

Prevention and treatment of hepatic artery thrombosis after liver transplantation

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BACKGROUND: Hepatic artery thrombosis (HAT) which is a serious complication after orthotopic liver transplantation (OLT) remains a significant cause of graft loss. The purpose of this study was to sum up our experiences in the prevention, diagnosis and management of HAT after liver transplantation.

METHODS: From April 1993 to September 2003, a total of 198 patients underwent OLT at our hospital. The hepatic artery was anastomosed using 7/0 prolene with running continuous suture in 96 patients (group 1) and with interrupted suture in 102 (group 2). Ultrasonography was performed every day in two weeks after operation and selectively afterwards.

RESULTS: HAT occurred in 6 patients (6.3%, 6/96) of group 1, and in 1 (1%, 1/102) of group 2 ($\chi^2=4.027$, $P=0.045$). Six patients received emergency thrombectomy, and 1 conservative therapy but died from tumor recurrence eventually. Biliary complication developed in 3 patients after thrombectomy of whom 2 died of liver failure and one waited for retransplantation. In the other 3 patients after thrombectomy, 1 died of renal failure, and 2 survived. The mortality of patients with HAT was 57.1% (4/7).

CONCLUSIONS: The technique of hepatic arterial anastomosis is the key factor for the prevention of HAT. Routine ultrasonography is very important in early detection of HAT after OLT. Biliary complication is a severe outcome secondary to HAT.

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KEY WORDS: liver transplantation; hepatic artery thrombosis; vascular complication; ultrasonography

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Introduction

Hepatic artery thrombosis (HAT) is the most serious vascular complication after orthotopic liver transplantation (OLT). It is an important course for graft loss and patient's death. Many surgical and nonsurgical risk factors are found to be associated with HAT. Nonsurgical factors which damage the vascular endothelium or change hemodynamics include rejection,^[1] cold ischemic time (CIT),^[2] infection of cytomegalovirus (CMV),^[1,3] over transfusion of frozen fresh plasma (FFP)^[4] and cigarette smoking.^[5] Surgical factors seem to play even more important roles in the pathogenesis of HAT, particularly in its early presentation; but most of these factors remain controversial.

A total of 198 orthotopic liver transplantations were performed at our center. Seven of them developed thrombosis of the hepatic artery. To summarize our experience, we retrospectively analyzed the clinical data of the 198 patients.

Methods

The 198 patients with various end-stage liver diseases, 172 men and 36 women, underwent liver transplantation at our center from April 1993 to September 2003. The mean age of recipients was 44.3 ± 8.7 years, and the mean age of donors was 27.6 ± 5.4 years. Of the 198 patients, 121 received liver transplantation for benign diseases and 77 for malignant diseases.

In the 198 patients, the hepatic arteries were anastomosed with running continuous suture in 96 patients (group 1) and with interrupted suture (Fig. 1) in 102 (group 2). Anatomical variations of the hepatic arteries were found in 26 recipients (10 in group 1 and 16 in group 2).

A triple regimen of cyclosporine (CsA), azathioprin (Aza)/mycophenolate (MMF) and steroids was used as the first line immunosuppressants after liver transplantation, followed by a dual regimen of immunosuppressive therapy consisting of tacrolimus (FK506) and steroids.^[6] Ultrasonography was performed every day with-



Fig. 1. The hepatic artery was anastomosed with intermittent suture (arrow).

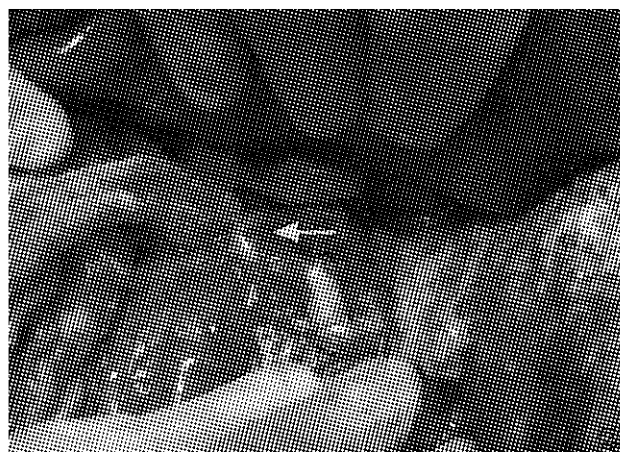


Fig. 2. HAT developed in the first day after OLT (arrow).

in two weeks after operation and then was given on clinical request. Blood coagulation and liver function were monitored. Prostaglandin E₁ was used routinely in two weeks after operation. Prothrombin time, international normalized ratio (INR), partially activated thromboplastin time, and platelet count were evaluated meticulously to decide whether FFP, albumin or platelet were needed. If INR was more than 1.8, FFP was supplied; if INR was less than 1.8, the albumin was supplied instead of FFP. In the first 24 hours after operation, the platelet was supplied if it was less than $60 \times 10^9/L$, and it was not supplied in principle if there was no bleeding beyond 24 hours after operation. The hematocrit was maintained at about 30%.

