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Case Report

Long-term results of vascular stent placements for portal vein stenosis following liver transplantation

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Abstract: Portal vein stenosis (PVS) is a serious complication after liver transplantation (LT) and can cause increased morbidity, graft loss, and patient death. The aim of this study was to evaluate the long-term treatment effect of vascular stents in the management of PVS after LT. In the present study, follow-up data on 16 patients who received vascular stents for PVS after LT between July 2011 and May 2015 were analyzed. Of these, five patients had portal hypertension-related signs and symptoms. All procedures were performed with direct puncture of the intrahepatic portal vein and with subsequent stent placement. Embolization was required for significant collateral circulation. Technical and clinical success, patency of portal vein, and complications were analyzed. The analysis found that both technical and clinical success was achieved in all 16 patients. Embolization therapy for collateral circulation was performed in 1 patient with hematemesis. All stents remained patent without further interventional treatments during the follow-up (32.1±14.5 months). No portal hypertension-related symptoms reoccurred during follow-up. Postprocedure abdominal bleeding occurred in 1 patient and an additional surgical procedure was performed. In conclusion, percutaneous transhepatic portal vein stent (PTPS) for PVS after LT is feasible and effective with good long-term results. However, possible fatal complications should be kept in mind.

Keywords: Liver transplantation, portal vein stenosis, percutaneous transhepatic portal vein stent, portography

Introduction

Portal vein complications following liver transplantation (LT) include portal vein stenosis (PVS) or portal vein thrombosis. Although infrequent, potential life-threatening sequelae including graft loss and mortality can occur [1-4]. Surgical treatments including revascularization, thrombectomy, or retransplantation have been considered as the main approaches in the management of such complications after LT [4-6]. However, these invasive surgical procedures are limited because of technical difficulties and are associated with significant morbidity, mortality, and recurrence rates [1, 6]. Moreover, since there is a paucity of suitable hepatic allografts, timely retransplantations cannot usually be performed for these critically ill patients. A more effective and minimally invasive procedure, namely, percutaneous transhepatic portal vein stent (PTPS) placement has been considered as an alternative treatment for PVS after LT [1, 4, 7, 8]. However, PTPS placements for PVS after LT, as well as long-term follow-up, has not been widely reported. The aim of this study was to review the long-term results of PTPS placements for treating PVS after LT.

Materials and methods

Patients

From July 2011 to May 2015, 16 patients (15 male and 1 female) underwent PTPS placements for PVS after LT. All of the existing cases of stenosis were reported near the portal venous anastomosis. One patient was referred from outside our hospital. The patients ranged in age from 9 to 60 years (median age 48

Table 1. Demographic characteristics of patients

Case	Gender	Age, y	Type of Transplantation	Time interval of PTPS after LT (d)	Primary Disease	Clinical Manifestations
1	M	48	OLT	38	Hepatocellular carcinoma	Distension, Ascites
2	M	49	OLT	310	Hepatitis B virus cirrhosis	Abnormal LFT
3	M	9	OLT	202	Hepatitis B virus cirrhosis	Abnormal LFT
4	M	49	OLT	98	Hepatitis B virus cirrhosis	Abnormal LFT
5	M	48	OLT	129	Hepatitis B virus cirrhosis	Distension, Ascites
6	M	42	LDLT	184	Hepatitis B virus cirrhosis	Abnormal LFT
7	M	55	OLT	51	Intrahepatic Cholangiocarcinoma	Abnormal LFT
8	M	39	OLT	57	Hepatocellular carcinoma	Abnormal LFT
9	M	38	OLT	89	Hepatitis B virus cirrhosis	Abnormal LFT
10	M	60	OLT	746	Hepatitis B virus cirrhosis	Esophageal variceal bleeding
11	M	51	OLT	346	Hepatitis B virus cirrhosis	Abnormal LFT
12	F	35	OLT	18	Hepatocellular carcinoma	Distension, Ascites
13	M	46	OLT	91	Hepatitis B virus cirrhosis	Abnormal LFT
14	M	48	OLT	95	Hepatitis B virus cirrhosis	Abnormal LFT
15	M	60	OLT	59	Hepatitis B virus cirrhosis	Distension, Ascites
16	M	49	OLT	38	Hepatocellular carcinoma	Abnormal LFT

