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Original Article

In-hospital and follow-up outcomes of patients undergoing orthotopic liver transplantation after hepatic artery reconstruction with an iliac interposition graft

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Abstract: Introduction: This study was to explore the indications, surgical method, and postoperative treatment of orthotopic liver transplantation (OLT) after hepatic artery (HA) reconstruction with an iliac interposition graft. Methods: This study analyzed in-hospital and follow-up outcomes of 34 Chinese patients: 17 who received conventional OLT ("non-bypass" group) and 17 who received OLT with hepatic artery reconstruction by iliac interposition bypass ("bypass" group). Complications were tracked using findings from clinical presentation, liver function, and HA ultrasound. Results: Compared to the non-bypass group, the bypass group had a longer average surgery time (48.47±11.86 min vs. 82.29±22.00 min, respectively; $P < 0.01$) and more blood loss (4,841.18±1,268.39 mL vs. 7,047.06±976.04 mL; $P < 0.01$). The postsurgical hepatic function of both groups quickly recovered and, by 10 days, there was no significant difference in the HA peak blood flow velocity between groups. The bypass patients were followed for an average of 45.2 months (range: 20-56 months), with no arterial-related complications (e.g., artery stenosis or arterial thrombosis) or fatalities. Conclusions: Iliac arterial interpositional graft is an effective and reliable method of HA reconstruction in OLT, when the use of the HA is not possible.

Keywords: Orthotopic liver transplantation, hepatic artery reconstruction, Iliac artery graft, Doppler ultrasonography, blood flow velocity

Introduction

Orthotopic liver transplantation (OLT) is the only definitive therapeutic modality for patients with end-stage liver disease [1]. With refinements in surgical procedures, immunosuppressive protocols, and patient care, patient survival rate has greatly improved over the last decade [2, 3]. However, complications (such as renal dysfunction, hypertension, diabetes mellitus, hyperlipidemia, etc.) continue to reduce the long-term outcomes of transplanted patients [4, 5]. Hepatic artery (HA) reconstruction and the maintenance of a good hepatic arterial blood supply are essential for a successful liver transplantation and for reducing postoperative complications [6, 7].

A direct anastomosis between the grafted and recipient HA (i.e., anatomical HA reconstruction) is technically simple and is the first technique used by most surgeons for HA reconstruction [6]. However, the recipient HA may be unsuitable for reconstruction-it can be scarred from a previous operation or intraoperative arterial dissection, or can be a different diameter as the graft HA [8, 9]. In these cases, reconstruction is performed with arteries other than the HA (termed "extra-anatomical HA reconstruction"), including saphenous vein grafts [10], and recipient splenic [11] or right gastroepiploic arteries [12]. A number of studies have suggested that an iliac arterial interpositional graft was an acceptable transplantation alternative for the arterial revascularization of a liver allograft, when the use of the HA was not possible [13-15], however, there are no reports documenting in-hospital and follow-up outcomes in such cases. In the present study, we discuss the indications, surgical method, and postoperative treatment of 17 patients who underwent OLT with HA reconstruction by iliac interposition bypass, in order to determine if an iliac artery graft is an acceptable alternative for arterial reconstruction during liver allograft.

Materials and methods

Patients

This study was performed from May 2006 to December 2010 at the department of No. 1 Hepatobiliary Pancreatic Surgery in the First People's Hospital of Kunming City (Kunming, China). We selected 17 patients who underwent OLT with HA reconstruction by iliac interposition bypass ("bypass" group) and randomly selected 17 matching patients who underwent standard liver transplantation ("non-bypass" group) simultaneously. The study was approved by the Ethics Committee of the First People's Hospital of Kunming City and written consent was obtained from all donors' immediate family and recipients.

