Acta Cardiol Sin 2015;31:152–157
Brief Report
doi: 10.6515/ACS20140503A

Percutaneous Transluminal Angioplasty and Stenting for Hepatic Vessel Stenosis after Orthotopic Liver Transplantation

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Background: This study aimed to evaluate the efficacy of vascular intervention in percutaneous transluminal angioplasty (PTA) for the treatment of hepatic artery and hepatic vein stenosis after liver transplantation (LT), including thrombotic total occluded lesions.

Methods: Percutaneous transluminal angioplasty after orthotopic liver transplantation was performed to re-open hepatic vessel lesions. We daily used routine Doppler ultrasound during admission for early detection of graft hepatic vessel lesions, including hepatic artery and vein lesions. In outpatients, Doppler ultrasound was performed every month. Urokinase was delivered with a dose of 150,000-300,000 IU by catheter before PTA for thrombotic total occlusion of the graft for hepatic artery patients. Laboratory data were collected to evaluate the effects of the PTA procedure.

Results: The study involved a total of seven patients, six of whom were successfully treated by a first PTA procedure. Thrombolysis use of urokinase in totally occluded donor hepatic arteries post-LT following stenting was successful in three patients. One complication occurred, an arterial dissection and perforation, finalizing the success rate at ~86% and the complication rate at ~14%. Therefore, our study has a primary patency rate of 100% at 1 and 3 months. Also, the graft survival rate was 100 % and 86 % in the first and third months, respectively.

Conclusions: PTA with stenting is an effective treatment for hepatic vessel stenosis, including hepatic arteries and hepatic veins, after a liver transplantation without an increase in the complication rate. In addition, thrombolysis using urokinase intra-artery infusion in graft thrombotic total occluded patients is a good treatment strategy as well.

Key Words: Angioplasty • Complication • Liver transplantation

INTRODUCTION

Liver transplantation (LT) is the optimal treatment choice for patients with liver failure. Although balloon angioplasty has been accepted as a safe and effective initial treatment to manage hepatic artery and venous flow abnormalities, it may induce a rupture of the fresh anastomosis, and it also may be ineffective at eliminating various etiologies of vessel inflow or outflow lesions in the early post-transplant hepatic patient. Therefore, the purpose of the present study was to evaluate the effectiveness and complications of PTA and stenting for hepatic vessel lesions, including hepatic arteries stenosis, total occluded thrombotic artery lesions and hepatic veins stenosis after a cadaveric liver post-transplant hepatic vessel flow abnormality. The following parameters were documented retrospectively: technical

Received: September 24, 2013 Accepted: May 3, 2014
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success and complications. The primary patency rate implies uninterrupted patency following the PTA procedures by ultrasound evaluated. Also, graft survival rate is the patient survival rate after liver transplantation.

METERIALS AND METHODS

Patient population

From 2009 to January 2014, eighteen patients received a liver transplant at our facility. Eight patients received a hepatic angiogram post-LT. Seven of those were diagnosed with hepatic vessel lesions: three patients with hepatic artery stenosis, three patients with hepatic artery thrombotic total occlusion, and one with hepatic vein stenosis. Doppler ultrasound was used to evaluate the hepatic vessel stenosis. We evaluated the hepatic arteries and measured the resistive index (maximal systolic velocity − end diastolic velocity/maximal systolic velocity) and the systolic ascending time. The hepatic artery was considered to be stenotic when the resistive index (RI) was less than 0.5 and/or the systolic ascending time was greater than 10 milliseconds. During hospitalization, in our policy, screening Doppler ultrasound was performed by following protocol for early detection of hepatic artery stenosis. Doppler ultrasound was performed twice a day during the first week after transplantation, once a day during the second week, and once a week after the third week until discharge. If we found any problem in serum liver function test, we did not hesitate to perform Doppler ultrasound as soon as possible. Unknown reasons causing hemodynamic compromise prompted the use of emergency ultrasound or computerized tomography as needed to define vascular complications. After discharge, we used ultrasound to evaluate the post-PTA primary patency rate monthly. Three patients showed complete thrombotic total occlusion of a hepatic artery, as shown in Figures 1A and B. Urokinase (UK) was delivered with a dose of 150,000-300,000 IU by catheter before PTA for those patients. PTA was performed as early as 12 hours to as late as 166 days in patients ranging from 40 to 71 years of age (Table 1). Liver enzyme levels were measured before and after the procedure to detect any improvements in the allograft liver function.

