tive trial of prophylactic immunosuppression with ATG-Fresenius versus OKT3 after renal transplantation. Transplantation 1995; 59: 830.
15. Racusen LC, Solez K, Colvin RB, et al. The Banff 97 working classification of renal allograft pathology. Kidney Int 1999; 55: 713.
16. Hunningake GW, Monick MM, Geist LJ. Cytomegalovirus infection–regulation of inflammation. Am J Respir Cell Mol Biol 1999; 21: 150.
17. Waldman WJ, Knight DA, Adams PW, Orosz CG, Sedmak DD. In vitro induction of endothelial HLA class II antigen expression by cytomegalovirus-activated CD4+ T cells. Transplantation 1993; 56: 1504.
18. van Dorp WT, van Wieringen PA, Marselis JE, et al. Cytomegalovirus directly enhances MHC class I and intercellular adhesion molecule-1 expression on cultured proximal tubular epithelial cells. Transplantation 1993; 55: 1367.
19. Grundy JE, Downes KL. Up-regulation of LFA-3 and ICAM-1 on the surface of fibroblasts infected with cytomegalovirus. Immunology 1993; 78: 405.
20. D Geist LJ, Dai LY. Cytomegalovirus modulates interleukin-6 gene expression. Transplantation 1996; 62: 653.
21. Srivastava R, Curtis M, Hendrickson S, Burns WH, Hosenpud JD. Strain specific effects of cytomegalovirus on endothelial cells: implications for investigating the relationship between CMV and cardiac allograft vasculopathy. Transplantation 1999; 68: 1568.
22. Valantine HA, Gao SZ, Menon SG, et al. Impact of prophylactic immediate posttransplant ganciclovir on development of transplant arteriosclerosis: a post hoc analysis of a randomized, placebo controlled study. Circulation 1999; 100: 61.
23. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D. Improved graft survival after renal transplantation in the United States, 1988 to 1996; N Engl J Med 2000; 342: 605.

Received 1 June 2000.
Accepted 19 July 2000.

0041-1337/01/7106-767/0
TRANSPLANTATION
Vol. 71, 767–772, No. 6, March 27, 2001
Printed in U.S.A.

UNI- AND MULTI-VARIATE ANALYSIS OF RISK FACTORS FOR EARLY AND LATE HEPATIC ARTERY THROMBOSIS AFTER LIVER TRANSPLANTATION

CHANG-KWON OH, SHAWN J. PELLETIER, ROBERT G. SAWYER, A. RASHARD DACUS, CHRISTOPHER S. MCCULLOUGH, TIMOTHY L. PRUETT, AND HILARY A. SANFEY[1]

The Charles O. Strickler Transplant Center, University of Virginia, Department of Surgery, Charlottesville, VA 22908-0709

Background. **Hepatic artery thrombosis (HAT) is a significant cause of morbidity after liver transplantation. The aims of this study are to identify and compare risk factors that might contribute to HAT.**

Methods. **A total of 424 liver transplants performed at the University of Virginia were reviewed. HAT was defined as complete disruption of arterial blood flow to the allograft and was identified in 29 cases (6.8%). HAT was classified as early (less than 1 month posttransplant, 9 cases: 2.1%) or late (more than 1 month posttransplant, 20 cases: 5.4%). Possible risk factors for HAT were analyzed using Pearson χ^2 test for univariate analysis and logistic regression for multivariate analysis.**

Results. **Multiple transplants, recipient/donor weight ratio >1.25, biopsy-proven rejection within 1 week of transplant, recipient negative cytomegalovirus (CMV) status, arterial anastomosis to an old conduit (defined as a previously constructed aorto-hepatic artery remnant using donor iliac artery), and CMV negative patients receiving allograft from CMV positive donors were found to be significant risk factors for developing early HAT. After logistic regression, factors independently predicting early HAT included arterial anastomosis to an old conduit [odds ratio (OR)=7.33], recipient/donor weight ratio >1.25 (OR=5.65), biopsy-proven rejection within 1 week posttransplant (OR=2.81), and donor positive and recipient negative CMV status (OR=2.66). Female donor, the combination of female donor and male recipient, recipient hepatitis C-related liver disease, donor negative CMV status, and the combination of recipient CMV negative and donor CMV negative were found to be significant risk factors for late HAT. Factors independently predicting late HAT by logistic regression included negative recipient and donor CMV status (OR=2.26) and the combination of a female donor and male recipient (OR=1.97).**

Conclusion. **Therefore, in nonemergency situations attention to these factors in donor allocation may minimize the possibility of HAT.**

[1] Address correspondence to: Hilary A Sanfey, MD, Department of Surgery, University of Virginia HSC P.O. Box 800709, Charlottesville, VA 22908-0709.