The chi-square test was employed for statistical analysis.

Results

Six patients (6.3%, 6/96) developed HAT in group 1, and only 1 patient developed HAT (1.0%, 1/102) in group 2. There was a significant difference between group 1 and group 2 ($\chi^2=4.027$, $P=0.045$). In the 7 patients who developed HAT (Fig. 2), 6 presented with early HAT (less than 30 days after surgery) and 1 presented with late HAT (more than 30 days after surgery).^[7,8] Except in 1 patient who was confirmed by laparotomy, HAT in 6 patients was detected by ultrasonography. Emergency thrombectomy and arterial reconstruction were performed in 6 patients with early HAT and blood flow recovered well after operation (Figs. 3 and 4). Biliary complications after thrombectomy occurred in 3 patients (death caused by liver failure, 2 and retransplantation, 1) (Fig. 5). Of the other 3 patients, 1 died of renal failure and 2 survived after thrombectomy. Late HAT was detected by ultrasonography

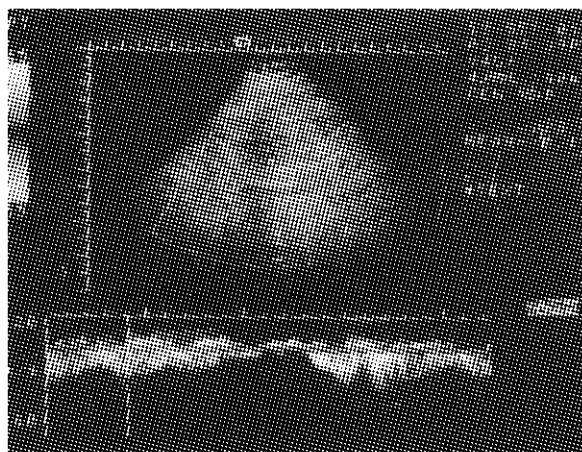


Fig. 3. Ultrasonography before thrombectomy. HAT developed in the first day after OLT. The blood flow of the hepatic artery could not be detected by ultrasonography.

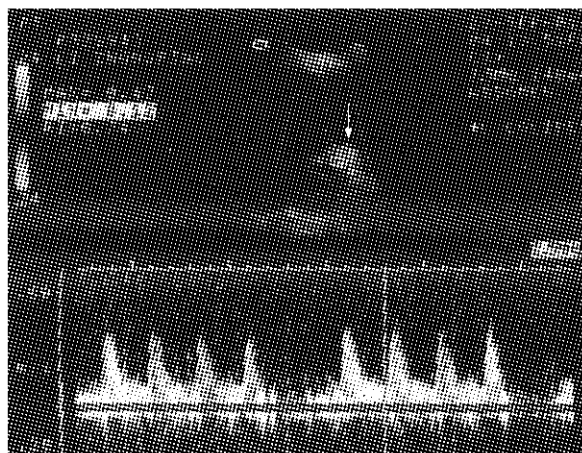


Fig. 4. Ultrasonography after thrombectomy and arterial reconstruction. The blood flow of the hepatic artery was detected by ultrasonography again after thrombectomy and arterial reconstruction, the maximum hepatic artery blood flow was 0.47 m/s.

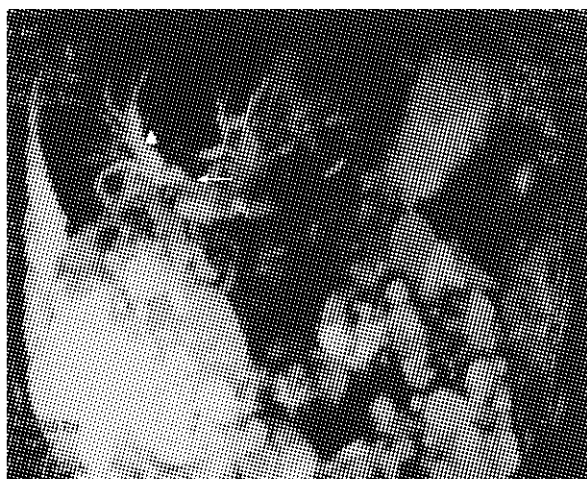


Fig. 5. The stricture of the common bile duct after thrombectomy. The stricture of the common bile duct (arrow) and the dilation of the intrahepatic biliary duct (triangle) were detected by MRCP after thrombectomy.

