World Journal of Gastroenterology

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DOI: 10.3748/wjg.v20.i41.15367

World J Gastroenterol 2014 November 7; 20(41): 15367-15373
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

CLINICAL TRIALS STUDY

New strategies for prevention and treatment of splenic artery steal syndrome after liver transplantation

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Received: March 1, 2014 Revised: May 5, 2014
Accepted: July 22, 2014
Published online: November 7, 2014

Abstract

AIM: To explore a prophylactic procedure to prevent splenic artery steal syndrome (SASS), as well as a therapeutic intervention to correct it.

METHODS: Forty-three liver transplant patients were enrolled in a non-randomized controlled trial, with the eligible criterion that the diameter of the splenic artery is more than 5 mm and/or 1.5 times of the diameter of the hepatic artery. The procedure of splenic artery banding was performed in 28 of the 43 patients, with the other 15 patients studied as a control group. SASS and other complications were compared between these two groups. A new therapeutic intervention, temporary incomplete blockade of the splenic artery with a balloon, was performed to treat SASS in this study.

RESULTS: The incidence of SASS was decreased by banding the splenic artery (0/28 *vs* 5/15, $P = 0.006$), and the same result was observed in total complications associated with prophylactic procedures (2/28 *vs* 6/15, $P = 0.014$). Five patients in the control group developed SASS within 5 d after OLT, 2 of whom were treated by coil embolization of the splenic artery, whereas the other 3 by temporary blockade of the splenic artery. Reappeared or better hepatic arteries with improved systolic amplitude and increased diastolic flow were detected by Doppler ultrasonography in all the 5 patients. Local splenic ischemic necrosis and nonanastomotic biliary stricture were diagnosed respectively in one patient treated by coil embolization, and no collateral complication was detected in patients treated by temporary blockade of the splenic artery.

CONCLUSION: SASS should be avoided during the operation by banding the splenic artery. Temporary blockade of the splenic artery is a new safe and effective intervention for SASS.

Key words: Organ transplantation; Liver transplantation; Splenic artery steal syndrome; Vascular complication; Angiography

Core tip: Splenic artery steal syndrome (SASS) is a rare but severe vascular complication after orthotopic liver transplantation (OLT). Splenic artery embolization has been reported to treat SASS, which could induce local ischemic necrosis of the spleen, infection and septicemia. We proved that banding the proximal splenic artery, whose diameter exceeds 5 mm and/or 1.5 times of the diameter of the hepatic artery, during the OLT was an effective preventive intervention. We also recommend occluding the splenic artery temporarily as a new therapeutic intervention, by which, the possible complications of splenic artery embolization could be avoided.

Song JY, Shi BY, Zhu ZD, Zheng DH, Li G, Feng LK, Zhou L,

Wu TT, Du GS. New strategies for prevention and treatment of splenic artery steal syndrome after liver transplantation. *World J Gastroenterol* 2014; 20(41): 15367-15373 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i41/15367.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i41.15367

INTRODUCTION

The survival rate of patients undergoing liver transplantation has increased in recent years. However, some scarce postoperative vascular complications, such as splenic artery steal syndrome (SASS), is recognized as a real threat[1,2]. SASS was defined by Langer *et al*[3] first in 1990. Its incidence was reported to be 0.6% to 10.1% in orthotopic liver transplant (OLT) recipients[4-11]. The characteristic of SASS is hypoperfusion of the hepatic artery, which is caused by a competitive shunt of blood flow into the splenic artery from the celiac trunk, and can result in hypoxic injury, subsequent inflammation and bile duct proliferation[12,13]. Patients with SASS may present with elevated liver enzyme levels, cholestasis and hepatic arterial thrombosis[14], possibly, biliary complication and graft dysfunction in some severe cases[6,15,16]. SASS can be diagnosed by Doppler ultrasonography, which is reported to be the preferred way with a sensitivity of 91% and a specificity of 99%[6,17-20]. It can also be diagnosed by CT imaging and angiography[3,6-10,21,22]. However, the reliable diagnostic criteria have not been defined, and the pathogenesis of SASS has not been clarified to date. It was reported that increased resistive index (RI) after ischemia/reperfusion (I/R) injury may decrease the blood flow of the hepatic artery in the early period after OLT[23,24]. Additionally, portal hypertension and enlarged splenic artery in patients who underwent OLT have not been relieved. All the above factors lead to a competitive blood shunt from the hepatic artery into the splenic artery, thereby causing SASS. Based on the above findings, some scholars believe that SASS should be diagnosed before OLT[10,25]. Wojcicki *et al*[26] reported that SASS could be forecast by direct pressure gradient measurement between the hepatic and radial artery. Many institutions have reported that SASS should be treated by embolization with a coil[7,14-16,27-34]. Nevertheless, coil embolization of the splenic artery after OLT can induce local ischemic necrosis of the spleen, infection and septicemia[7,15,16,33-35]. In this study, we explored a prophylactic procedure to reduce the incidence of SASS, as well as a therapeutic intervention to correct it.