M = male; F = female; OLT = orthotopic liver transplantation; LDLT = living donor liver transplantation; PTPS = percutaneous transhepatic portal vein stent; LT = liver transplantation ; LFT = liver function test.

years). Fifteen patients had received orthotopic LT and one patient had received a living donor LT. The average interval between LT and PTPS procedures was 159 days±183 (range, 728 days). The interval between diagnosis of PVS and PTPS procedures was within 1 week in 6 patients, 2 weeks in 7 patients, and within 1 month in 3 patients. The underlying diseases included posthepatitic cirrhosis (n=11) and primary hepatic carcinoma (n=5). Five patients mainly exhibited with portal hypertension-related symptoms including abdominal distension and ascites in 4 patients and esophageal variceal bleeding in 1 patient. Eleven of the 16 patients were asymptomatic but presented elevated liver function test results. The information of patient characteristics is shown in the **Table 1**.

Diagnosis of PVS was confirmed with doppler ultrasonography (DUS) and/or computed tomography angiography (CTA). When the DUS showed a more than three-fold shift in angle-velocity at the focal point narrowing more than the proximal portion of the portal vein, a suspicion was raised of PVS that was confirmed by CTA [8-10]. The main indication for PTPS placements in patients with PVS was that the patients had to have abnormal liver function test results and a CTA showing >50% narrowing of the main portal vein simultaneously [8, 10]. The abnormal liver function test results included prolonged prothrombin time with a sudden rise in alanine transaminase and aspartate transaminase due to insufficient portal flow, and/or signs of portal hypertension, such as ascites, melena, or hematochezia [8-11]. Before PTPS placement, hyperacute rejection, primary non-function, or severe preservation injury of allografts and other vascular complications of liver grafts, including hepatic vein stenosis, hepatic artery thrombosis, or massive hepatic necrosis, should be excluded by CTA [11].

The Ethics Research Committee of First Affiliated Hospital, School of Medicine, Zhejiang University approved this retrospective study and agreed that informed consent was not necessary because of the observational nature of the study. All data were anonymized and de-identified prior to analysis.

Procedure

Under ultrasonographic guidance, a portal vein branch was percutaneously punctured with a 18-gauge PTC needle (Kyowa Hakko Co., Ltd, Japan) under local anesthesia, then a 4-F coaxial dilator and a 7F sheath (Terumo Co., Ltd, Tokyo, Japan) were introduced over a 0.035-inch angled hydrophilic guide wire (Terumo Co., Ltd, Japan). The guide wire was manipulated to traverse the stenotic portion, and a portal