Indications and surgical method

Indications for HA reconstruction with iliac interposition bypass included: 1) the donor's and recipient's HAs were not suitable for direct anastomosis, even after anatomical reconstruction, because of a diameter discrepancy between the graft and recipient HA (2 patients); 2) the presence of hepatic arterial thrombosis leading to liver retransplantation (3 patients); 3) the presence of severe atherosclerosis of the HA (3 patients); 4) the HAs were not suitable for anastomosis because of a separation between the intima and adventitia or intima edema and crisp (5 patients); 5) the presence of an HA-dissecting aneurysm (1 patient); or 6) proper HA injury resulting from HA infusion chemotherapy (HAIC) under digital subtraction angiography (DSA, 3 patients).

Living transplantation bridge and vascular preparation

Donor livers were harvested after cardiac death of the donor patient. Resection included the left and right common iliac arteries, the internal and external iliac arteries, and part of the femoral artery. The left and right common iliac arteries were separated from their origination in the common iliac artery, which was further cleaned of connective tissue. Arterial quality was evaluated to avoid working with severely injured or atherosclerotic arteries. Until they were needed for HA abdominal aorta bypass surgery, the donor graft iliac arteries were preserved at 4°C in UW solution supplemented with 2.5% dimethyl sulfoxide (DMSO) and 10% fetal calf serum (FCS) [2]. The solution and tissue were enclosed within three layers of aseptic plastic bags (the outer was a non-sterile bag), each of which was sealed with silk ligation. The average time of donor tissue preservation was 8.12±1.35 hours, after which packaged iliac arteries were immediately moved to cooling equipment for a gradient cooling program.

For recovery of the cryopreserved donor artery, a program was used similar to that for cryopreserved cells. The stored donor artery was quickly rewarmed in bath water at a constant 37°C until the UW solution was completely dissolved. At that point, the outer fungus layer and the two layers of sterile packaging were removed and the sterile iliac artery was placed on a stage and repaired for further usage.

Bypass surgical procedures between the HA and the abdominal aorta

To prepare the recipient for receiving the graft, a 5-cm segment of the abdominal aorta below the renal artery level was isolated to partially block blood flow in the abdominal aorta. A 3-cm incision was then made in the aortic wall using a small sticker. One end of the donor graft iliac artery was anatomized with the recipient's abdominal aorta using a continuous 4-0 or 5-0 prolene suture and the other end was occluded with an arterial clamp. The clamp blocking the recipient's abdominal aorta was then released and the donor bypass iliac artery was passed through a retropancreatic or antepancreatic tunnel, and was anatomized with the recipient's common HA or celiac trunk through a continuous 7-0 prolene suture.

After the arterial blocking clamps were completely released, the grafted liver was confirmed to have a ruddy appearance and the arterial blood flow was assessed by intraoperative B-mode and Doppler ultrasonography. In all cases, a sufficient pulsatile HA flow was confirmed throughout the entire grafted liver tissue, after which the peritoneum in front of the bypass artery was closed.

Table 1. Clinical characteristics of patients in the bypass and non-bypass groups

	Groups	
	Bypass (n=17)	Non-bypass (n=17)
Male	13	15
Female	4	2
Average age (years)	54.35±5.16	48.71±7.67
Average weight (kg)	55.41±8.45	57.06±7.15
Hepatitis B cirrhosis	7	9
Fulminant liver failure	4	1
Re-transplant	3	1
Auto-immune hepatitis	1	2
Hepatocellular carcinoma	3	1
Alcoholic cirrhosis	1	2

Table 2. Surgery characteristics of patients in the bypass and non-bypass groups

	Groups	
	Bypass (n=17)	Non-bypass (n=17)
Surgery time (min)	82.29±22.00*	48.47±11.86
Blood loss (mL)	7,047.06±976.04*	4,841.18±1268.39

*Compared with non-bypass groups, $P < 0.01$.

