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# URGENT REVASCULARIZATION OF LIVER ALLOGRAFTS AFTER EARLY HEPATIC ARTERY THROMBOSIS<sup>1</sup>

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Between April 1993 and May 1995, 17 adult orthotopic liver transplant recipients were found to have early hepatic artery thrombosis (HAT) after a median of 7 postoperative days (mean, 11). The HAT was diagnosed in all cases by duplex ultrasound. Thrombectomy was performed with urgent revascularization (UR), using an interposition arterial graft procured from the cadaveric liver donor, and arterial patency was verified with intraoperative angiography. In seven cases, intra-arterial urokinase was administered after the thrombectomy. Fifteen (88%) of the livers remained arterialized throughout the follow-up period (median, 15 months); the remaining two patients developed recurrent HAT after 6 and 8 months. Although there was a high rate of subsequent complications, 11 (65%) of the patients are alive without retransplantation, with a mean follow-up of 17 months. Despite having a patent hepatic artery, the remaining six patients (35%) died from infectious complications that usually were present before the UR. Thus, UR effectively restored arterial inflow in 88% of the patients with early HAT. The ultimate outcome was determined mainly by the presence of intra-abdominal complications at the time of UR. In conclusion, UR, rather than retransplantation, should be considered the prime treatment option for patients who develop early posttransplant HAT.

Hepatic artery thrombosis (HAT\*) remains one of the most dreaded complications after orthotopic liver transplantation (OLT). Earlier series reported that HAT occurred in about 10% of recipients (1-6), with even higher rates reported for children (1, 2, 7-12). In early days, up to 50% of these patients died without retransplantation; significantly more died when HAT developed in the early posttransplant period (2, 13). Those who did survive with HAT suffered significant morbidity, primarily related to septic hepatic gangrene of the liver and complications of the biliary tree (1, 2, 13-20). Although retransplantation has been credited with reducing the mortality of HAT (2, 13, 21), the inadequate supply of donor organs has limited this option.

While the feasibility has been reported of using urgent revascularization (UR) to avoid the need for retransplantation (22-24), this alternative strategy depends on early diagnosis. Innovations in duplex ultrasound (DUS) technology

have provided an accurate noninvasive method for detection of HAT before irreversible ischemic damage of the allograft occurs (25). Here, we report our results with UR in 17 adult OLT recipients with early HAT.

## PATIENTS AND METHODS

Between April 1993 and May 1995, 492 liver transplantations were performed in adult recipients at the University of Pittsburgh. Seventeen of these patients underwent UR for HAT within 30 days of OLT. Follow-up information was available in all cases. Patient selection, organ procurement, the recipient operation, intraoperative anesthetic management, and tacrolimus-based immunosuppression were performed using standard protocols, in which tacrolimus-based immunosuppression was routinely used (26).

Postoperative DUS examinations were not routinely done, but they were ordered promptly when clinically indicated. If HAT was diagnosed by DUS, angiographic confirmation frequently was obtained before UR was performed. During the period covered in this article, the technique of UR became increasingly standardized (Table 1). After balloon catheter thrombectomy, intraoperative angiography was performed to confirm patency of the intrahepatic arterial branches. When intrahepatic thrombus could not be cleared, urokinase (50,000-100,000) was administered directly into the donor hepatic artery (n=7). The hepatic arterial flow was restored with an iliac interposition arterial graft, which usually was based on the infrarenal aorta (27, 28).

After UR, all patients were treated with intravenous heparin and low molecular weight dextran for 7 days, followed by long-term, low-dose aspirin. The heparin dosage was designed to achieve a partial thromboplastin time between 1.5 and 2.0 times baseline. In selected patients who were at high risk for recurrent HAT, long-term anticoagulation with warfarin sodium was used. In these patients, the aim was to achieve 1.5-1.8 times prothrombin time prolongation by international normalized ratio.

## RESULTS

During the 2-year period of this study, UR was attempted in 17 adult OLT recipients with HAT 3-30 days after OLT (median, 7 days; mean, 11 days). The HAT occurred with 12 primary allografts, 4 second allografts, and 1 third allograft. Table 2 shows the type of arterial reconstruction that had been used previously. In 14 of the 17 cases, the anastomosis

TABLE 1. Urgent revascularization after HAT (n=17)

Technique
(a) Thrombectomy
(b) Intraoperative angiography
(c) Interposition arterial graft (n=10)
(d) Residual distal thromboses (n=7)
Intra-arterial urokinase (50-100,000 U)
Interposition arterial graft
(e) Systemic heparin and dextran 40

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\* Abbreviations: DUS, duplex ultrasound; HAT, hepatic artery thrombosis; OLT, orthotopic liver transplant; UR, urgent revascularization.