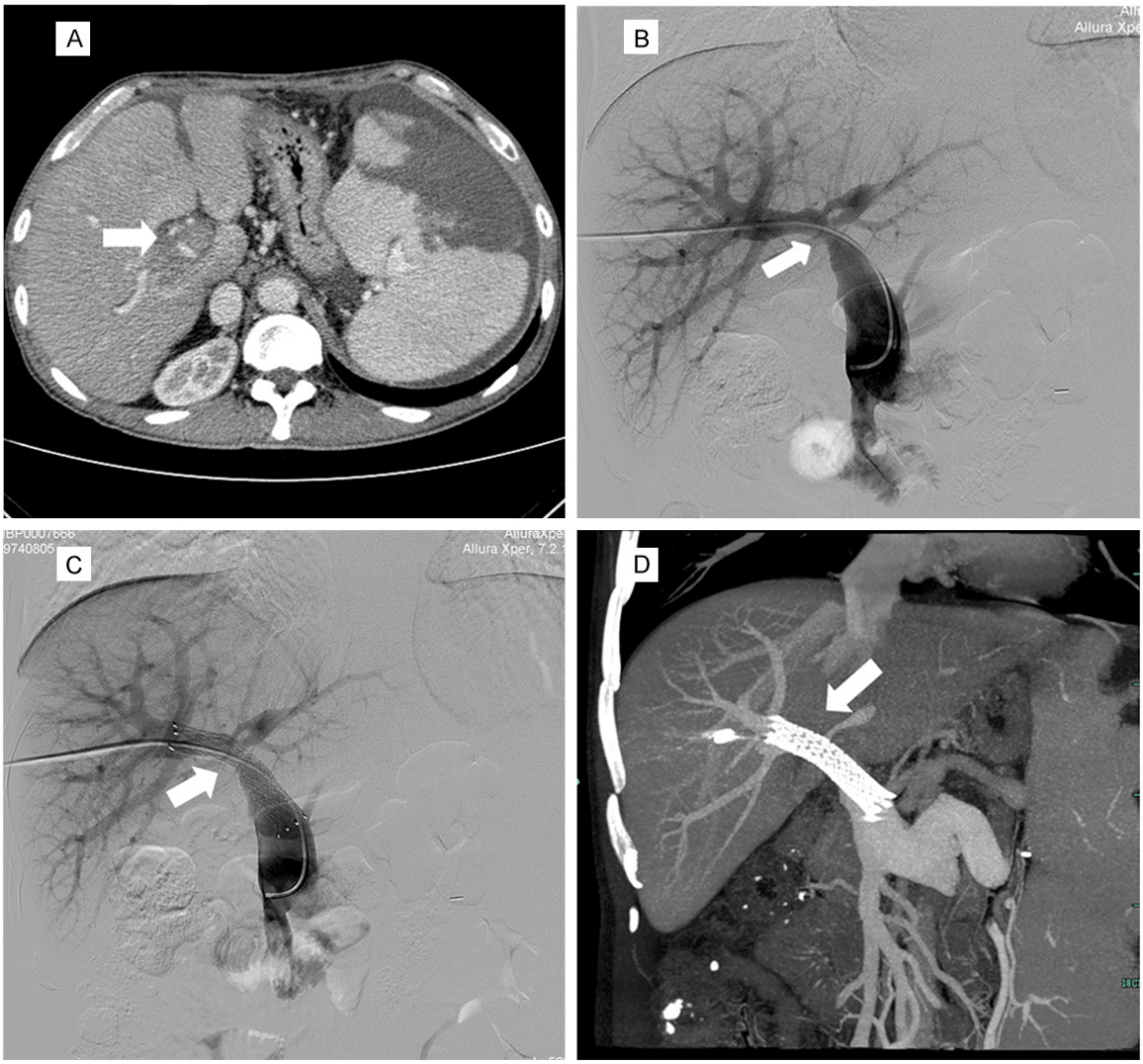

Figure 1. A 39-year-old male patient demonstrated main PV stenosis at 50 days after LT. A. Enhanced computed tomography showed that periportal fibrosis at porta hepatis(arrow) seemed to have led to PVS. B. Before stent placement, transhepatic portography also revealed a PVS at porta hepatis(arrow). C. Portal venogram obtained immediately after metallic stent placement (arrow) displayed no further PVS. D. The follow-up abdominal CTA showed patency of the metallic stent (arrow) in the portal vein of the liver graft. PV = portal vein, LT = liver transplantation, PVS = portal vein stenosis, CTA = computed tomography angiography.

venography was obtained to determine the length of the stenotic portion and the surrounding collateral circulation through a 5F C2 angiographic catheter (Cordis Corporation, Miami Lakes, FL, USA). The vascular stent (Cordis Corporation, Miami Lakes, FL, USA) was placed in the stenotic portion according to the stenotic length (**Figure 1**). Embolization with several coils (Cook Corporation, Denmark, USA) was required for serious collateral circulation or low hepatopetal blood flow. The transhepatic tract was embolized with coils routinely. Low-molecular-weight heparin calcium (100 U/kg) was used as anticoagulation therapy twice daily after PTPS for 7 days to produce a partial thrombin time 1.5-2.0 times. Oral and antiplatelet agents (aspirin 100 mg/d and dipyridamole 75 mg/d) were also prescribed for at least for 6 months [1, 8, 10, 12].

