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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Stent insertion and balloon angioplasty for portal vein stenosis after liver transplantation: long-term follow-up results

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PURPOSE
It is not easy to determine whether balloon angioplasty or stenting should be performed in patients with portal vein stenosis after liver transplantation. We aimed to propose appropriate indication by evaluating long-term outcomes of balloon angioplasty and stent insertion in adult liver transplant patients.

METHODS
We retrospectively reviewed 31 patients with portal vein stenosis among 1369 patients who underwent adult liver transplantation from January 2001 to December 2015. When stenosis was confirmed by venography, angioplasty was performed first. When there was no flow improvement or pressure gradient was not decreased after angioplasty, stent insertion was performed. We also performed primary stent insertion without angioplasty for diffuse stenosis, kinking, external compression, and near occlusion of portal vein in venography. We assessed patency in patients who underwent percutaneous transluminal angioplasty and stent insertion through regular outpatient follow-up and evaluated technical and clinical success and long-term results.

RESULTS
Technical success was 85% and 100% in balloon angioplasty and stent insertion, respectively. Clinical success was achieved in 78% of balloon angioplasties and in 100% of stent insertions. At 1, 5, and 10 years after balloon angioplasty, patency rates were 87%, 82%, and 68% respectively, and the rates of stent patency were all 100%. Portal vein size measured during the operation of patients with and without recurrence were 19±4.2 mm and 19±3.0 mm ($P = 0.956$), respectively. The balloon size of patients with and without recurrence were 11±1.95 mm and 14±1.66 mm, respectively ($P = 0.013$), when balloon angioplasty was performed after stenosis diagnosis.

CONCLUSION
Stent insertion can be considered when fibrotic changes are expected due to repeated inflammation and when the balloon size to be used is small. Balloon angioplasty seems less risky for anastomotic ruptures in portal vein stenosis in the early post liver transplantation period.

Liver transplantation is considered the only treatment for end-stage liver disease (1). Successful vascular anastomosis is an important factor for successful liver transplantation. Portal vein reconstruction is the most important part of the surgery and portal vein complications can cause graft failure (2). Portal vein complications are anastomotic portal vein stenosis (PVS) or portal vein thrombosis (3). Portal vein stenosis (PVS) is rare and occurs in 5% of all liver transplantations (4). PVS is more common in living donor liver transplantations (LDLT) (4%) and pediatric liver transplantation (7% to 27%) (3, 5), but is uncommon (< 2%) in adult whole liver grafts (6, 7).

Since Olcott et al. (8) published the first study on post liver transplantation portal vein angioplasty and stent insertion, percutaneous transhepatic balloon angioplasty and stent insertion have been commonly used and are considered safe methods to treat PVS after liver transplantation (9–11). However, balloon angioplasty still has a higher recurrence rate than stent insertion. Previous studies reported a recurrence rate of 26.7% (12) and 25.6% (13) for percutaneous transluminal angioplasty (PTA). For stent insertion, the reported recurrence

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rate was 0% (14, 15). Although stent insertion has the advantage of low recurrence rate, it makes vascular anastomosis difficult at re-transplantation. In addition, stent insertion may result in excessive treatment for patients who may be adequately treated with balloon angioplasty alone. In these circumstances, determining whether to perform balloon angioplasty or stent insertion in PVS patients is a difficult issue. Therefore, the purpose of this study was to identify appropriate treatment to reduce recurrence and excessive treatment of PVS by evaluating long-term outcomes of interventions in adult liver transplantation patients.

Methods

Patients

At our institution 283 patients over 18 years of age underwent deceased donor liver transplantation (DDLT) and 1086 underwent LDLT between January 2001 and December 2015. Of these patients, 31 patients underwent balloon angioplasty or stent insertion for PVS. These 31 patients ranged in age from 25 to 62 years (mean, 52 years) and included 28 men and 3 women. The interval between transplantation and initial intervention ranged from 4 days to 49 months (mean, 15.4 months).