Techniques of vascular intervention

If Doppler ultrasound defined RI less than 0.5, patients received hepatic angiography. Written informed consent was obtained from each patient. A selective femoral artery or right internal jugular vein approach, hepatic angiogram (n = 6) and venography (n = 1) were performed. A 0.035-inch hydrophilic Roadrunner wire

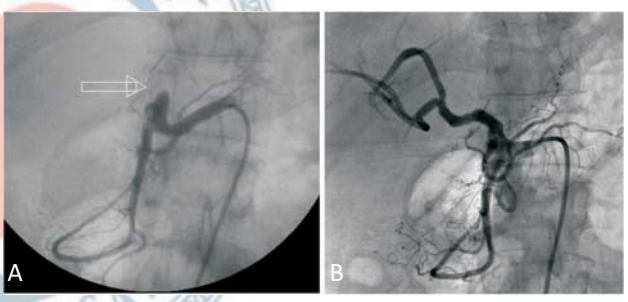

Figure 1. *Patient No. 1 revealed hepatic artery total occlusion post liver transplantation (A, white arrow). Post PTA with two stent (5.0 × 18 mm, 7.0 × 18 mm) restored hepatic artery flow (B).*

Table 1. Indication for LT and time interval from LT to PTA

Case No.	Age/Gender	Disease	Donor	TI after LT (days)
1	53/M	Alcoholic LC, HCC	Cadaveric	8
2	55/F	LC, HCV	Cadaveric	130
3	55/M	LC, HCV, HCC	Cadaveric	34
4	61/M	LC, HBV, HCC	Cadaveric	166
5	71/M	Alcoholic LC, HCC	Autotransplant*	6
6	40/M	Alcoholic LC	Cadaveric	30
7	56/F	LC, HCV	Cadaveric	0.5
Mean ± SD		53.5 ± 66.5		

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitic C virus; LC, liver cirrhosis; LT, liver transplantation; PTA, percutaneous transluminalangioplasty; SD, standard deviation; TI, time interval.

* Patient had huge hepatoma, the surgeon removed whole liver from patient and embedded tumor-free liver to patient during operation.

(Cook) and a 7F JR guiding catheter (Terumo, Japan) were used to do selective angiogram. A 0.014-inch PT2 moderate support guide wire (Boston Scientific) was introduced to cross the lesion. Stent placement was performed with an SD stent, an express coronary stent or a Wall stent (Boston Scientific, Galway, Ireland). Heparinization was not by intravenous bolus during the procedures because of abnormal liver function and fear of coagulopathy in these patients.

Statistical analysis

The statistical package software (Version 11.5.0.0, MedCalc, Ostend, Belgium) was used for analysis. All data of continuous variables are expressed as mean ± standard deviation. Categorical variables were analyzed using the Chi-square test with Yates' correction. Between-group differences in continuous variables were measured by Student's *t*-test. A probability value of $p \leq 0.05$ was considered statistically significant.

RESULTS

The patients who received PTA had a median age of 55 years. The time interval from LT to PTA was 53.5 ± 66.55 days (Table 1). Six of seven patients were successfully treated without complications. One patient died of hepatoma recurrence 92 days post-LT (Table 2). Additionally, our study had a primary patency rate of 100% at 1 and 3 months. Also, the graft survival rate was 100% and 86% in the first and third months, respectively. We observed significant improvement of liver function after PTA ($p < 0.001$) (Table 3). In one patient, a hepatic artery was perforated after PTA, likely due to the dissection of the artery. We used the stenting procedure in this patient to compress the intimal flap, utilizing a three-millimeter-diameter balloon inflated for three minutes. Eventually, the hepatic artery was reopened and the stenosis disappeared. At two months after PTA, the patient's diagnosis appeared normal. Six of the seven procedures (85.7%) were successful, and complications only occurred in one procedure (14.3%). Delayed complications did not occur during the follow-up period, which was an average of 243 days after PTA (Table 2). Thrombolysis use of UK in totally occluded donor hepatic arteries post-LT following stenting was successful in three patients (Table 2).

DISCUSSION

Hepatic vessel steno-occlusive disease is the most common complication following LT. This includes hepatic artery and hepatic vein stenosis and aneurysms.[1,2] Hepatic artery thrombosis (HAT) is defined as a thrombotic occlusion of the hepatic artery and has been classified into two types depending on the time of presentation as follows: early HAT (within the first 30 days after

Table 2. Catheterization parameter

Case No.	Lesion characteristic	Urokinase	Guide catheter (F)	Balloon DA (mm)	Stent (mm)	Complication	Follow-up (day)	Clinical outcome**
1	Hepatic artery thrombotic*	150k	JR (7)	3.0 × 20	5.0 × 18 7.0 × 18	no	430	Patency
2	Hepatic artery thrombotic*	300k	JR (7)	2.5 × 20 5.0 × 20	4.5 × 16	no	372	Patency
3	Hepatic artery stenosis	no	JR (7)	no	3.5 × 15	no	270	Patency
4	Hepatic artery stenosis	no	JR (7)	4.0 × 20	no	no	269	Patency
5	Hepatic vein stenosis	no	no	3.0 × 20 12 × 40	14 × 60 16 × 60	no	92	Died
6	Hepatic artery stenosis	no	JR (7)	3.5 × 12	no	no	180	Patency
7	Hepatic artery thrombotic*	300k	JR (7)	3.5 × 12 2.0 × 20 4.5 × 20	4.5 × 16	perforation	90	Patency
Mean ± SD							243 ± 131	

DA, diameter; JR, Judkins Right (Terumo). * Thrombus 100% occlusion; ** Meaning graft primary patent during following time.