MATERIALS AND METHODS

Four hundred and ninety-eight consecutive OLTs were performed in our institute between April 2002 and December 2013. Donor livers were harvested in accordance with the current regulations of the Chinese Government and the guidelines of the Declaration of Helsinki. All of the OLTs and the present study were approved by the Ethics Committee of the 309th Hospital of PLA. Written informed consent from each patient was obtained. Forty-six patients had been selected from 386 OLT recipients since January 2005 by preoperative CT imaging. The eligible criterion was that the diameter of the splenic artery exceeds 5 mm and/or 1.5 times of the diameter of the hepatic artery. Forty-three cases were studied, except one case with variant hepatic artery and 2 cases who died in the postoperative period. A study had verified the rationality of the criterion. It had been reported that the cutoff points for abnormal splenic artery diameter and abnormal splenic artery diameter/proper hepatic artery diameter (S/P) ratio in cirrhosis-induced portal hypertension were > 5.19 mm and > 1.40, respectively[36].

Surgical technique, immunosuppression, and grouping

Standard OLT without venovenous bypass were performed in all the 43 patients. End-to-end anastomosis was performed between the donor's common hepatic artery and the recipient's proper hepatic artery. No variant artery was detected in all the donors. The gastroduodenal artery was ligated after the hepatic artery anastomosis during transplantation. The patient received a tacrolimus-based immunosuppressive protocol, *i.e.*, tacrolimus (Tac), mycophenolate mofetil (MMF) and steroid, after transplantation. Tac was administered orally with the dose titrated according to the blood concentrations, targeting for 8-12 ng/mL during the first three months, 5-8 ng/mL from the 4th to 12th month, and 3-5 ng/mL thereafter in both groups. Intravenous methylprednisolone (500 mg) was administered intraoperatively. Then 20 mg/d prednisone was administered orally, progressively tapered, and finally withdrawn at the end of the first month. In the 43 cases, the trunk of the splenic artery was ligated uniformly in 28 recipients (24 males and 4 females; mean age, 48.9 ± 8.5 years; range: 35-62 years). Nothing was done to the splenic artery in the other 15 patients (13 males and 2 females; mean age, 50.2 ± 7.9 years; range: 40-63 years). There was no statistical difference in age or sex between these two groups.

Prevention of SASS

Artificial stenosis of the splenic artery was performed during OLT in the 28 patients as a preventive intervention. The proximal splenic artery was searched above the neck of the pancreas. We put a latex tubing (12F) beside the trunk of the splenic artery, then tied the latex tubing and the artery together with a nonabsorbable suture (Prolene 3-0; Ethicon, Inc., United States) loosely. A standardized diameter (3 mm) of the splenic artery remained after pulling out the latex tubing. An uninterrupted and weakened splenic artery was detected by intraoperative Doppler ultrasonography.