INTRODUCTION

After liver transplantation, hepatic artery thrombosis (HAT) can lead to devastating outcomes. The incidence of hepatic artery thrombosis varies widely, with a reported frequency of 2.6–20% in adult recipients (*1–4*), 9–14.9% in the pediatric population (*1–3*), and as high as 30% in children younger than 1 year old (*5*). HAT is most commonly diagnosed less than 1 month after transplantation (*2*). Clinical presentations range from fulminant hepatic failure, recurrent biliary sepsis, or delayed biliary leaks to an asymptomatic presentation with abnormal liver function tests (*3*, *4*, *6*, *7*). Arterial thrombosis occurring early after transplantation is more likely to be associated with an aggressive course and a higher rate of allograft loss and patient mortality in comparison to late onset HAT, which has been described as having a more benign course (*8*). Diagnosis can be suggested by Duplex ultrasonography (*9–11*), and confirmed by angiography (*12*), exploratory laparotomy, or autopsy. In the current predicament of serious organ shortage, hepatic allograft rescue with the use of urgent revascularization sometimes is an effective means of either avoiding retransplantation or providing a bridge until a suitable donor becomes available (*13–15*). With the help of interventional radiology and medical therapy, the recipient with HAT can be temporarily or permanently supported (*16*). Despite efforts to salvage hepatic allograft, many patients eventually require retransplantation, which is associated with considerable morbidity including decreased allograft survival, higher cost, and longer length of hospitalization (*17*). The reported mortality for liver transplant recipients developing HAT has been quite variable, ranging from 30 to 75%, and may be due to the variable clinical course that can occur in this patient population (*1*, *8*, *18*).

A clear definition of HAT, based on defined risk factors, is necessary to potentially reduce the incidence of HAT and to formulate guidelines and protocols for the management of this dreadful complication. Although identifiable technical problems, such as a relatively small recipient receiving a small allograft, retransplantation, the method used for arterial reconstruction, and anatomic variation of the donor hepatic artery may be responsible in some cases, the etiology of HAT is not always identifiable. Although the risk is substantially increased in children (*1–3*), particularly in infants under the age of 12 months (*19*), older age is also an important factor influencing the occurrence of atherosclerotic lesions in arterial vasculature (*20*). An increased incidence in patients undergoing retransplantation has also been noted (*1*), possibly due to the more complex methods of arterial reconstruction necessary. The incidence of HAT is higher in patients requiring a vascularallograft (23.8 vs. 5.4%) than patients undergoing conventional arterial reconstruction (*3*). Uncontrolled rejection has been implicated as predisposing to HAT (*6*, *21*), possibly related to the increased resistance to blood flow through an edematous allograft (*22*). Viral infections such as cytomegalovirus (CMV) may also contribute, because CMV can infect endothelial cells and may potentially lead to a rapid procoagulant response (*23*, *24*). Abbasoglu et al.(*25*) recently demonstrated the association between low hepatic artery blood flow (less than 400 ml/min) with more than a 5-fold increased incidence of early hepatic artery complications. This led to the recommendation for measuring hepatic artery flow at the time of liver transplantation, which may help predict early, but not late posttransplant hepatic artery complications.

Despite many reports on the possible risk factors for HAT after liver transplantation, systematic analysis with multivariate testing to compare the significance of each risk factor has not been published. Therefore, this study of univariate and multivariate analysis for early and late HAT was performed to identify the independent risk factors contributing to HAT.

PATIENTS AND METHODS

A total of 425 liver transplants performed at the University of Virginia Health System from February 7, 1988 to December 31, 1998 were reviewed. Allograft was preserved with University of Wisconsin (UW) solution. Immunosuppression consisted of cyclosporine or tacrolimus, corticosteroids, and, in some cases, azathioprine or mycophenolate mofetil. Before the availability of ganciclovir, no prophylactic therapy for CMV infection was used. After its introduction (October, 1995), oral ganciclovir (1 g three times daily for 6 weeks, dose appropriately adjusted for renal dysfunction) was routinely administered to CMV serology negative patients receiving an organ from a CMV serology positive donor and, in some cases, to recipients considered to be at high risk for CMV infection (such as those treated with OKT3 or high dose steroids for rejection). The University of Virginia Blood Bank did not routinely screen Blood products for CMV.