In DDLT, the entire liver was used and was not split. In LDLT, only the right liver was transplanted. Anastomosis of the portal vein during liver transplantation was achieved by the standard end-to-end technique. Portal vein anastomosis was performed with sufficient growth factor to avoid stenosis. In 4 transplantation patients, the length of the portal vein was short and the cadaveric iliac vein graft was inserted between the recipient and the donor. In all patients, flow was confirmed by Doppler ultrasonography (US) to ensure no abnormalities after anastomosis of the vessels.

The initial diagnosis modality of PVS was Doppler US on days 1, 3, and 7 after liver transplantation. If abnormal results such as portal vein narrowing to >50%, absence of flow or flow rate acceleration in the stenotic part >3 times the rate in the prestenotic portal vein were confirmed with Doppler US and when definite stenosis was suspected, venography was performed. When stenosis was suspected via Doppler US based on the patient's condition, intervention was performed after computed tomography (CT) angiography. This study complied with the Declaration of Helsinki and was approved by the Institutional Review Board of Samsung Medical Center (2018-04-062).

Main points

- Portal vein stenosis after liver transplantation may induce serious morbidity, including graft failure due to portal hypertension.
- Balloon angioplasty may be safe and effective for early portal vein stenosis.
- Stent insertion should be considered when fibrotic change is expected around the hepatic hilum due to repeated inflammation.

Balloon angioplasty and stent placement

Informed consent was obtained from all patients or their guardians. The procedure was performed in the operating room under local anesthesia in 30 cases and under general anesthesia in one case. The transplanted liver was punctured with a 22G Chiba needle using fluoroscopic and US-guidance, which was aimed at the peripheral blood vessels of the liver portal under the capsule. After the portal puncture was confirmed via injection tests, a 0.018-inch platinum-coated nitinol guidewire (M.I.Tech) was placed in the main portal vein. We changed the nitinol guidewire to a 0.035-inch guidewire (Glidewire, Terumo) and then inserted a 6–8 F vascular sheath (Cook Medical). Portal venogram was obtained. Angioplasty was performed using an ultra-thin balloon dilatation catheter (Boston Scientific) with balloon diameter equal to or greater than 10% of the diameter of the nonstenotic portal vein. Careful and continuous rise of pressure was achieved using inflation devices (Merit Medical Systems), and instrument expansion continued until it lost its waist. Increased balloon pressure at full expansion was maintained for 2 minutes. After balloon dilatation was completed, portal angiography was performed. However, when stenosis remained in the stenotic site as compared to the nonstenotic site, stent insertion was performed with a self-expandable stent (Boston Scientific) that was then completely ballooned.

Primary stent insertion was attempted using a Wallstent (Boston Scientific). Stents with the same diameter or 10% larger than that of the nonstenotic portal vein were used. Balloon angioplasty was performed if the deployed stent showed a residual stenosis greater than 50% of its normal diameter. In the final angiogram, portal vein flow improved significantly and the procedure was completed without any other immediate complications.

Follow-up

According to the liver transplant protocol after angioplasty and stent insertion, follow-up Doppler US was generally performed the next day or later in admission by a radiologist at our hospital. If there was an abnormality, CT angiography was performed to confirm whether the problem was with the portal vein. In the absence of any abnormalities on US or laboratory findings on follow-up examination for hepatocellular carcinoma patients, Doppler US and liver CT were alternately performed every 3 months after liver transplantation during the first year and every 6 months after the first year. Patients who were not diagnosed with hepatocellular carcinoma underwent Doppler US 6 months after liver transplantation and liver CT at 1 year, followed by alternating Doppler US and liver CT every other year.

Definition and analysis

Technical and clinical success, patency rate, and complications were reported retrospectively. Successful PTA can be defined as a reduction in residual stenosis within 30% compared with normal portal vein after balloon angioplasty on venography. Reduced pressure gradient and improved flow were considered technological successes. Successful stent insertion was defined as placement of the stent at the intended location of the portal vein and improved portal vein flow. We defined clinical success with improvements in clinical patterns associated with liver function and portal hypertension. We defined major complications as those that required increased levels of care, additional surgery or interventional manipulation, adverse sequelae, or death. Other complications were defined as minor. Intervention patency rates were evaluated by Doppler US and CT scans.