TABLE 2. Urgent revascularization after HAT: arterial anastomosis at the time of OLT

Donor/recipient	No. of patients (%)
Celiac axis/common hepatic artery	14 (83)
Celiac axis/iliac arterial graft	2 (11)
Common hepatic artery/right hepatic artery	1 (6)

had been between the donor celiac axis and the recipient common hepatic artery.

#### Diagnostic Accuracy

DUS correctly revealed the HAT in all 17 patients. These scans almost invariably were obtained to evaluate the cause of allograft dysfunction or injury, most often manifested by elevations of bilirubin and/or canalicular or hepatocellular enzymes. Five patients had unexplained sepsis (Table 3). Fourteen of the 17 patients underwent confirmatory angiography, but three patients were explored based on the DUS findings alone.

#### Causes of HAT

A clear mechanical cause for HAT was identified in five patients. In two cases, an intimal dissection was found. A bile leak with an associated mycotic aneurysm of the hepatic artery and distal thrombosis was found in two other patients, both of whom were recipients of second transplants after chronic rejection of their primary allografts. The fifth patient received a liver from a non-heart-beating donor. Intraoperative angiography performed after thrombectomy revealed diffuse donor arterial spasm. In five additional patients, a positive cytotoxic antibody cross-match was a nonmechanical risk factor for HAT. In the remaining seven patients, no specific etiologic factor could be identified.

#### Operative Procedures

UR was accomplished in all 17 patients. In one patient, the interposition arterial graft was anastomosed to the recipient splenic artery to avoid instrumentation of the atherosclerotic aorta. In another patient, the anastomosis to the usual infrarenal aortic position used in 15 of the 17 cases was technically difficult, causing the supraceliac aorta to be used (1, 29). In seven cases, the arteriogram obtained after thrombectomy showed residual thrombi in the small intrahepatic branches. Dissolution of these clots within the allograft was accomplished by administering 50,000–100,000 U of urokinase directly into the donor hepatic artery.

#### Patient Survival

None of the patients has had retransplantation. The long-term patency rate after UR was 88% (15/17). However, six patients (35%) died with a patent hepatic artery after a mean period of 33 days (range, 6–120 days; median, 17 days). In all

TABLE 3. Indications for DUS after OLT in 17 patients with HAT

Indication	No. of patients (%)
Increased liver function tests and fever	4 (24)
Increased liver function tests	6 (35)
Bile leak	2 (12)
Sepsis	5 (29)

the patients who died, the patency of the hepatic artery was established with a DUS before the terminal event and/or at autopsy (when performed). Eleven patients (65%) are still alive, with follow-up of 1–25 months (mean, 17 months; median, 15 months). Table 4 shows the mean values of the liver function tests at 3, 6, 9, and 12 months. Two of these 11 patients had recurrent HAT at 6 and 8 months after UR, with a single episode of cholangitis at the time of the recurrent HAT without further symptoms or complications.

*Ostensible candidates for retransplantation.* Ten of the 17 patients were considered to be candidates for retransplantation at the time of HAT, but did not have the procedure because no allografts were immediately available. One of the 10 “deprived” patients died of *Aspergillus* pneumonia 5 months after UR. The other nine patients became long-term survivors, and seven still have a patent hepatic artery (Table 5).

*Noncandidates for retransplantation.* Because of intra-abdominal infections at the time HAT was diagnosed, the other seven recipients were not considered candidates for retransplantation. Two (28.5%) of the seven patients are still alive, while the other five patients continued a complex septic course to death (Table 5).

#### Morbidity after Revascularization

All of the patients were anticoagulated with heparin and low-molecular-weight dextran. Only one patient (6%) required reoperation for bleeding after UR. The bleeding site at the anastomosis was repaired, and anticoagulation resumed.

*Vascular.* Despite anticoagulation, three patients (18%) developed occlusion of intrahepatic artery branches. One had an asymptomatic thrombosis (diagnosed by DUS) of an anomalous right hepatic artery branch. In two other patients, thrombosis of an anomalous left hepatic arterial branch required left lateral segmentectomy for the treatment or prevention of septic hepatic gangrene.

#### Biliary

Within 2 weeks after UR, one patient developed a bile leak and two other patients had distal common bile duct strictures. Biliary reconstruction was successful in all three cases. None of the survivors with patent hepatic artery developed intrahepatic biliary strictures.

#### Other

Three patients had worsening of hepatic dysfunction, due to allograft rejection (n=2) or from a combined hepatitis B virus/cytomegalovirus hepatitis (n=1).