HAT was defined as the complete disruption of arterial blood flow to the allograft and was identified by Doppler ultrasound, angiography, surgical exploration, or autopsy. HAT was classified as early (less than 1 month posttransplant) or late (more than 1 month posttransplant). Possible risk factors included: duration of donor hospitalization, cause of donor death, donor and recipient age, gender, race, CMV status, ABO/Rh/HLA matching, body weight ratio, the etiology of recipient end-stage liver disease, prior liver transplantation, Child-Turcotte-Pugh (CTP) scores, ischemic times, presence of allograft arterial aberrancies, use of a Carrel patch, ligation of the gastroduodenal artery, the method of intraoperative arterial reconstruction, and the number and severity of posttransplant rejection episodes. For our study, an "old conduit" was defined as a previously constructed aortohepatic artery remnant using donor iliac artery.

For univariate analysis, categorical variables were analyzed using Pearson χ^2 testing. All values are expressed as a percentage of the group from which they were derived (categorical variables). On univariate analysis, $P \leq 0.05$ was considered significant. Logistic regression was then performed to identify risk factors for HAT after liver transplantation. Variables with a $P < 0.100$ in the univariate analysis were entered into a forward stepwise logistic regression analysis to estimate the odds ratio (OR) of early or late HAT (dependent variables) and the presence or absence of potential prognostic factors (independent variables). The odds ratio was defined as the exp[β-coefficient] with 95% confidence intervals (95% CI). Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences, Chicago, IL) 7.0 software for Windows (SPSS.

RESULTS

Of the 424 cases reviewed, 29 episodes of HAT (6.8%) occurred during the study period with 72.4% of cases identified by Doppler ultrasound, 79.3% confirmed or diagnosed by angiography, 6.9% by surgical exploration, and 13.8% by autopsy. Nine patients (2.1%) were diagnosed with early HAT although 20 patients (4.7%) were diagnosed with late HAT. The time interval between transplantation and the diagnosis of HAT ranged from 8 days to 8.4 years (mean$\pm$SE, 381$\pm$118 days). Thirty-one percent (9 cases) of all patients

with HAT were diagnosed within 1 month after transplantation, 41.4% (12 cases) between 1 month and 1 year after transplantation, and 27.6% (8 cases) more than 1 year post-transplantation. Forty-five other patients (10.6%) either died or experienced allograft loss for reasons other than early HAT during the first month after transplantation.

Early hepatic artery thrombosis

Table 1 demonstrates donor and recipients characteristics associated with early HAT. By univariate analysis, the number of previous transplants was found to be associated with early HAT. The incidence of early HAT in 50 patients with multiple transplants was 6.0%, significantly higher than that of primary transplant patients ($P=0.043$). The incidence of early HAT for 8 patients receiving a third liver allograft was 12.5% and for 42 patients receiving a second liver allograft, 4.8%, compared with 1.6% of 374 primary transplants. Early HAT occurred more frequently in recipients with negative pretransplant CMV serology (n=106, 5.7%) when compared with patients with positive pretransplant CMV serology ($P=0.003$). CMV negative patients receiving an allograft from CMV positive donors had a significantly higher incidence of early HAT (7.7% of 65 cases, $P=0.001$) when compared with other combinations. The incidence of early HAT in 22 recipients less than 15 kg was 9.1%, compared with 1.8% to recipients weighing more than 15 kg (n=351, $P=0.022$). Body weight ratios (recipient/donor) greater than 1.25 (n=117) were associated with an incidence of early HAT of 6.0% compared to 0.8% of the 259 cases with a ratio<1.25 ($P=0.002$). During retransplantation, the use of a previously placed arterial conduit for reconstruction was associated with a 16.7% incidence of HAT compared to 2.0% for other types of arterial reconstruction ($P=0.016$). The incidence of early HAT among recipients with an episode of biopsy-proven rejection within 1 week of transplantation (8.6% of 35 cases) was significantly higher than that for those without rejection (1.6% of 371 cases, $P=0.008$). There was no significant difference in the incidences of early HAT between recipients grouped by age, gender, race, etiology of recipient end-stage liver disease, recipient pretransplant VZV and EBV status, ABO or Rh blood type or matching, duration of donor admission, and cause of donor brain death.

