatzer-assisted RTO, patients were assessed for thrombosis of the SRSs by CT during hospitalization. Once the patients were discharged from the hospital, Doppler was used to check for thrombosis every month in the first 3 months and at the 6th and 12th months. Subsequently, their follow-up clinical and laboratory data were taken from the patient's medical record or electronic information database. Information regarding their status or death was obtained by telephone from all patients or their families.

Assessments and Definitions

The study end points were technical success, procedure-related complications, and clinical success. The standard of technical success was as follows: after the Amplatzer was successfully placed in the SRS, the blood flow of the SRS was significantly reduced or disappeared, and the PV was well displayed. Clinical success was defined as an increase in PV blood flow and obvious improvement in liver function index after interventional therapy.

Diagnostic criteria for PVS (6) were as follows: PVS was confirmed if the extent of PVS was >50% and/or obvious varices were noted in the lateral branch vein with the pressure

MAIN POINTS

- *Spontaneous SRSs cause significant vascular steal from the liver, and its combination with PVS after OLT will seriously affect the blood flow of the PV.*
- *RTO is proven to be an effective method for gastric fundal varices (GFVs) with SRSs.*
- *Amplatzer-assisted RTO is safe and effective for the treatment of SRSs, which can completely block SRSs with a very high success rate.*

Table 1. Patient characteristics and clinical outcomes (n=5).

Case No	Age (years)	Sex	Original disease	LT type	LT time (d)	Amplatzer size (D1/D2)	Procedural complications	PV patency	Shunt patency	Child-Pugh score Before PTA	Child-Pugh score After PTA	Follow-up period (months)	Alive
1	47	M	LC (HBV)	WLT	15-7-31	24/28 mm	No	Yes	No	10	5	28	Yes
2	54	M	LC (HBV)	WLT	15-10-5	28/32 mm	No	Yes	No	9	5	25	Yes
3	49	M	LC (PBC)	WLT	13-11-8	26/30 mm	No	Yes	No	11	6	26	Yes
4	48	M	HCC, LC (HCV)	WLT	11-07-07	28/32 mm	No	Yes	No	6	5	31	Yes
5	34	M	HCC, LC (HBV)	WLT	16-12-07	26/30 mm	No	Yes	No	10	5	9	Yes

HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; LC: liver cirrhosis; LT: liver transplantation; M, male; PTA: percutaneous transluminal angioplasty; PV: portal vein; WLT: whole liver transplantation.

gradient between the 2 ends of the stenosis being >5 mm Hg. The criteria indicating successful treatment of PVS were defined as having at least one of the following: pressure gradient ≤5 mm Hg; pressure gradient reduced by ≥50% from baseline, and residual venography stenosis ≤30%. Complications were classified as major and minor according to the clinical practice guidelines of the Society of Interventional Radiology Standards of Practice Committee (7).

Statistical Analysis

The paired-sample t test was used to compare the donor lateral PV blood flow velocity before and after Amplatzer-assisted RTO. The statistical analysis was performed using commercially available SPSS Statistics for Windows version 17.0 (SPSS Inc., Chicago, IL, USA). $p<0.05$ was considered statistically significant.

RESULTS

Characteristics and Clinical Outcomes of Patients

Patient characteristics and clinical outcomes are presented in Table 1. All patients were men and underwent transplantation owing to liver cirrhosis. Their mean age was 46.4 years (range: 34–54 years). All 5 patients had abnormal liver function, with a Child-Pugh score ranging from 6 to 11 before percutaneous transluminal angioplasty. The blood pressure in the donor lateral PV ranged from 6 to 19 mm Hg, and blood flow velocity of the donor lateral PV ranged from 8.2 to 23.1 mm Hg. Two of the patients exhibited PVS. All patients had PV patency but no shunt patency.