Statistical analysis

Between nonrecurrent and recurrent patients, paired t-test was performed to analyze the difference between balloon size measured in venogram and graft portal vein size measured in operation. We used the Kaplan-Meier method to analyze patency rate. We compared rates using the log-rank test and considered a *P* value less than

Table 1. Characteristics of patients who underwent portal vein dilatation because of portal vein stricture

No	Sex	Age (years)	POD (days)	Graft liver	Portal vein size (at OP)	Balloon size (at PTA)	Patency	Patent period	F/U period (months)	Biliary complication	Management (number of changes)
1	M	38	224	RL		14	Yes		197	No	
2	M	56	42	RL	25	14	Yes		10	Stricture	PTBD (1)
3	M	58	318	RL	14	16	Yes		173	No	
4	M	58	530	RL	24	16	Yes		165	No	
5	M	43	1048	RL	15	10	Yes		35.07	No	
6	M	41	867	Whole liver	17	16	Yes		132	No	
7	M	46	463	RL		9	No	68.0	133	Stricture	PTBD (13)
8	M	60	98	RL	22	12	Yes		14	Stricture	PTBD (1)
9	M	48	1264	RL	22	10	No	5.5	101	Leakage	ERBD (3)
10	F	62	594	RL	20	12	Yes		71	No	
11	M	47	135	RL	20	16	Yes		53	No	
12	M	51	688	Whole liver	20	14	No	4.3	64	No	
13	M	25	500	RL	15	12	No	21.7	57	Leakage	PTBD (9)
14	M	57	90	Whole liver	26	12	Yes		50	No	
15	M	53	171	Whole liver		14	Yes		51	No	
16	M	61	777	RL	20	14	Yes		48	Stricture	ERBD (5)
17	M	60	144	Whole liver	18	12	No	0.16	7	Leakage	ERBD (1)
18	M	60	378	RL	18	14	Yes		45	Stone	PTBD (1)
19	M	68	4	RL	17	14	Yes		44	No	
20	M	48	1236	RL	18	14	Yes		44	Stricture	PTBD (3)
21	M	49	30	RL	11	14	Yes		37	Stricture	PTBD (7)
22	M	58	434	RL	14	14	Yes		31	Stricture	PTBD (4)
23	M	50	186	RL	17	12	Yes		21	Stricture	PTBD (3)

POD, postoperative days; OP, operation; PTA, percutaneous transluminal angioplasty; F/U, follow-up; M, male; F, female; RL, right lobe; PTBD, percutaneous transhepatic biliary drainage; ERBD, endoscopic retrograde biliary drainage.

0.05 statistically significant. We performed all statistical analyses using SAS version 9.4 (SAS Institute, Inc.).

Results

Seven (2.4%) of the 283 DDLT patients and 24 (2.2%) of the 1086 LDLT patients were diagnosed with portal vein stenosis and underwent radiologic intervention. A total of 1369 liver transplantations were performed. Of the 31 patients who underwent intervention, PTA was performed in 27 patients except 4 patients who underwent primary stent placement. Stent insertion was performed in 4 patients who had failed PTA. The results of the 31 patients are shown in Tables 1 and 2. Percutaneous balloon angioplasty was attempted in 27 patients, percutaneous transhepatic stent placement was attempted in 4 patients, and primary stent insertion was performed in 4 patients. Stent insertion was performed when recoiling was observed after balloon dilatation or pre- and post-stenotic lesion pressure gradient difference was not resolved. Lack of pressure gradient reduction means that the stenotic sites did not dilate sufficiently after balloon dilatation. In percutaneous balloon angioplasty, technical success was achieved in 23 patients (85%). In the post-intervention venogram, flow improvement and pressure gradient resolution were confirmed. However, 3 patients showed residual stenosis of less than 10%, and 4 patients had residual stenosis between 15% and 30%. Although these patients showed residual stenosis, they were considered technical successes because they showed improved flow and resolution of the pressure gradient. In percutaneous transhepatic stent placement, all 8 patients showed technical success.