Diagnosis of SASS after OLT

Doppler ultrasonography was scheduled once daily in the first week after OLT. Emergency angiography was

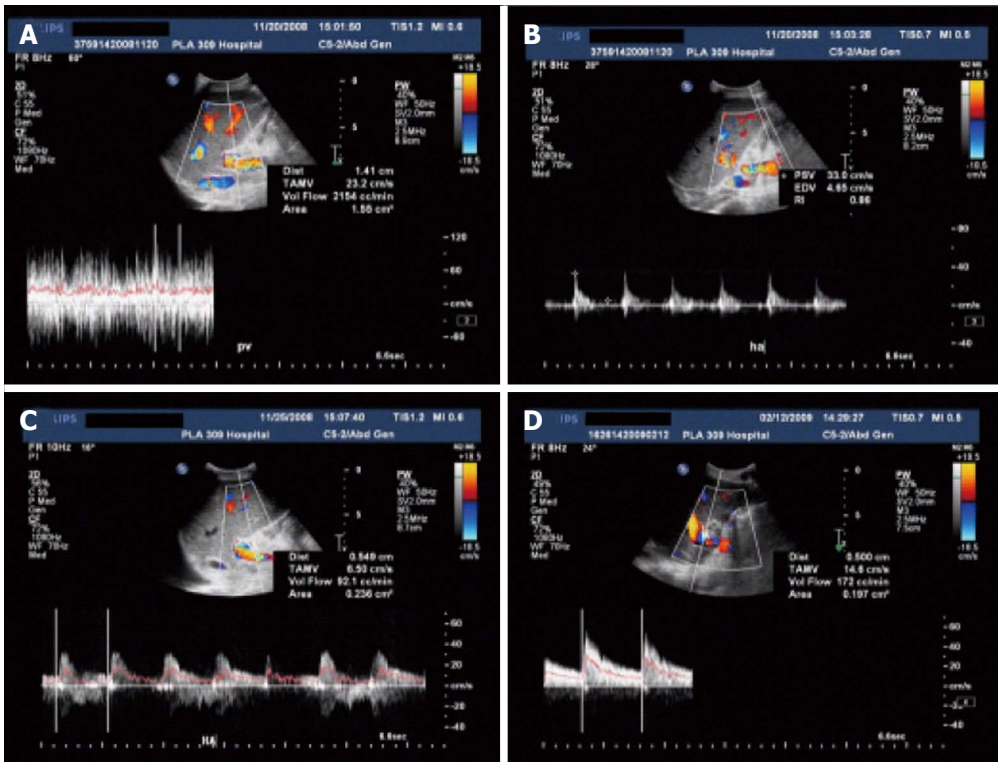

Figure 1 Doppler images during occluding the splenic artery. A: Normal portal vein and disappeared hepatic artery flow signal as revealed by Doppler ultrasonography on the 2nd day after transplantation; B: Reappearance of the hepatic artery flow signal revealed by Doppler ultrasonography after the treatment by occluding the splenic artery temporarily; C: Better hepatic artery flow signal on the 5th day after the treatment; D: Normal hepatic artery flow signal at the end of the 3th month after the orthotopic liver transplantation.

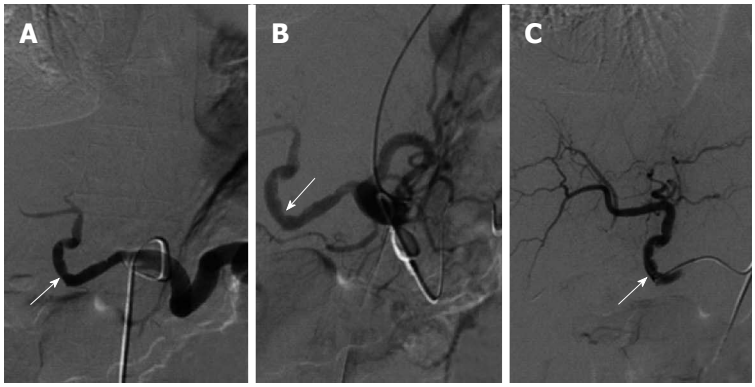

Figure 2 Radiological images during occluding the splenic artery (arrow is the anastomotic site). A: Selective celiac trunk arteriogram shows reduced hepatic artery perfusion and enlarged splenic artery perfusion; B: Increased hepatic arterial perfusion was seen after occluding the splenic artery temporarily; C: Normal hepatic arterial flow was reestablished 5 d after the treatment.

immediately performed while the hepatic artery flow signal weakened or disappeared as revealed by Doppler ultrasonography (Figure 1A). SASS was diagnosed when there were the following findings: there was no stenosis or thrombosis in the hepatic artery; the filling of the intrahepatic arterial branches by contrast material was delayed significantly in comparison with the filling of splenic arterial branches; the contrast material into an enlarged splenic artery (the diameter was more than 5 mm and/or 1.5 times of the diameter of the hepatic artery) was evacuated quickly (Figure 2A).