Table 3. The level of glutamic-pyruvic transaminase of patients in bypass and non-bypass group (U/L)

Postoperative time (Days)	Groups	
	Bypass (n=17)	Non-bypass (n=17)
1	231.06±87.26	249.65±150.67
2	207.88±112.04	193.00±102.26
3	171.59±71.48	168.89±77.94
4	149.18±67.00	146.65±62.10
5	122.06±46.65	129.24±51.28
6	107.35±34.45	109.71±37.94
7	83.94±15.95	89.29±26.92

Postoperative treatment

An assessment of the development of OLT-associated complications was made using findings of clinical presentation, liver function, HA ultrasound, and HA DSA angiography. Depending on their postoperative coagulative function, recipients were treated with an anticoagulant (e.g., fraxiparine) and Kaishi for 2 weeks, and thereafter with an oral bayaspirin or persantine to maintain a target international normalized ratio (INR) of 1.5 (a coagulation index within 1.5 fold of normal). In order to guard against the development of thrombosis, patients' hemoglobin and hematocrit levels were maintained at about 100 g/L and < 30%, respectively. The blood flow within the HA was daily monitored using Doppler ultrasonography during the 2 weeks following the operation. Following their discharge, patients were followed up every month for the first 6 months, every 2 months for the second 6 months, every 3 months for the second year, and every 6 months for the third year and thereafter.

Statistics

Continuous data are expressed as mean ± standard deviation. The chi-square test and one-way ANOVA with repeated measures were used for statistical analyses where appropriate. Analyses were performed by the SPSS software (Statistical Package for the Social Sciences version 11.5, SPSS Inc.). $P < 0.05$ was considered statistically significant.

Results

Clinical data

Clinical data for patients of the bypass group and non-bypass group are listed in **Table 1**. There were no statistical differences between the groups in terms of age, sex, and primary disease. The average surgery time of the bypass group was longer than that of the non-bypass group (82.29±22.00 vs 48.47±11.86 min, $P < 0.01$; **Table 2**). Recipients of bypass also had more blood loss than those in the non-bypass group (7047.06±976.04 vs 4841.18±1268.39 mL, $P < 0.01$; **Table 2**).

Incidence of arterial complications

Of those patients in the bypass group, one patient suffered from a biliary fistula, but was fully recovered within 15 days after sufficient drainage and nutrition support. Another patient developed a biliary infection, combined with intrahepatic bile neoplasia, but these complications were remedied using percutaneous transhepatic biliary drainage (PTCD), anti-infection measures, and nutritional support treatment. The remaining 14 patients did well postopera-

Table 4. The level of total bilirubin of recipients in bypass and non-bypass group (μmol/L)

Postoperative time (Days)	Groups	
	Bypass (n=17)	Non-bypass (n=17)
1	60.99±22.37	88.69±50.41
2	57.07±30.14	83.03±50.59
3	47.90±19.85*	77.73±49.94
4	44.31±14.17*	69.46±41.16
5	40.61±11.05*	63.04±37.16
6	38.14±12.77*	59.29±36.67
7	35.64±10.37*	51.92±33.35

*Compared with non-bypass groups, $P < 0.01$.

Table 5. Hepatic artery peak velocity in bypass and non-bypass groups (cm/s)

Postoperative Time (Days)	Groups	
	Bypass (n=17)	Non-bypass (n=17)
1	92.00±10.04	89.00±16.83
2	131.05±12.66	68.60±21.92
3	150.30±12.30	70.10±31.40
4	109.65±3.32	63.65±28.21
5	109.25±88.74	87.50±14.00
6	95.60±2.97	85.85±23.12
7	77.90±34.22	88.14±14.16
8	86.10±22.63	37.00±0.14
9	90.35±31.75	50.85±19.86
10	131.45±71.92	99.50±4.38

tively. Overall, there were no differences between the groups in terms of complications.