Technical elements were evaluated for their potential association with the development of early HAT. Hepatic arterial aberrancies were found in 23.8% of the 424 cases evaluated during the study period, including left hepatic (13.4%), right hepatic (13.0%), and both (2.7%). The incidence of early HAT in patients transplanted with allografts which had arterial aberrancies (n=79) was 0% compared to 2.8% occurring in recipients transplanted with allografts with normal anatomy (n=253, $P=0.135$). In addition, there was no difference in the rate of early HAT for cases involving hepatic artery anastomosis using a Carrel patch (2.0% of 101 recipients) when compared to hepatic artery anastomosis without a Carrel patch (1.8% of 112 recipients, $P=0.917$) or those with or without ligation of the gastroduodenal artery (1.8% of 163 recipients versus 1.7% of 58 recipients, respectively; $P=0.971$).

Factors independently predictive of early HAT are listed in Table 2. After logistic regression, independent predictors of HAT included the type of arterial reconstruction ($P=0.047$, odds ratio=7.33, 95% confidence interval: 1.03–52.26), body weight ratios ($P=0.022$, odds ratio=5.65, 95% confidence interval: 1.28–24.91), the occurrence of biopsy-proven rejection within 1 week of transplantation ($P=0.023$, odds ratio=2.81, 95% confidence interval: 1.16–6.84), and the combination of CMV negative recipients with CMV positive donors CMV ($P=0.021$, odds ratio=2.66, 95% confidence interval: 1.16–6.08).

The rate of mortality for the nine patients with early HAT was 55.6%. Four patients died from liver failure although one died from sepsis with a partially functioning allograft. All four of the surviving patients with early HAT required retransplantation.

Late hepatic artery thrombosis

Donor and recipient characteristics associated with the development of late HAT are demonstrated in Table 3. The

TABLE 1. Risk factors associated with early HAT

Variables	Category	Incidence (%)	Total no.	*P*
No. of allograft	3rd	12.5	8	
	2nd	4.8	42	
	1st	1.6	374	0.047
CMV status	Negative	5.7	106	
Recipient	Positive	0.7	268	0.003
Combination	D+R−	7.7	65	
	D−R−	2.5	40	
	D+R+	0.7	139	
	D−R+	0.8	120	0.009
Recipient body weight	<15 kg	9.1	22	
	>15 kg	1.8	391	0.022
Recipient/donor body wt. ratio	>1.25	6.0	117	
	<1.25	0.8	259	0.002
Reconstruction of hepatic artery	To hepatic artery	2.1	336	
	Supraceliac conduit	0	6	
	Infrarenal conduit	1.9	53	
	To old conduit	16.7	6	0.201
Biopsy-proven rejection within 1 wk	Yes	8.6	35	
	No	1.6	371	0.008

Abbreviations: CMV, cytomegalovirus; D+R−, the combination of pretransplant CMV serology of recipient negative and donor positive.

TABLE 2. Independent predictors of early HAT after liver transplantation

Variable	*P*	OR	95% CI	
			Lower	Upper
Arterial anastomosis to old conduit	0.0468	7.3303	1.0282	52.2625
Recipient/donor wt. ratio >1.25	0.0223	5.6468	1.2799	24.9142
CMV combination D+R−	0.0209	2.6550	1.1595	6.0796
Episode of rejection within 1 wk	0.0226	2.8112	1.1559	6.8370

Abbreviations: CMV, cytomegalovirus; D+R−, the combination of pretransplant CMV serology of recipient negative and donor positive; CI, confidence interval; OR, odds ratio.

TABLE 3. Risk factors associated with late HAT

Variables	Category	Incidence (%)	Total no.	*P*
Combination of gender	Female to male	14.9	74	
	Male to female	3.7	81	
	Male to male	3.0	165	
	Female to female	2.0	50	0.001
Donor gender	Female	9.7	124	
	Male	3.3	246	0.010
Recipient liver disease	Hepatitis C related	9.8	82	
	Nonhepatitic C	4.2	288	0.048
	Hepatitis B related	7.5	53	
	Nonhepatitis B	5.0	317	0.456
	Hepatitis B or C related	8.7	127	
	Nonhepatitis B or C	3.7	243	0.045
CMV status-Combination	D−R−	19.4	36	
	D−R+	5.8	104	
	D+R+	3.2	125	
	D+R−	1.7	59	0.001
Donor	Negative	9.6	156	
	Positive	2.4	205	0.003

Abbreviations: CMV, cytomegalovirus; D−R−, the combination of pretransplant CMV serology of recipient negative and donor negative.