Treatment of SASS

When SASS was confirmed by angiography, transcatheter splenic artery occlusion with a coin (8-4; Cook Int, United States) was performed by selective catheterization of the splenic artery in the first two cases. The latter three cases were treated by temporary blockade of the splenic artery. We inserted the balloon catheter (10-4 Xtreme; Invatec, Italy) into the proximal trunk of the splenic artery and filled the balloon by contrast material. The weakened splenic arterial flow and the obviously improved hepatic arterial flow were observed when

Table 1 Complications associated with prophylactic procedures for splenic artery steal syndrome after orthotopic liver transplantation *n* (%)

Complication	Banding the splenic artery (*n* = 28)	Standard arterial reconstruction (*n* = 15)
SASS	-	5 (33.3%)
Local ischemic necrosis in the spleen	-	1 (6.7%)
Splenic arterial thrombus	1 (3.6%)	-
Non-anastomotic biliary stricture	1 (3.6%)	2 (13.3%)
Total	2 (7.1%)	6 (40.0%)[1]

[1]The infarction of the spleen and a case of the nonanastomotic biliary stricture occurred in recipients with splenic artery steal syndrome (SASS), respectively.

the angiography was performed from the right radial artery (Figure 2B, C). The exoteric part of the balloon catheter was locked on the body surface. The hypodermic injection of low molecular heparin (2125 u/d) was performed daily in the following six days. From then on, anticoagulation therapy with aspirin (0.1 g/d) was used for two months. Antibiotic prophylaxis was given and the vital signs were monitored after the treatment. Biochemical examination and Doppler ultrasonography were scheduled once daily before removing the balloon catheter from the body.

Statistical analysis

Statistical analyses were performed using SPSS 13.0 statistical software. Continuous data were tested for normal distribution and are expressed as mean ± standard deviation (SD) or median (range) as appropriate. Continuous data were compared by the Mann-Whitney *U* test. Categorical data were analyzed using Pearson's χ^2 test or Fisher's exact test if any expected cell frequency was less than 5. $P < 0.05$ was considered statistically significant.

RESULTS

Complications in the investigated recipients

Based on the criteria, none of the 28 patients with banding of the splenic artery developed SASS after OLT, whereas SASS was detected in 5 patients of the control group ($P = 0.006$). The total complications associated with prophylactic procedures were also decreased by banding the splenic artery (Table 1; $P = 0.014$). Besides, the liver function of the patients who underwent banding of the splenic artery recovered faster than that of the patients in the control group (Figure 3). SASS was diagnosed within 5 d after OLT in all the 5 recipients.

Outcome of patients with SASS

Regular Doppler ultrasonography in the patients who underwent coil embolization showed a reappeared hepatic artery with improved systolic amplitude and increased diastolic flow, meanwhile a disappeared splenic artery. Local ischemic necrosis was detected in one patient's spleen. The same characteristics of the hepatic artery were detected in the patients who underwent temporary blockade of the splenic artery (Figure 1B). But the splenic arteries were still there and became weakened. Local ischemic necrosis of the spleen was not detected in all the three patients who underwent temporary blockade of the splenic artery. An increased hepatic arteriopalmus and a recuperative splenic arteriopalmus were detected when we drew the contrast material out from the balloon on the 5th day after the treatment (Figure 1C). We pulled out the balloon from the body on the next day. The liver function of all the five patients recovered smoothly after the treatment (Figure 4). Non-anastomotic biliary stricture happened in one patient who underwent coil embolization, whose SASS had been diagnosed on the 5th day after OLT. No more complication related to the artery and biliary duct was identified in the 5 patients during the 6-mo follow-up (Figure 1D).