In-hospital outcomes of recipients

The level of glutamic-pyruvic transaminase of all patients included in this study decreased gradually, so that, by 7 days after transplantation, there was no difference between the two groups (**Table 3**). The levels of total bilirubin also decreased gradually in all patients, and, at postoperative days 3, 4, 5, and 6, the levels of total bilirubin in the bypass group were lower than those in the non-bypass group (**Table 4**; $P < 0.05$). In the continuous 10 days following the procedure, there was no significant difference in the HA peak blood flow velocity between the bypass group and the non-bypass group (**Table 5**).

Long-term follow up

The bypass patients were followed for an average of 45.2 months (range: 20-56 months). These patients developed no additional complications, including arterial stenosis or thrombosis, and experienced no arterial-related fatalities.

Three-dimensional CT vascular remodeling

For 2 of the 17 bypass patients, an abdominal CT scan was performed at the 38th and 42nd month after transplantation. The three-dimensional vascular remodeling clearly exhibited vascular structures of interest, such as the anastomotic stoma between the bypass artery and hepatic artery, the circuitous splenic artery, etc. (**Figure 1**).

Discussion

HA reconstruction is considered to be essential for a successful liver transplantation and for reducing the incidence of postoperative complications; however, in some conditions, the recipient HA is often unsuitable for direct anatomical reconstruction [8, 9, 16]. A number of studies have used a donor iliac artery for arterial reconstruction in liver transplantation. For instance, Del Gaudio *et al.* [13] found that an iliac arterial interpositional graft was an alternative solution for arterial revascularization of the liver allograft after retransplantation, when the HA was not useable. A composite graft of the iliac artery and the inferior mesenteric vein (IMV) was found to yield a satisfactory outcome in one patient and may be a valuable addition to the arterial grafts available to the liver transplant surgeon [14]. Hwang *et al.* [17] felt that a cryopreserved iliac arterial graft could be used as an interpositional vessel graft for middle hepatic vein reconstruction of a right liver graft, when cryopreserved iliac vein grafts were not available. In our study, we sought to minimize the use of cryopreserved iliac arteries because of the potentially increased risk of complications associated with cryopreserved vessels [18, 19]. Overall, these studies suggest that iliac artery graft is an alternative procedure for arterial revascularization of liver allograft and that cryopreserved iliac artery is also suitable when the use of fresh artery is not possible.

In the present study, we performed HA reconstruction using iliac artery interpositional bypass between the HA and abdominal aorta. We found that the surgical time of the bypass group was longer than that of the non-bypass group and that recipients of bypass had more blood loss than those in the non-bypass group.

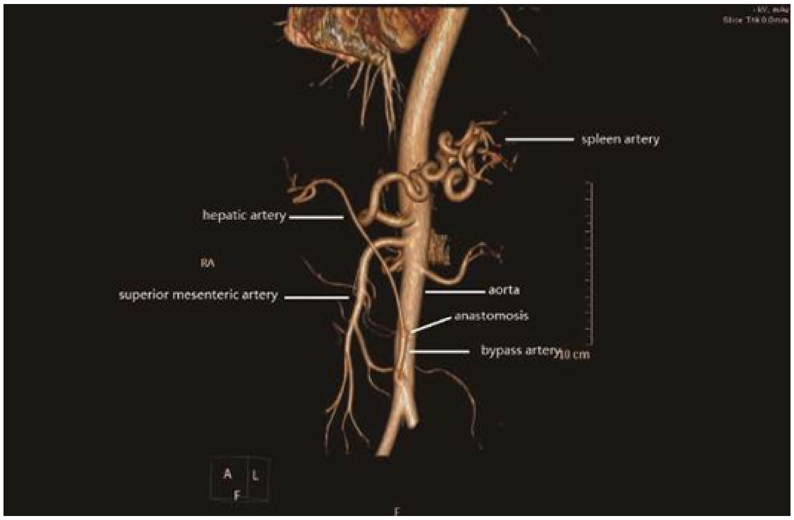

Figure 1. Three-dimensional computed tomography vascular remodeling. The white line exhibits the vascular structures of postoperative interest, such as the anastomotic stoma between the bypass artery and hepatic artery and the circuitous splenic artery.