Table 3. Laboratory data

	Pre-PTA	Post-PTA	p
White blood cell (/uL)	11250 ± 4945	8283 ± 3197	0.36
Hemoglobin (g/dL)	11.6 ± 2.99	10 ± 1.33	0.1
Platelet (×104/uL)	8.48 ± 5.92	8.78 ± 5.49	0.87
Glutamate oxaloacetic transaminase (U/L)	893.2 ± 1838	91.6 ± 151.5	< 0.001
Glutamate pyruvate transaminase (U/L)	106.5 ± 83.58	67.8 ± 72.2	0.76
Creatinine (mg/dL)	1.58 ± 1.2	1.38 ± 1.21	0.98
Bilirubin, total (mg/dL)	6.95 ± 7.76	8.21 ± 10.22	0.56
Bilirubin, direct (mg/dL)	5.23 ± 6.26	5.82 ± 7.67	0.67
Prothrombin time (secs)	15.6 ± 5.17	14.9 ± 3.29	0.4
Alkaline phosphatase (U/L)	330.2 ± 156.8	282.8 ± 71.29	0.16
r-Glutamyl transpeptidase (U/L)	145.75 ± 123.3	64 ± 19.87	0.01

Post-PTA, means blood sampling one week post PTA; Pre-PTA, means blood sampling in the same day or before PTA.
PTA, percutaneous transluminal angioplasty.

LT) and late HAT (30 or more days after LT).[3] Hepatic artery thrombosis carries a mortality rate of 27-58%. Early HAT has been associated with a higher mortality of 33.3% (range: 0-80%).[3,4] Many explanations have been suggested to explain hepatic artery stenosis after LT, including ischemia of the anastomotic site, diagonal anastomosis, torsion and angulation by a bagged anastomotic vessel, small vascular diameter, external compression, problems with the operative procedure, rejection, reactive edema, thrombus, endoluminal hyperplasia, and fibrosis.[5,6] However, it is difficult to clearly specify the precise cause, and a variety of issues may be associated with stenosis. It is well-understood that stenosis of the hepatic artery causes thrombosis because the hepatic arterial flow is static, resulting in hepatic necrosis.[7] Acute hepatic necrosis and complications of the biliary system greatly influence the survival rate following a graft. Therefore, hepatic artery stenosis requires immediate treatment.[8,10] To early on detect post-surgical graft hepatic vessel lesions, we routinely used Doppler ultrasound during hospitalization every day for inpatients, and monthly for outpatients. In patient no. 7, we diagnosed thrombotic total occlusion of the graft hepatic artery within 12 hours post-operation by routine screening Doppler ultrasound. Unknown reasons caused increasing serum bilirubin and persisting jaundice, enlargement of the donor liver size and increased a portal vein diameter similar to congestive liver reported by ultrasound. In these situations, hepatic vein occlusion should be suspected. A selective venogram for hepatic vein was necessary for patient no. 5 (as shown in Figures 2A, B, C, and D). The delivery by catheter of a thrombolytic agent has been used as a continuous infusion, bolus or a combination of the two. Clinical safety and efficacy have been demonstrated with different dosing regimens. Bovyat et al.[11] recommended a dose of 1-3 mg recombinant tissue plasminogen activator or 50,000-250,000 IU UK. For total occlusion thrombus lesions in hepatic arteries, UK intra-hepatic artery bolus infusion effectively restored blood flow in the hepatic