DISCUSSION

SASS is a rare vascular complication after OLT. It has not been paid enough attention by clinicians. A 1.3% (5/386) incidence was found in this study even SASS was prevented partly. Perhaps it was merely the symptomatic part of all the cases. The potential incidence of SASS is 11.9% (46/386) if all of the 46 patients had been calculated. The I/R injury lasts longer if reduced hepatic blood flow could not be improved in time. Hepatic arterial thrombosis and obliteration, even graft failure and recipient death would happen in some severe cases. The consequences of SASS are positively related to the time that the hepatic artery has suffered the ischemia. Therefore, SASS should be avoided during OLT and be diagnosed and treated as early as possible. How to recognize this complication before OLT and prevent it during OLT has become extraordinarily important. In this study, we identified the potential risk factor (thickened splenic artery) of SASS and treated it by banding the splenic artery during the OLT. By the way, we routinely ligated the gastroduodenal artery during the OLT in all recipients because the gastroduodenal artery can also steal some blood flow from the hepatic artery[37,38]. The distribution ratio of celiac trunk flow was corrected and the hepatic arterial infusion increased. The incidence of SASS was decreased obviously by the intervention, and it also provided benefit to the recovery of liver function. There was no increased complication incidence in the patients after the intervention.

The outcome of SASS is related obviously to the time that hepatic artery has suffered the ischemia. Therefore, it is especially important to diagnose and treat the complication as early as possible. Additionally, many other complications after OLT are characterized by elevated liver enzyme levels, cholestasis and graft dysfunction. SASS is often ignored by clinicians because of these confusing symptoms. Actually, it can be detected as

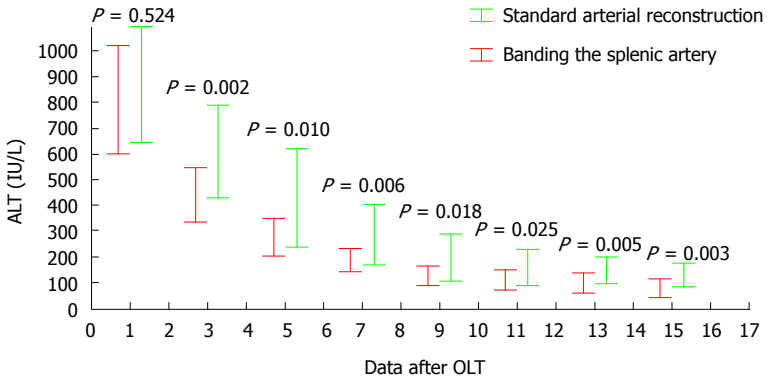

Figure 3 Fluctuation of mean alanine transarninase in the recipients in the two groups after the treatments. The alanine transarninase (ALT) in the patients who underwent banding the splenic artery decreased faster than that in the patients in the control group. OLT: Orthotopic liver transplantation.

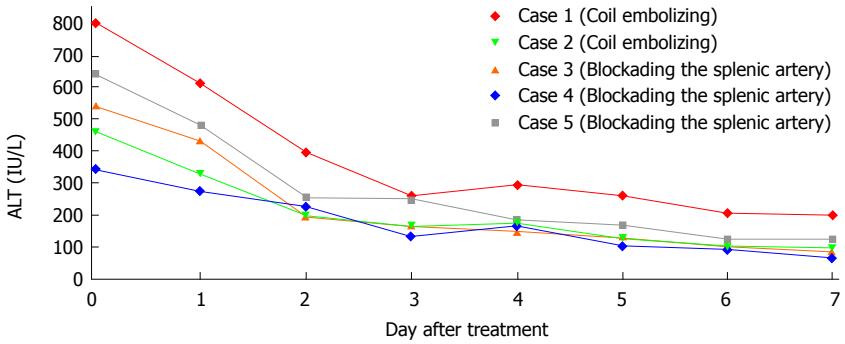

Figure 4 Fluctuation of alanine transarninase in the patients with splenic artery steal syndrome after the treatments. ALT: Alanine transarninase.