Follow-up

The technical and clinical success rate, complications, and stent patency were noted. Technical success was defined as successful stent placement with subsequent improvement of portal vein flow. Clinical success was defined

Table 2. Outcomes of percutaneous transhepatic portal vein stent treatment in 16 patients

Case	Technical results	Clinical results	PVS Extension	Procedure-related complications	Follow-Up, mo
1	S	S	Limited	None	59
2	S	S	Limited	None	55
3	S	S	Limited	None	50
4	S	S	Limited	None	47
5	S	S	Limited	None	36
6	S	S	Limited	Intra-abdominal hemorrhage	36
7	S	S	Limited	None	35
8	S	S	Limited	None	33
9	S	S	Limited	None	28
10	S	S	Limited	None	26
11	S	S	Limited	None	25
12	S	S	Limited	None	22
13	S	S	Limited	None	19
14	S	S	Limited	None	15
15	S	S	Limited	None	15
16	S	S	Extensive	None	13

S = success, PVS = portal vein stenosis. Limited: <50% of the whole length of the main portal vein; Extensive: >50% of the whole length of the main portal vein.

as subsequent amelioration of liver function and improvement of portal hypertension-related clinical signs and symptoms. Major complications were defined as those necessitating an additional interventional or surgical procedure or causing adverse sequelae or death [8]. The patency of the portal vein was evaluated by follow-up DUS and/or CTA. The DUS surveillance was routinely performed on postprocedural Day 1, Day 2, Day 3, and then weekly until the patient was discharged. Then, DUS was performed every 3 months thereafter. A CTA was required in the case of abnormal US results.

Results

The outcomes of PTPS are shown in **Table 2**. Technical success of PTPS was achieved in all 16 patients (100%). Portograms showed limited PVS (<50% of the whole length of the main portal vein) in 15 patients and extensive stenosis (>50% of the whole length of the main portal vein) in one patient. Collateral circulation embolization was performed in one patient due to hematemesis. The clinical success rate was 100% in all patients. Portal hypertension-related symptoms in five patients, including abdominal distension, ascites, or esophageal variceal bleeding, resolved after PTPS without recurrence during the follow-up. The abnormal liver function in 11 patients improved after PTPS, and has remained good in all thus far. Portal venous patency has been maintained for 13-59 months (mean time, 32.1±14.5 months) in all 16 patients. Suspected portal vein restenosis was observed by DUS in one patient 22 months after PTPS. However, CTA revealed patency of the portal vein. At the time this study was completed, all stents have remained patent without further interventional treatments.

Procedure-related complications occurred in one patient. The patient complained of abdominal distension after the procedure, followed by a progressively increasing heart rate. Urgent blood tests showed that hemoglobin decreased quickly from 132 to 98 g/L. Diagnostic abdominocentesis revealed uncoagulated blood, which was considered to be an active intra-abdominal hemorrhage. Emergency surgery was performed and pulsating bleeding from the transhepatic tract was observed. The bleeding was stopped by a local suture.