TABLE 4. Independent predictors of late HAT after liver transplantation

Variable	P	OR	95% CI	
			Lower	Upper
CMV combination D−R−	0.0025	2.2552	1.3309	3.8213
Gender combination (F to M)	0.0080	1.9674	1.1935	3.2430

Abbreviations: CMV, cytomegalovirus; D−R− the combination of pretransplant CMV serology of recipient negative and donor negative; F to M, male recipient and female donor; CI, confidence interval; OR, odds ratio.

combination of female donors and male recipients was found to be a significant risk factor for late HAT ($P=0.001$). The incidence of HAT among male recipients who received an allograft from a female donor (14.9% of 74 cases) was significantly higher than that for other gender combinations (3.0% of 296 cases, $P<0.001$). Allograft from female donors also were associated with late HAT ($P=0.010$). Recipients transplanted for end-stage liver disease associated with hepatitis C virus infection had a higher incidence of late HAT (9.8% of 82 cases) than those transplanted for other etiologies (4.2% of 288 cases, $P=0.048$). Late HAT was more common among the 156 donors with negative pretransplant CMV serology (9.6%) when compared with the 205 donors with positive CMV serology (2.4%, $P=0.003$). The combination of negative donor CMV and negative recipient CMV also had a higher incidence of late HAT ($P=0.001$). There was no significant difference in the incidences of late HAT between patients grouped by the number of transplants, age, race, recipient gender, recipient pretransplant VZV and EBV status, ABO or Rh blood type and matching, method for arterial reconstruction, presence biopsy-proven rejection within 1 week after transplantation, duration of donor admission, or cause of brain death.

Technical elements were evaluated for their potential associations with the development of late HAT. The incidence of late HAT in patients transplanted with allografts who had arterial aberrancies (n=72) was 2.8% compared with 6.6% occurring in recipients transplanted with allografts with normal anatomy (n=226, $P=0.219$). In addition, there was no difference in the rate of late HAT for cases involving hepatic artery anastomosis using a Carrel patch (3.2% of 95 recipients) when compared with hepatic artery anastomosis without a Carrel patch (2.9% of 102 recipients, $P=0.930$) or those with or without ligation of the gastroduodenal artery (3.2% of 156 recipients vs. 4.2% of 48 recipients, respectively; $P=0.900$).

Logistic regression was used to identify factors independently associated with late HAT (Table 4). These included a combination of a pretransplant CMV of negative recipient with a CMV negative donor ($P=0.003$, OR=2.26, 95% confidence interval: 1.33–3.82) and the combination of a male

recipient and with a female donor (P=0.008, OR=1.97, 95% confidence interval: 1.19–3.24).

The rate of mortality for the 20 recipients with late hepatic artery thrombosis was 15.0%, all with an attributable mortality due to liver failure. Fourteen recipients (70.0%) required retransplantation although 3 patients (15.0%) survived without retransplantation. One of the three patients who survived without retransplantation after late HAT underwent left lobectomy secondary to liver infarction and multiple biliary revisions due to a delayed bile leak and biliary stenosis. The second patient had multiple biliary stenoses that were drained percutaneously. The third patient's posttransplant course was complicated by a complete obstruction of the proximal common hepatic artery leading to necrosis of the left hepatic lobe. This patient experienced a spontaneous recovery while on the waiting list for retransplantation.

DISCUSSION

Hepatic artery thrombosis after liver transplantation is a relatively infrequent, but possibly devastating complication often requiring urgent retransplantation. Patients with HAT may present with a fulminant clinical course or a subtle and indolent course. The time of onset of HAT has been correlated with the severity of subsequent complications, with late HAT thought to have a more benign course. However, outcomes still vary considerably, although the reasons for this are unclear.

Ligation of a hepatic artery branch (right, left, or segmental) in a nontransplant patient is a safe adjunct for control of hemorrhage and rarely results in biliary necrosis (*26*). Generally, only a transient rise in liver enzymes is seen, perhaps due to collateral flow from spared hepatic arterial branches and maintenance of oxygenated portal blood flow. Traditionally, ligation of either the proper or common hepatic artery has been considered more dangerous. Although the transplanted liver is considered less likely to tolerate diminished arterial flow, even complete ligation of the hepatic artery after transplantation is not invariably associated with biliary tree necrosis. In a report of seven cases of ligated or embolized hepatic artery pseudoaneurysms after liver transplantation, one of the patients suffered acute hepatic failure and underwent retransplantation, two cases died from peritonitis, and four cases have been alive for several years (*27*). In addition, transcapsular arterial collateralization of a liver allograft after hepatic artery occlusion in an adult has been noted by using color Doppler ultrasonography (*28*). The arterial collateralization came from peridiaphragmatic vessels into both right and left lobes of the transplanted liver. These mechanisms may be a possible explanation for the wide variation in clinical course after HAT.