soon as possible by regular Doppler ultrasonography and emergency angiography. Many institutions reported that SASS should been treated by embolization with a coil[7,15,16,27-34]. But the patient with SASS usually has a coarse splenic artery, the diameter of which is more than 5 mm. The fast splenic arterial flow can often push the coil into the branch of the splenic artery, which could induce local ischemic necrosis of the spleen, infection and septicemia[7,15,16,33-35]. The incidence of infection after embolization was even reported as 50%[15]. Infection and septicemia after coil embolization did not happen in these two cases, but local ischemic necrosis of the spleen was identified in one case. Non-anastomotic biliary stricture happened in the other patient who underwent coil embolization, whose SASS was diagnosed on the 5th day after OLT. We attributed it to the long time ischemia. Quantifying increased hepatic arterial flow with test balloon occlusion of the splenic artery in OLT recipients with SASS has been reported[39]. It showed that occlusion of the splenic artery in patients with SASS could double the hepatic arterial flow (1.7- to 2.6-fold)[39]. To our knowledge, temporary blockade of the splenic artery to treat the SASS has not been reported. We treated 3 patients with SASS successfully by occluding the splenic artery temporarily. The blockade of the splenic artery can help the allograft to live through the high-resistance period caused by I/R injury and rectify the competitive shunt of blood flow. At the same time, the blockade can also decrease the splenic artery flow with no irreversible influence, which could avoid the local ischemic necrosis in the spleen. The I/R injury in the allograft continues 5-10 d after OLT[23,24], in view of which, we pulled out the balloon on the 6th day after it was placed. The splenic arterial flow recovered when the balloon had been pulled out, and no concomitant complications, such as local ischemic necrosis of the spleen and infection, were observed. However, the value of temporary blockade of the splenic artery should be studied further because of the shortage of sample capacity in this study.

In summary, SASS is a rare but severe complication after OLT. The diameter of the splenic artery exceeding 5 mm and/or 1.5 times of the diameter of the hepatic artery is a risk factor for SASS. We should avoid it as possible as we can. Banding the splenic artery during the OLT is a safe and effective intervention to prevent SASS. Temporary blockade of the splenic artery is a new effective therapeutic intervention to SASS.

COMMENTS

Background

Splenic artery steal syndrome (SASS) is a rare but severe complication after orthotopic liver transplantation (OLT). It is characterized by hypoperfusion of the hepatic artery secondary to a competitive shunt of blood flow into the splenic artery from the celiac trunk. SASS can cause elevated liver enzyme levels, cholestasis, thrombosis of the hepatic artery, and even graft failure in some severe cases. However, SASS has not received enough attention yet. Its reliable diagnostic criteria, extensional preventive and therapeutic interventions have not been defined to date.

Research frontiers

SASS can cause thrombosis of the hepatic artery, non-anastomotic biliary stricture, and even graft failure in some severe cases. The reliable diagnostic criteria, extensional preventive and therapeutic interventions have not been defined to date, all of which are hotspots.

Innovations and breakthroughs

This study offered a possible risk factor of SASS, which is the diameter of splenic artery exceeding 5 mm and/or 1.5 times of the diameter of the hepatic artery. The authors proved that treating the risk factor by banding the proximal splenic artery could decrease the incidence of SASS. Occluding the splenic artery temporarily was recommended as a new therapeutic intervention for SASS in this article.

Applications

The preventive intervention for SASS mentioned in this article can decrease the incidence of SASS dramatically. At the same time, occluding the splenic artery temporarily provides clinicians a new therapeutic intervention for SASS.

Terminology

Splenic artery steal syndrome (SASS) is caused by a competitive shunt of blood flow into the splenic artery from the celiac trunk, the result of which is hypoperfusion of the hepatic artery.

Peer review

The author examined clinical usefulness of banding the splenic artery after OLT. Also, they advocate the feasibility of temporary occlusion of the splenic artery for splenic artery steal syndrome. The manuscript is interesting and worth publication.

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P- Reviewer: Endo I **S- Editor**: Ma YJ
L- Editor: Wang TQ **E- Editor**: Liu XM

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ISSN 1007-9327