Clinical success was achieved in 78% of patients (18/23 patients) in ballooning and 100% of patients (8/8 patients) in stenting. Two (patients 7 and 17) of the 5 recurred patients were not given further treatment due to deteriorating conditions. Patient 7

Table 2. Characteristics of patients who underwent portal vein stent insertion because of portal vein stricture

No	Sex	Age (years)	POD (days)	Graft liver	Portal vein Size (at OP)	Stent size (at stenting)	Patency	F/U period (M)	Biliary complication	Management (number of changes)
1	M	50	1494	RL	13	10/6	Yes	170	Stricture	PTBD (4)
2	M	55	274	RL	20	14/4	Yes	83	Stricture	PTBD (9)
3	M	50	1399	RL	14	12/4	Yes	67	Leakage	PCD
4	M	55	665	Whole liver	22	14/4	Yes	59	Stricture	PTBD (8)
5	M	55	5	Whole liver	16	14/4	Yes	58	No	
6	F	53	27	RL	15	14/4	Yes	44	No	
7	M	54	19	RL	20	14/8	Yes	34	Stricture	ERBD (8)
8	F	46	227	RL	15	12/6	Yes	33	Stricture	ERBD (3)

POD, postoperative days; OP, operation; F/U, follow-up; M, male; F, female; RL, right lobe; PTBD, percutaneous transhepatic biliary drainage; PCD, pigtail catheter drainage; ERBD, endoscopic retrograde biliary drainage.