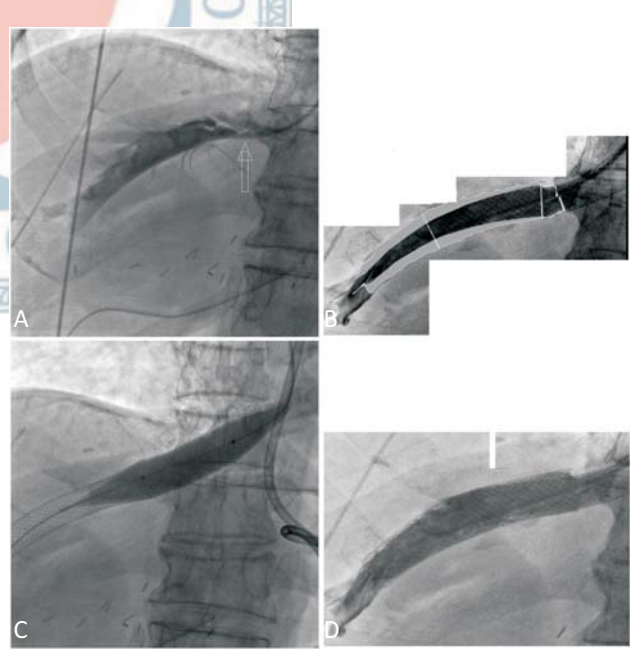

Figure 2. *Patient No. 5 revealed hepatic vein drainage outlet surgical anastomosis stenosis (A, white arrow), post two Wall stent (14 × 60 mm, 16 × 60 mm) deployed showed without full expansion (B). Post dilated with balloon (12 × 40 mm) showed full expansion of Wall stent and returned venous flow (C and D).*

arteries.[12,13] Zhou et al.[14] used up to nine million units of UK without any complications in one particular patient. The duration of thrombolytic therapy has been reported to vary. Zhou et al.[14] recommended 2-4 days of therapy to complete the treatment, successfully using different dosing regimens. Careful monitoring of coagulation profiles and clinical symptoms is necessary during thrombolysis treatment. Several authors have also mentioned the use of prothrombin time and activated partial thromboplastin time and fibrinogen levels for monitoring. In our cases, thrombolysis was performed with UK via a catheter-based infusion when an angiogram showed a totally occluded hepatic artery before the guide wiring was introduced. Initially dosage of UK is 150000 IU. After the guide wiring was introduced, the hepatic artery flow returned in all three cases. Therefore, this is the reason we know that thrombotic lesions are involved. This appears to be very useful in restoring the hepatic artery flow, and Zhou et al.[14] described the same results. After hepatic artery flow returned, significant stenosis lesion distal to the previous thrombus site was always found, which needed to be dilated with a balloon and stenting provided in all three patients.[15,16] Our study demonstrated that patients benefitted from significantly improved liver function ($p < 0.001$), but more data regarding the biliary system are required to support the beneficial developments post-PTA. Most patients showed improved biliary system function up to two months after the procedure and returned to normal function 3 months post-PTA, with the exceptions of no. 5 (Table 4). Hepatic artery thrombotic total occlusion patients appeared to show an increased incidence in the young and a prolonged operation time. However, more data are needed to support these issues. The graft hepatic stenosis rate was high in this study for two reasons. One: rarely donor source, we still in learning curve; two: all donors were cadaveric. Although this study included only a few cases, and we need more long term data, our manuscript emphasizes that not only hepatic arteries, but also hepatic veins and total thrombotic occlusion hepatic arteries could be subjected to successful vascular interventions. This could improve liver function and preserve the donor organ from damage.

In conclusion, PTA with vascular intervention is effective for the treatment of hepatic artery stenosis in LT, including hepatic veins and thrombotic total occlusion

Table 4B. Laboratory data in glutamate pyruvate transaminase (ALT) series

Patient No.	Pre-PTA ALT (U/L)	Post-PTA One week ALT (U/L)	Post-PTA One month ALT (U/L)
1	101	32	16
2	235	188	0.14
3	59	44	25
4	-	-	-
5	174	123	34
6	9	7	6
7	61	13	14

ALT, glutamate pyruvate transaminase; Post-PTA, means blood sampling one week, one month, post PTA; Pre-PTA, means blood sampling on the same day before PTA; PTA, percutaneous transluminal angioplasty.

Table 4A. Laboratory data in bilirubin series

Patient no.	Pre-PTA bilirubin, total/direct (mg/dL)	Post-PTA one week bilirubin, total/direct	Post-PTA one month bilirubin, total/direct	Post-PTA two months bilirubin, total/direct	Post-PTA three months bilirubin, total/direct
1	1.6/0.9	6.8/5.4	0.9/0.4	0.6/0.2	0.9/0.5
2	24.7/19.1	22.2/17.5	24.3/19.2	17.7/12.7	-
3	1.1/0.4	1.2/0.5	0.6/0.2	0.6/0.2	0.7/0.3
4	-	-	8.8/7.4	2.1/1.4	1.1/0.4
5	17.4/11.2	5.2/3.7	40.7/28.4	46.8/39.8	-
6	1.8/1 .	1.9/1.2	1.3/0.9	0.7/0.3	1/0.3
7	2.7/2.3	4.4/3.1	1.7/1	0.5/0.3	0.7/0.2

ALT, glutamate pyruvate transaminase; Post-PTA, means blood sampling one week, one month, two months, three months post PTA; Pre-PTA, means blood sampling in the same day before PTA; PTA, percutaneous transluminal angioplasty.

hepatic arteries, without significantly increasing the complication rate.

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