Retrograde Transvenous Obliteration in Patients with Splenorenal Shunts After Orthotopic Liver Transplantation

The transfemoral approach and percutaneous transhepatic PV were used in all patients. Amplatzer placement was technically successful in all 5 patients, with 2 of them successfully implanted into the stents owing to PVS. Digital subtraction angiography was performed immediately after Amplatzer deployment and stent implantation to confirm the correct position and the appropriate sizing of the Amplatzer. None of the Amplatzer and stents migrated after detachment. The mean procedure time from Amplatzer placement to Amplatzer detachment was 16 minutes, with a range of 6 to 33 minutes. There were no procedure-related complications in any patient. The mean blood pressure in the donor lateral PV after RTO was significantly promoted compared with that before RTO ($p<0.05$; 19.80±2.27 mm Hg vs 11.80±5.35 mm Hg) (Table 2).

Follow-Up Results

Follow-up CT studies were performed within 1 week after Amplatzer-assisted RTO. SRS in a 47-year-old man after LT is shown in Figure 1. A large SRS appeared (a), and appropriate balloon catheter (b) and balloon-expandable stents (c) were selected to perform blood vessel angioplasty at the stenosis section. The Amplatzer (black arrow) was placed in the SRS and led to better PV perfusion (d,e). CT image shows SRS before Amplatzer-assisted RTO (f) and complete obliteration of the SRS after Amplatzer-assisted RTO (f). In addition, follow-up Doppler performed within 1 week after Amplatzer-assisted RTO showed that the donor lateral PV blood flow velocity was 15.56±6.80 mm Hg (range: 8.2–23.1 mm Hg) and 36.94±5.26 mm Hg (range: 29.8–47.7 mm Hg) before and after RTO, respectively. There was a significant difference between 2 groups ($p<0.05$) (Table 3). The Child-Pugh score was decreased after RTO (5.20±0.15 points) compared with that before RTO (9.2±1.18 points) ($p<0.05$) (Table 4). Ascites of 2 patients disappeared within 1 week after surgery.

Table 2. Blood pressure in donor lateral PV before and after RTO.

	Blood pressure in donor lateral PV (mm Hg)					
	Case 1	Case 2	Case 3	Case 4	Case 5	t test (mean±SD)*
Before RTO	6	17	19	6	9	11.40±6.19
After RTO	16	22	26	17	18	19.80±4.15

*p<0.05 between after RTO and before RTO.
PV: portal vein; RTO: retrograde transvenous obliteration; SD: standard deviation.

Table 3. Blood flow velocity of donor lateral PV before and after RTO.

Blood pressure in donor lateral PV (mm Hg)						
	Case 1	Case 2	Case 3	Case 4	Case 5	t test (mean±SD)*
Before RTO	21.4	9.5	8.2	23.1	15.6	15.56±6.74
After RTO	47.7	32.5	29.8	41.2	33.5	36.94±7.36

*p<0.05 between after RTO and before RTO.
PV: portal vein; RTO: retrograde transvenous obliteration; SD: standard deviation.

Table 4. Child-Pugh score before and after RTO.

	Child-Pugh score (points)					
	Case 1	Case 2	Case 3	Case 4	Case 5	t test (mean±SD)*
Before RTO	10	9	11	6	10	9.20±1.92
After RTO	5	5	6	5	5	5.20±0.45

*p<0.05 between after RTO and before RTO.
RTO: retrograde transvenous obliteration; SD: standard deviation.

DISCUSSION

OLT performed in almost all cases is usually the only curative therapeutic option for patients with acute and chronic liver failure and a hepatocellular carcinoma (8). Insufficiency of PV blood flow after OLT can lead to abnormal liver function and even graft failure, and the PVS and SRS may be the main causes of a lack of PV blood flow (9). The varicose veins of the fundus of the esophagus often converge into the left renal vein to form the portal-cavity channel owing to portal hypertension, making OLT technically high, difficult, and risky (10). Spontaneous SRSs cause significant vascular steal from the liver, and its combination with PVS after OLT will seriously affect the blood flow of the PV (11). In our study, it was found that the technical and clinical success rates are both 100%, and none of the patients had any procedure-related complications. The causes of PV anastomotic stenosis are as follows: the intima of the PV is not smooth, the growth factor of the PV is not expanded, the anastomotic suture is too tight, the PV is distorted, and the PV has a lesion before transplantation.