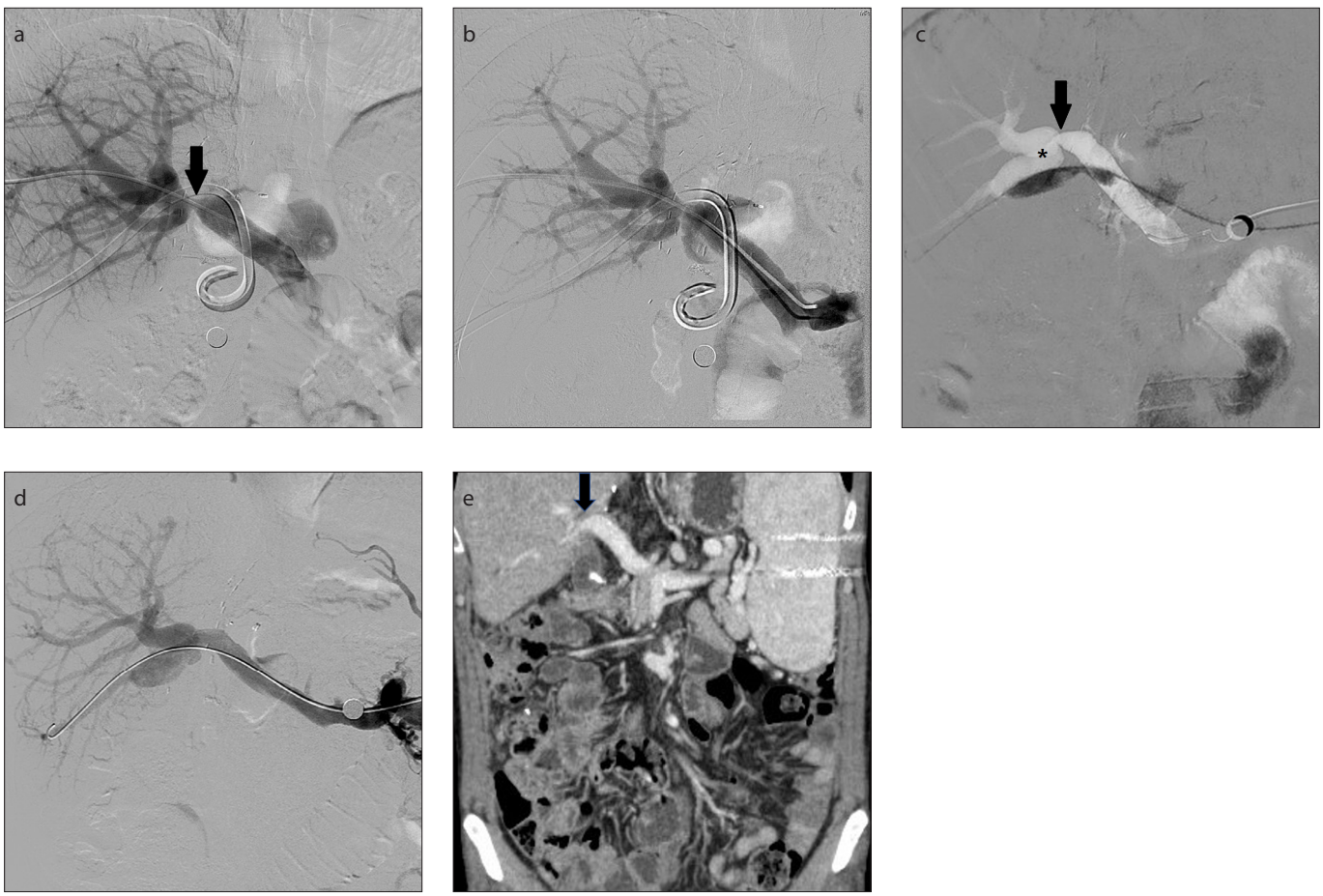

Figure 1. a–e. A 25-year-old man underwent right lobe living donor liver transplantation. Portal vein stenosis was suspected at POD 500, and percutaneous transhepatic portography was performed. The PTBD was inserted because of bile leakage at the duct anastomosis site, and the tip of the PTBD was in the duodenum. An angiogram **(a)** obtained before treatment shows an anastomotic structure *(arrow)*. Post-ballooning angiogram **(b)** showed improved blood flow through the portal vein, but there was residual stenosis. At 23 months after the first intervention, the angiogram **(c)** showed poststenotic dilatation *(asterisk)* and stenosis *(arrow)*. In the second intervention, post-ballooning angiogram **(d)** showed improved blood flow in portography, but there was residual stenosis as in the first intervention. CT angiography was performed **(e)** and showed recurrent stenosis *(arrow)* 17 months after the second intervention.

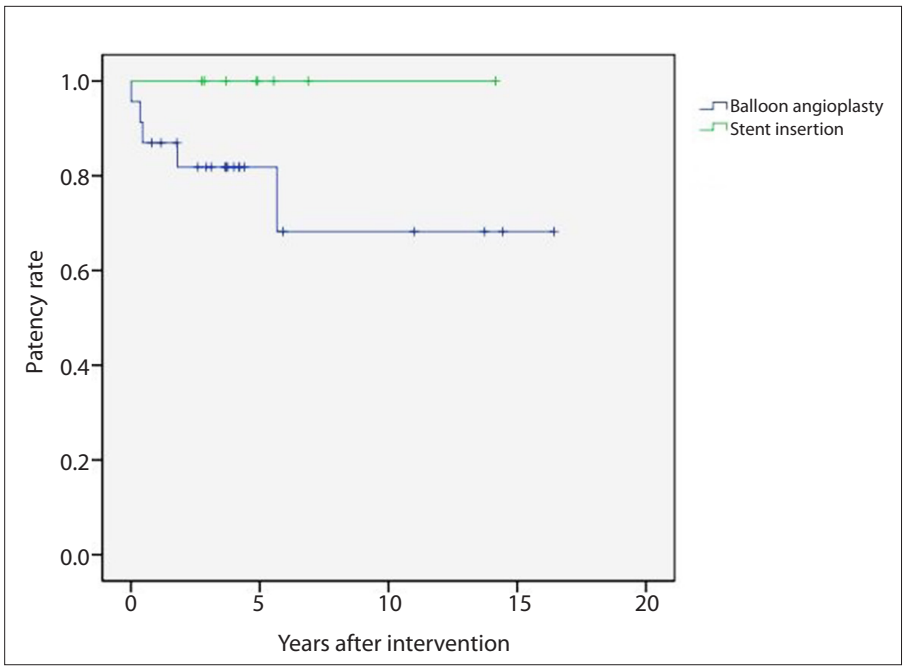

Figure 2. Kaplan-Meier curves showing primary stent insertion and balloon angioplasty patency rates ($P = 0.16$).