However, only two bypass patients developed postoperative complications. We also found that there was no difference between the bypass and non-bypass groups in terms of hospital outcomes, as measured by hepatic function and the HA peak blood flow velocity. Also in our study, 3 cases were retransplanted and 2 cases used cryopreserved iliac artery graft, all of which had satisfactory hospital outcomes. These results suggest that performing an HA reconstruction using iliac artery interpositional bypass is suitable and effective.

Based on our experiences, two important procedures should be carefully performed: the positioning of the anastomosis between the iliac artery graft and the abdominal aorta, and the establishment of conduit tunnels for the graft. Theoretically, the graft artery becomes shorter when the iliac artery is anastomosed with the suprarenal aorta [20]. Shaked *et al.* [21] even found that the routine use of the supraceliac aorta for difficult HA reconstruction decreased the need for arterial grafts, the incidence of HA thrombosis, and the loss of hepatic grafts. However, compared with the infrarenal aorta, the suprarenal aortic anatomy is more complicated and its dissection is more difficult [20]. When dissecting the upper abdominal aorta, the risk of developing complications (e.g., pneumothorax) is higher. Moreover, renal perfusion may be decreased due to a clamp on the suprarenal aorta, which would result in inducing or worsening renal function damage [22]. In our study, no patient suffered from artery-related complications. Therefore, we felt that the infrarenal positioning of the anastomosis between the iliac artery graft and that abdominal aorta was preferential for HA reconstruction using iliac interposition bypass.

The establishment of the conduit tunnel for the graft should be based on the portal vein pressure and the status of surrounding tissue adhesions [23]. The retrocolic antepancreatic tunnel should be chosen when collateral vessels of the portal vein are rich and there are severe adhesions. In all other cases, the retropancreatic tunnel should be chosen. After confirming a sufficient blood flow throughout the entire grafted artery, the peritoneum in front of the bypassed artery should be closed.

HA complications are a major problem affecting the long-term outcomes of liver-transplanted patients [4, 5], thus it is very important to timely diagnose, prevent, and treat vascular complications. For instance, the delicate balance between bleeding and thrombosis should be strictly maintained to avoid the development of HA thrombosis [24]. According to postoperative protocol, recipients of our study were treated with anticoagulants (e.g., fraxiparine) and Kaishi for 2 weeks, and then taken orally with bayaspirin or persantine to maintain a target international normalized ratio (INR) of 1.5 (a coagulation index within 1.5 fold of normal). In order to prevent the development of thrombosis, hemoglobin was kept to about 100 g/L and hematocrit levels were kept to below 30%. As anticipated, no patient in this study experienced HA thrombosis. Also, we used Doppler ultrasonography, an extremely sensitive technique for the detection of HA thrombosis, during the immediate postoperative period to monitor HA blood flow [25, 26] and found that there was no significant difference of HA peak blood flow velocity between the bypass and non-bypass groups.

Study limitations

Potential limitations in this study included: small population size, less patient demographic and disease characteristic data, and relatively short period of ultrasound examination. These limitations precluded the ability to perform multivariate analyses, in order to more effectively determine which factors were independently linked to outcomes and the incidence of arterial complications in patients who underwent OLT with HA reconstruction by iliac interposition bypass. A larger study is planned to evaluate this surgical method as an effective and reliable method in place of conventional arterial reconstruction.

Conclusions

In the present study, 17 patients underwent OLT with HA reconstruction by iliac interposition bypass. We found that there were no differences between the bypass and non-bypass groups, in terms of hospital outcomes and incidence of arterial complications. Therefore, iliac arterial interpositional graft is an effective and reliable method of HA reconstruction in OLT when the use of the HA is not possible.

Disclosure of conflict of interest

None.

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