RTO including balloon-occluded RTO, coil-assisted RTO, or plug-assisted RTO is a standardized therapeutic procedure for the treatment of the esophagogastric fundus venous shunt (12-19). Most importantly, RTO is proven to be an effective method for gastric fundal varices (GFVs) with SRSs (20, 21). RTO has been applied for the treatment of recurrent hepatic encephalopathy in patients with GFVs (22, 23). Recently, RTO was demonstrated to improve liver function in patients with decompensated cirrhosis (24). The clinical manifestations of PV insufficiency after OLT are not specific. They are often related to the degree of anastomotic stenosis and the blood flow of splenic and diverted veins, which are mainly manifested by abnormal liver function (25). Based on

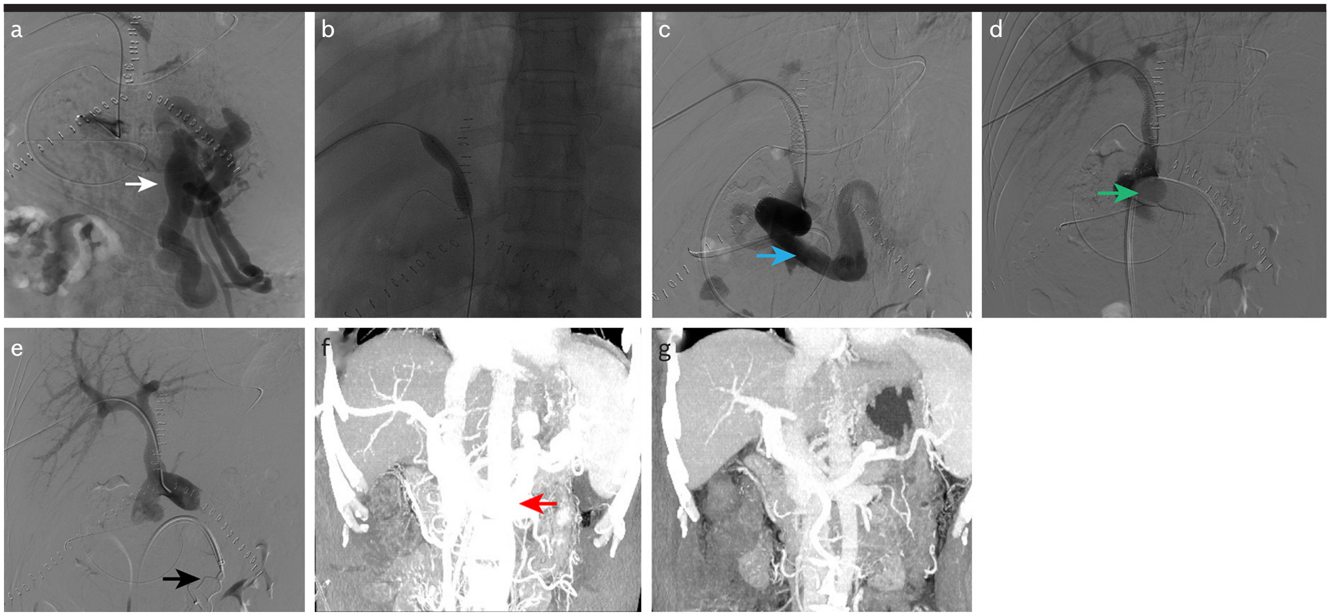

Figure 1. a-g. SRS in a 47-year-old man after LT. A catheter was placed in the superior mesenteric vein, and digital subtraction angiogram (DSA) showed a large SRS (white arrow) (a). Appropriate balloon catheter and balloon-expandable stents were selected to perform blood vessel angioplasty at the stenosis section, but the SRS was still in a severe varicose state (blue arrow) and affecting portal vein perfusion (b, c). We tried to use a 20-mm-diameter balloon catheter to occlude the left renal vein (green arrow); the portal vein perfusion improved, and the Amplatzer (black arrow) was placed in the SRS, resulting in better portal vein perfusion (d, e). Contrast-enhanced CT image obtained before Amplatzer-assisted RTO shows SRS (red arrow) (f). Contrast-enhanced axial CT image obtained 1 week after Amplatzer-assisted RTO shows complete obliteration of the SRS (g).