underwent PTBD insertion and was diagnosed with recurrent cholangiohepatitis resulting in liver cirrhosis. The patient was diagnosed with PVS during the follow-up period but did not receive further treatment. Eventually, the patient underwent re-transplantation. The other patient died from an intraabdominal infection without further treatment. Three of 5 recurred patients underwent additional treatment, one patient with stent insertion and two with additional balloon angioplasty. One patient who underwent an additional balloon angioplasty was suspected of recurrence but had no other symptoms (Fig. 1).

At the time of surgery, the portal vein size of patients with and without recurrence were 19±3.0 mm and 19±4.2 mm ($P = 0.956$), respectively. The balloon sizes of patients with and without recurrence were 11±1.95 mm and 14±1.66 mm ($P = 0.013$), respectively, when balloon angioplasty was performed after diagnosis of stenosis. Portal vein size at the time of surgery was not different between recurred and nonrecurred cases, but balloon size was different. The size of the balloon used in balloon angiography was equal to or slightly larger than the size of the nonstenotic extrahepatic PV.

Fig. 2 shows the primary patency rates for balloon angioplasty and stent insertion for patients with portal vein stenosis after liver transplantation. The median follow-up period was 54.2 months (range, 0.5–192.4 months). For ballooning, comprehensive 1-, 5-, and 10-year primary patency rates were 87%, 82%, and 68%, respectively. For stent insertion, the overall 1-, 5-, and 10-year rates were 100%. For ballooning, a total of 5 patients failed to maintain patency, and their median maintenance period was 19.8 months (range, 0.2–67.9 months). One of these patients underwent re-transplantation due to liver failure. Another patient did not obtain further management for portal vein stenosis because of an intraabdominal infection.

Complications occurred in one patient. The patient suffered a hematoma along the transhepatic guide tract, compression was performed post-ballooning, and angiography was terminated after confirmation of no bleeding. Thereafter, the patient recovered without additional bleeding. In other patients, there were no major complications such as hemoperitoneum, thrombosis formation, anastomosis rupture, or large hematoma associated with the procedure.

Of the 23 patients who underwent PTA, 12 (52%) had biliary complications. Biliary complications included stricture (8/12), leakage (3/12), and stone (1/12). Most patients underwent percutaneous transhepatic biliary drainage (PTBD) or endoscopic retrograde biliary drainage (ERBD) to manage biliary complications. Patients with recurrent PVS had a higher biliary leakage rate and more PTBD or ERBD changes. In stent insertion patients, 6 of 8 patients had stricture (5/6) or leakage (1/6) and were also managed by insertion of PTBD and ERBD. The number of PTBD and ERBD changes was found to be higher than in PTA patients.

Discussion

Previous studies have reported the effectiveness and feasibility of intervention treatment on PVS (8, 10, 14, 16). However, controversy remains over whether balloon angioplasty or stent insertion should be performed. Shibata et al. (17) reported that recurred cases (28.5%) underwent additional balloon angioplasty. Although it is the outcome of pediatric patients and the early period results of PTA, Funaki et al. (18) reported that seven (63%) of 11 patients who underwent initial venoplasty without stent placement developed recurrent stenosis between 1 and 13 months (mean, 6.3 months). Based on these results, balloon angioplasty has a risk of recurrence. Regarding stent insertion, although Shim et al. (14) reported low recurrence rate, radiologists tend to insert primary stent in the immediate post liver transplantation period due to possibility of anastomotic site rupture. (15) On the contrary, if the second liver transplantation is considered, it is difficult to make the decision to perform stent insertion. Therefore, a detailed indication of stent insertion and PTA is required.