Discussion

Although the incidence of PVS after full-sized LT has been reported to be <3% [1-4], the results of such an event are usually catastrophic. Graft failure, portopulmonary hypertension, and esophageal varices due to portal hypertension have been reported [13]. Surgical repair or retransplantation has long been the standard treatment for PVS after LT [4-6, 8, 12]. Unfortunately, the role of surgical treatments is limited due to either the scar tissue that surrounds the transplant or the length of the involved venous structures, making it impossible to perform some procedures on critically ill patients, or because of a shortage of liver grafts [11, 12]. Additionally, surgeries are invasive and associated with significant risks including morbidity, mortality, and recurrence rates [9, 12]. Because of advancements in

interventional radiology, we decided to use PTPS placements for PVS after LT.

Since portal vein angioplasty and PTPS were first reported by Olcott et al. [14] in 1990, they have subsequently been established as widely accepted, safe, and effective approaches for treating PVS after LT [10, 15-17]. Wang JF et al. [15] later reported the intermediate results of percutaneous transhepatic balloon dilation with stent deployment in nine patients with PVS after LT. Portal venous patency was maintained in all nine patients from 6 to 19 months (mean 10 months). Although Funaki et al. [16] reported that balloon dilation combined with stent implantations showed a patency of 100% over a follow-up of 47 months, stents were deployed only in recurrent stenoses or elastic portal venous stenoses. Thus, successful use of primary PTPS instead of balloon dilation for treatment of posttransplantation PVS for long-term effects is rare. In our study, only PTPS was used to treat PVS in order to improve hepatopetal blood flow in all patients, which was different from the study by Funaki et al. This was because the duration of the portal vein stenosis was much longer in our study, which meant the stenosis was likely to be unresponsive to balloon angioplasty. In addition, a high incidence of restenosis after balloon dilation of PVS has been reported previously [7, 18]. Shibata et al. [10] reported the patency of portal vein after balloon angioplasty for PVS was 71.4% with a mean follow-up of 24.4 months. They suggested that the stent placement should be considered for a residual significant stenosis or a recurrent stenosis within a few months after balloon angioplasty [12, 16]. In our study, we have maintained portal venous patency in all of these patients, even for up to five years in one patient. To date, there has been no recurrent stenosis of their stents.

One of the controversies of metallic stent deployment is that a stent placement may interfere with further retransplantation [19]. Some authors have suggested that repeat balloon dilation should be utilized instead of intravascular metallic stents due to the possible need for retransplantation in patients suffering from PVS [10]. Other authors have found that at the time of retransplantation, the stents can be excised or left *in situ*, and a jump graft from the superior mesenteric vein to the donor portal vein be placed [3]. However, these suggestions remain controversial. The long-term patency of stenting should also be considered [4, 18]. There is no unified standard for maintaining anticoagulation states to prevent thrombosis after PTPS [11, 15, 20, 21]. Anticoagulation therapies prescribed to our 16 patients after PTPS placements maintained the long-term patency of the stent.

The major complications of PTPS include bleeding and biliary injury. Postprocedure abdominal bleeding occurred in one patient in our study, possibly because of unstable embolization of the transhepatic tract. Reliable embolization or using a transjugular intrahepatic portosystemic shunt (TIPS) approach may reduce the risk of bleeding. The TIPS approach has also been reported as being useful for the treatment of portal vein thrombosis after LT, and is especially recommended in patients with significant coagulation disorders and ascites [22, 23]. Moreover, gentle and delicate manipulation of the puncture needle and guide wire is also crucial to minimize injury to the transplanted liver graft [24].

Nevertheless, there are some limitations to our study. First, the number of patients enrolled in this study was not large enough. Measuring the long-term results of larger patient pools is necessary for a more robust assessment of PTPS for PVS after LT. Secondly, this study was of a retrospective design. Randomized studies would be ideal to compare the long-term results of the use of PTPS and surgical treatment for PVS after LT. Thirdly, the pressure gradients were not obtained during the procedures.

In conclusion, PTPS is a feasible and effective alternative procedure for patients suffering from PVS after LT and shows excellent long-term outcomes. However, possible lethal complications of these procedures should be kept in mind.

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Disclosure of conflict of interest

None.

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