CT: computed tomography; DSA: digital subtraction angiogram; LT: liver transplantation; RTO: retrograde transvenous obliteration; SRS: splenorenal shunt.

our imaging data, it was suggested that all 5 patients developed complete thrombosis of SRS, and patients with PVS maintained patency when they were followed up for more than 9 months. Moreover, in 1 of the 5 patients with slender PV owing to long-term SRSs, the diameter of the PV increased from 0.8 cm before the operation to 1.1 cm 1 month after the RTO. The improvement in the Child-Pugh score was observed in all 5 patients (100%) within 1 month after Amplatzer-assisted RTO. RTO can be expected to increase the portal pressure gradient because of obstruction of the SRS. Once the SRS is blocked, the portal pressure will increase to the varying degrees, and some patients may temporarily have ascites (26). All 5 patients in this study showed abnormal liver function and hypoalbuminemia, with an ultrasound that suggested PV insufficiency. Combined with enhanced CT, PV blood flow insufficiency is considered owing to SRS and/or PVS.

The pathological basis of residual splenic shunts after OLT is still the portal hypertension caused by liver cirrhosis before LT. Kumamoto et al. (27) compared liver function and the long-term prognosis and suggested that SRS was responsible for the derangement of liver function and vital outcome, and RTO procedures may improve the outcomes of patients with SRSs. After reviewing the relevant literature (28-30) and after the venography of the PV and the treatment of the PVS, the patients received Amplatzer-assisted RTO in this study. Compared with the transdermal transhepatic method, Amplatzer-assisted RTO has several advantages. First, the liver is a substantial organ with an abundant blood supply, and these patients have abnormal coagulation combined with PV blood deficiency, leading to a push for more coarse occluders. After percutaneous transhepatic treatment, the risk of liver bleeding is greater, and it is easier to stop the bleeding by pressing the femoral vein puncture point. Second, the SRS is always tortuous, the vascular wall is very thin, and the coarse pushing of a device through the PV to the SRS is difficult, with a high risk of bleeding. Once the shunt is broken, it is difficult to surgically stop the bleeding. The path from the right femoral vein to the left renal vein and then to the SRS is relatively smooth, reducing the difficulty and risk of treatment (31). In patients with PV anastomosis stenosis, when choosing between the self-expanding stent and the balloon expanded stent, the author recommends the latter. Compared with fibrosis in the portal area after OLT, the PVS is often harder, and the balloon-expanded stent is stronger and the positioning is relatively accurate (32). Therefore, the balloon-expanded stent should be the first choice for PVS. In 1991, Raby et al. (33) first reported about balloon angioplasty for the treatment of PVS after OLT, and it is still the first choice for PVS (34).

There are several limitations in this study. First, the sample size is small. Although the technical success rate of interventional therapy for the 5 patients was 100% and the clinical effect is clear, there were only a few cases in this study. Therefore, the clinical efficacy of RTO on post-OLT SRSs in more patients remains to be further studied. Second, when is the best time to treat SRSs? We suggest that once the SRS leads to insufficiency of PV blood flow and liver function damage, RTO should be undertaken immediately. If there is PVS at the same time, we suggest that the SRSs can be blocked after the treatment of the PVS. Third, our results suggest that Amplatzer-assisted RTO is safe and effective for the treatment of SRSs, which can completely block SRSs with a very high success rate. Considering the complexity of the diagnosis and treatment of SRSs in OLT, this complication should be taken seriously. Further studies are needed to assess the true role of Amplatzer-assisted RTO in the treatment of these patients.

In conclusion, Amplatzer-assisted RTO was useful for the improvement of liver function even in patients with SRSs by increasing the PV flows, indicating that Amplatzer-assisted RTO is a choice for treatment of SRSs after OLT.

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