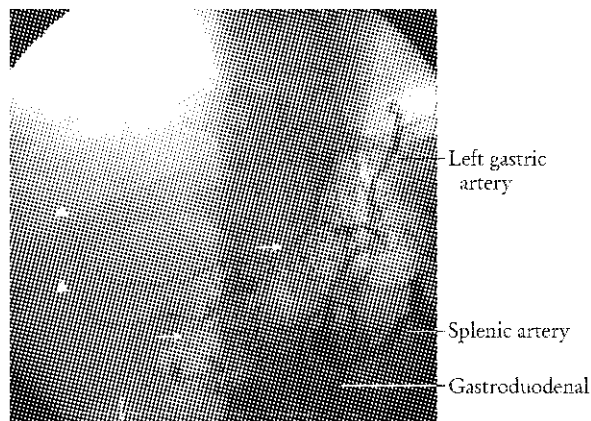


Fig. 6. Hepatic artery angiograph of the patient with late HAT. Late HAT was detected by ultrasonography 7 months after transplantation. Hepatic artery angiography could not show the common hepatic artery, but the intrahepatic artery (triangle) was well because of compensation of blood supply via rich collaterals (arrow) around the liver.

Table 1. The clinical data of patients with HAT

Patients	1	2	3	4	5	6	7
Blood type of donor/recipient	O/A	B/B	A/A	B/O	AB/AB	O/O	A/A
Hepatic artery suture	Running	Running	Running	Running	Running	Running	Interrupted
Hot ischemia (min)	3	4.5	4	5	5	5	4
Cold ischemia (min)	420	687	632	765	645	650	500
Anatomical variations of the hepatic artery	No	Yes	Yes	No	No	No	No
Diameter of the hepatic artery (mm)	4	5	4	3	6	5	3.5
Time for hepatic artery anastomosis (min)	15	11	15	17	12	16	10
FFP used intraoperatively (ml)	3560	3490	3050	2020	1040	1960	2960
Multiple organ transplantation	OLT	CLKT	OLT	OLT	OLT	OLT	OLT
Rejection	No	No	No	No	No	No	No

OLT; orthotopic liver transplantation; CLKT; combined liver-kidney transplantation.

Table 2. The clinical features of patients with HAT

Case	Time	Methods of detection	Treatment	Complication	Result
1	7 POM	Ultrasonography	Conservative treatment	No	Died of tumor recurrence
2	1 POD	Ultrasonography	Emergency thrombectomy and arterial reconstruction	No	Died of renal failure
3	18 POD	Laparotomy	Emergency thrombectomy and arterial reconstruction	Biliary necrosis	Died of liver failure
4	3 POD	Ultrasonography	Emergency thrombectomy and arterial reconstruction	Biliary leak	Died of liver failure
5	1 POD	Ultrasonography	Emergency thrombectomy and arterial reconstruction	No	Survived
6	5 POD	Ultrasonography	Emergency thrombectomy and arterial reconstruction	No	Survived
7	1 POD	Ultrasonography	Emergency thrombectomy and arterial reconstruction	Biliary stricture	Survived but waiting for retransplantation

POM; months of postoperation; POD; days of postoperation.

and confirmed by angiography in 1 patient in the seventh month after liver transplantation. The liver function of this patient was normal because of compensation of the hepatic artery blood supply via rich collaterals around the liver (Fig. 6). Thus conservative therapy was prescribed and the patient finally died of tumor recurrence. The mortality of the patients with HAT was 57.1% (4/7).

The detailed data of the 7 patients with HAT are presented in Tables 1 and 2.