#### DISCUSSION

HAT, or even acute ligation, is usually well tolerated in humans because abundant collateral arterial sources protect the native liver from ischemia (30). Although the total hepatectomy at transplantation disrupts these collaterals, the allograft may survive on portal flow only while arterial collaterals develop (1). We have estimated that one third of arterial thromboses are asymptomatic, one third are not immediately life threatening but lead to biliary tract ischemia syndromes, and one third cause parenchymal necrosis and rapid death if not rectified promptly (3, 7, 13–17).

Retransplantation has been considered the standard treat-

TABLE 4. Follow-up of the graft function after UR (n=11)<sup>a</sup>

	Pre-UR	Post-UR	3 mo	6 mo	9 mo	12 mo
Total bilirubin						
Median	3.4	1.6	1	1	0.9	1
Mean±SD	3.4±1.4	2.1±1.2	1.2±0.6	1.1±0.6	0.9±0.2	0.9±0.3
Aspartate aminotransferase						
Median	401	282.5	27	31	33	23.5
Mean±SD	402.8±280.9	288.9±215±4	52.5±66.5	44.7±45.7	31±9.6	24.5±12.5
Alanine aminotransferase						
Median	464	322.5	43	40	40.5	38
Mean±SD	413.3±268.7	346.5±277.8	69.7±66.2	53.5±37.8	40.3±12.1	40±15.8
γ-Glutamyltranspeptidase						
Median	116.5	59	62	56.5	94.5	83
Mean±SD	121.8±59.4	68.8±35.6	82±53.6	76.5±55	129.5±94.6	119.2±99.2

<sup>a</sup> Two patients with recurrent HAT.

TABLE 5. Urgent revascularization after HAT

	Revascularization alternative to re-Tx	Contraindication for re-Tx
No. of patients (%)	10 (59)	7 (41)
Patients surviving (%)	9 (90)	2 (28.5)
Hepatic artery patency (%)	8 (80)	7 (100)

ment for HAT. However, our recent experience showed that with early diagnosis, UR can eliminate the need for retransplantation in most cases. In the face of the deepening liver allograft dysfunctions, failure to attempt UR for early HAT is now considered a judgment error in our program. In recipients who were free from infection when diagnosed with HAT, long-term patient and graft survival rates after UR were 90%, as has been reported by others (24, 31). Although it was unusual, long survival was possible for patients who were infected and therefore not thought to be candidates for retransplantation. Recovery of nearly a third of these septic patients after UR may have been more frequent than would have been possible with the more radical operation of liver replacement.

The incidence of HAT can be reduced by careful case selection and attention to surgical technique at both the donor and recipient operations. We identified obvious mechanical and technical failures in 29% of the cases reported herein. In an additional 29%, HAT was associated with a positive cytotoxic antibody cross-match. In all cases, early diagnosis of HAT is critical if effective reintervention is to be done. We do not routinely schedule DUS to follow OLT in adult recipients unless there are increased risk factors, such as an older recipient or donor, a technically difficult arterial anastomosis, the use of an anomalous hepatic artery for rearterialization, or a positive cross-match.

During the 2-year duration of the study, there were no false-positive diagnoses of HAT using DUS scans, similar to the experience of Kubota et al. (32) in Sweden. Consequently, we currently obtain angiographic confirmation of HAT only when the DUS diagnosis is equivocal, as has been advocated by others (4, 24, 33, 34). Although false-negative DUS scans were not recorded during the present study, this can occur, particularly in pediatric patients (10, 11, 35). Once the diagnosis of HAT is established by either DUS or angiography, the symptomatic patient is quickly prepared for reoperation. However, if the patient is asymptomatic, the best course may

be careful monitoring rather than operation, because some such carefully monitored patients may continue to do well.

If the decision is made to operate, the standard strategy in our center includes thrombectomy and, if necessary, intrahepatic arterial thrombolysis with urokinase or other thrombolytic agents. Re-establishment of both the arterial outflow and the inflow are critical. We believe that most technical errors involve failure to accomplish the latter. With the flexibility allowed by the routine procurement of cadaveric iliac arterial grafts (27, 36), there is no excuse for acceptance of a weak pulse in the hilum. Autologous saphenous vein grafts also have been used (37).

We do not reuse the recipient celiac axis or hepatic artery for UR, or attempt to salvage a hepatic artery segment of the first liver graft, because inadequate flow or proximal intimal dissections in these vessels often have contributed cryptically to the HAT in the first place. Systematic reuse of these vessels for UR has been associated with a high failure rate (38). Our first choice is to base an interposition graft on the recipient aorta, preferably below the renal arteries.

Postoperative anticoagulation with heparin and dextran is of unproved value in adult liver recipients after HAT, but it has had a low complication rate (only 6% bleeding). Anticoagulation has been effective in preventing HAT in high-risk pediatric transplant patients (8).

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