In this study, 5 patients out of 23 had recurrence, and 3 underwent additional stent insertion and balloon angioplasty. Patients 9 and 13 had recurrent stenosis after first PTA and underwent a second PTA, and both patients had biliary leakage. Patients 9 and 13 had a history of repeat ERBD 3 times and PTBD 13 times, respectively. Patient 9 did not consider stent placement because of improved flow and decreased pressure gradient after the second PTA. At that time, stent insertion was not performed because the influence of biliary complication was not considered. After second PTA, PVS was suspected on follow-up CT and stent insertion would be required in the future. Even if we use high pressure balloons instead of standard balloons, flow is improved at the time of angioplasty, but stenosis is thought to recur because of fibrotic changes due to repeated inflammation. Stent insertion should be considered if the patient continues to require ERBD stent change. Although

patient 12 did not have biliary complications, diffuse stenosis from the portosplenic junction to the anastomotic site was confirmed in venography after recurrence and stent insertion was performed. There was no recurrence after stent insertion. One of the remaining two patients had repeated cholangiohepatitis and underwent re-transplantation for liver failure. The other patient died of sepsis from an intraabdominal infection. Eventually, the two patients died without further treatment.

Between recurrent and nonrecurrent cases, there was a difference in balloon size, but no difference in the size of the portal vein measured in liver transplantation surgery. Here, the portal vein size does not mean the normal portal vein size in the venography but the size of the graft portal vein at the time of surgery. These results suggest that a small balloon size is more likely to lead to a recurrence, and inserting a stent into a patient who will receive such a small balloon may reduce the need for additional procedures.

PVS occurs due to inflammation surrounding the portal vein (19). Inflammation around the portal vein occurs such as cholangitis and complicates fluid collection due to biliary leakage around the hepatic hilum. When inflammation and recovery is repeated, fibrotic change is also possible. Cholangitis is reported to occur in 1% of cases in which ERBD is inserted (20–22). Liver transplant patients who are immunocompromised due to the use of immunosuppressive agents are more likely to develop an infectious complication such as cholangitis (23). In our study, of the 5 patients with recurrent stenosis, 3 patients were regularly changing ERBD for leakage or stricture and all 3 patients were diagnosed with recurrent cholangitis. Although we do not entirely understand the mechanism for delayed PVS, it may be caused by fibrotic changes due to repeated inflammation. Therefore, if PVS occurs in patients who required regular replacement with ERBD, considering a stent insertion rather than balloon angioplasty may prevent repeated PVS procedures.

Ko et al. (15) performed primary stent insertion since the possibility of rupture of fresh anastomotic stricture could not be excluded. However, our results showed that balloon angioplasty with portal vein stenosis within 1 month occurred in only 2 of 23 cases. Both cases were performed with a 14 mm balloon size without any complications such as anastomotic site rupture and no recurrence. No rupture occurred in balloon angioplasty cases. Therefore, our results suggest that balloon angioplasty can be performed safely without rupture even within 1 month after liver transplantation. If the stent is inserted because of possibility of rupture, patency may be maintained for a long time, but this will be excessive treatment. The probability of anastomotic rupture is very low because a skilled surgeon performs an anastomosis and provides sufficient growth factors. Therefore, unless there is stenosis due to external pressure or kinking, PTA should be considered even within 1 month after liver transplantation.

Our study has several limitations. First, this study was retrospective and included a small sample of patients with portal vein complications. Therefore, we were not able to analyze risk factors. Second, pressure gradients were measured only in some patients. Third, patients with portal vein thrombosis were not included in our study. Fourth, we found that recurrence was likely if the balloon size was small, but we could not provide an exact size.

In conclusion, stent insertion can be considered when fibrotic changes are expected due to repeated inflammation and when the balloon size to be used is small. Balloon angioplasty seems less risky for anastomotic ruptures in PVS in the early post liver transplantation period.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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