Discussion

HAT as the most common serious vascular complication

occurs usually one month after OLT. It is encountered in about 1.6%–8% of adult patients, and 2.7%–20% of pediatric patients.^[9]

Many surgical factors are considered to be associated with HAT, and among them arterial reconstruction is predominantly important. First, the vasculature of donor and recipient should match accurately in terms of diameter and length. The incidence of HAT is reported to increase if the diameter of the hepatic artery was less than 3 mm.^[4] In our patients with HAT, the diameter of the hepatic artery was all greater than 3 mm. The anatomical variation of the hepatic artery has been confirmed to be a risk factor in the development of HAT.^[10,11] Two of our patients with anatomical variation of the hepatic artery developed HAT. Hence appropriate arterial reconstruction is important for recipients with anatomical variation of the hepatic artery. Second, microscopic techniques should be advocated.^[12,13] In our center, arterial reconstruction is performed using an operation microscope under the optical field with a magnification of approximately $\times 2.5$ zoom. The anastomosis was completed with 7-0 prolene, 8-0 or 9-0 dermalone. The manipulation during the operation should be slight and careful so as to avoid the damage of the vascular endothelium. Third, interrupted suture for arterial anastomosis could reduce the incidence of HAT significantly in liver transplantation. In this study, HAT occurred in 6 (6.3%) of the 96 patients who had accepted running continuous suture for hepatic arterial anastomosis, and in 1 (1%) of the 102 patients who received interrupted suture for hepatic arterial anastomosis ($\chi^2=4.027$, $P=0.045$). Interrupted suture is better than running continuous suture for hepatic arterial anastomosis.

Many nonsurgical factors are also related to HAT, especially hemodynamic derangement in the perioperative period, which is a high risk factor for HAT.^[14] An appropriate long-term coagulative state is of paramount importance. Blood coagulation function and liver function therefore should be monitored closely. Prothrombin time, INR, partially activated thromboplastin time, and platelet ought to be tested to decide whether FFP, albumin or platelet are needed. If INR is more than 1.8, FFP is supplied; if INR is less than 1.8, albumin is supplied instead of FFP. In the first 24 hours after operation, platelet should be supplied if it is less than $60 \times 10^9/L$ and not supplied if there is no bleeding beyond 24 hours after operation. Hematocrit should be maintained at about 30%. HAT will be induced if there are too much coagulation factors or a high level of hematocrit. In other organ transplantation centers, prophylactic anticoagulation treatment is routinely carried out after operation.

Rejection causes damage to vascular endothelial cells directly and increase the possibility of HAT.^[11] Immunosuppression regimen prescribed to avoid the occurrence of rejection is indicated for the prevention of

HAT. A triple regimen of CsA, Aza/MMF and steroids or a dual regimen of FK506 and steroid are both effective according to our experience.^[15,16] No rejection was detected in our patients who developed HAT.

Early diagnosis is of great importance in the treatment of HAT. Some authors reported that ultrasonography is very helpful in the early detection of HAT.^[17-23] In our center, ultrasonography is performed in patients every day in the first two weeks after liver transplantation, and changed according to their clinical manifestations two weeks after operation. If the velocity of blood flow in the left or right branches of the hepatic artery is faster than 0.4 m/s, HAT could be suspected. Six (85.7%) of 7 patients with HAT were detected by ultrasonography in this study, which has a sensitivity of 91% and a specificity 99.1%.^[24] The other one patient with massive ascites, which could not be detected by ultrasonography, was found to have HAT by laparotomy. So ultrasonography should be the first choice in detecting HAT. Angiography, however, is accurate and the gold standard in the diagnosis of HAT.^[7] CT^[25-27] and MRI^[28] are also helpful to diagnose HAT.

Once HAT is confirmed, thrombectomy and arterial reconstruction should be performed immediately.^[18,23,29] In this series, 6 patients with early HAT were subjected to emergency thrombectomy and arterial reconstruction as soon as HAT was confirmed. The blood flow of the hepatic artery recovered well after operation and the liver function returned to normal in a short period after operation (Figs. 3 and 4). Of the 6 patients, 1 died of renal failure, 2 survived, and 3 had biliary complication (2 died and 1 scheduled for retransplantation). Hepatic necrosis, hepatic abscess or serious biliary complication frequently occur after occurrence of HAT if thrombectomy and arterial reconstruction are not performed immediately. The blood supply of the hepatic and biliary systems was blocked completely after the development of HAT. Retransplantation is always needed if there is severe biliary complication or severe impairment of liver function. Thrombolysis is obscure in its effect and is frequently followed by the complication of bleeding. The treatment of late HAT is different from that of early HAT. Individualized treatment should be given to patients with late HAT. If the liver function is normal and there is no biliary complication, active treatment is not necessary. If there are severe biliary stricture or severe impairment of liver function, active treatments should be prescribed immediately, including biliary duct distention via endoscopic retrograde cholangiopancreatography, stent placement for biliary stenosis,^[30] biliary reconstruction and even retransplantation. One patient with late HAT in this study had a normal liver function received no active treatment but died of tumor recurrence.

Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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