The risk of HAT after transplantation has been associated with several factors. As with the different clinical manifestations of early and late HAT, the risk factors for these entities were found to be different. The number of transplants, type of arterial reconstruction, recipient/donor body weight ratio, an early episode of biopsy-proven acute rejection, and pretransplant CMV status were associated with early HAT by univariate analysis.

Multiple transplants with an arterial anastomosis to an old arterial conduit had a higher incidence of early HAT in our study. Secondary or tertiary transplants have been reported to be associated with a high incidence of conduit use for arterial reconstruction because of an unsuitable recipient hepatic artery, poor inflow, or intimal dissection (*1*). In the case of retransplantation, our study suggests that it may be prudent to avoid the use of old conduits.

Recipients who were transplanted with a liver from a small donor more frequently suffered early HAT. This impact of a discrepancy between the body weights of recipients and donors has not been documented. This complication potentially could be prevented by careful selection of recipients during the pretransplant decision making process, with a recipient/donor body weight ratio less than 1.25 appearing to be desirable.

During acute rejection, allograft vascular endothelialitis or edema may reduce the blood flow into a liver allograft (*21*, *22*). In support of this theory, Bell et al. showed that biopsy specimens obtained within a week of HAT revealed evidence of acute rejection in 9 of 10 cases (*6*). Our data confirmed that rejection within 1 week of transplantation is a risk factor for early HAT. Therefore, the aggressive control of acute rejection within 1 week of transplantation is recommended.

Interestingly, our data demonstrated that the impact of cytomegalovirus status on early HAT and late HAT is different. The combination of donor positive CMV and recipient negative CMV was associated with early HAT, although donor negative and recipient negative CMV status was associated with late HAT. The association of CMV with early HAT has previously been reported, with 50% of patients with early HAT found to be recipient CMV negative and donor CMV positive (*23*). CMV can establish lifelong latency after initial infection and may reactivate in many conditions associated with immunosuppression (*29*). In association with CMV infection, intercellular adhesion molecule-1 (ICAM-1) is induced in the vascular and sinusoidal endothelium of liver tissue within 24 hr of CMV infection (*30*). These alterations in the endothelial cell membrane may lead to the adherence of leukocytes and platelets (*31*), and the production of procoagulants within several hours after inoculation of the virus (*24*, *32*), and possibly subsequent HAT. Although the precise mechanism of HAT promoted by CMV reactivation or infection is still unknown, our finding of an increased incidence of early HAT in CMV negative recipients transplanted with livers from CMV positive donors and late HAT in CMV negative recipients from CMV negative donors supports the hypothesis that CMV is at least sometimes involved in the development of HAT. We currently use prophylactic treatment with ganciclovir for high-risk seronegative recipients who receive seropositive donor allograft. However, it is still unclear whether the extension of our criteria to include CMV prophylaxis for CMV negative patients who receive CMV negative donor livers in order to prevent the late onset HAT would be better.

As risk factors for late HAT, the importance of the gender combination of recipients and donors, recipient liver disease associated with hepatitis C virus, and the CMV combination of recipients and donors were suggested. The role of the gender combination of recipients and donors in the development of HAT after transplantation has not been reported although Brooks et al.(*33*) suggested that allograft survival from all causes was less when female donors were used.

The clinical correlation between hepatitis C virus and late onset HAT is new. In a previous study about allograft loss in the patients with chronic hepatitis C (*34*), the incidence of

HAT was not high at 1.6%, although a second report noted an incidence of 2.6% (*35*). Although the exact mechanism of the role of hepatitis C in HAT if it exists is still unknown, cytokines may play a role in this process since chronic activation of proinflammatory mediators in viral hepatitis predisposes to thrombosis (*36*, *37*).

How or if donor and recipient factors associated with HAT should influence liver allocation in the current era of extreme organ shortages is unclear. For groups at increased risk of early and late HAT as described above, however, prophylactic anticoagulant treatment or frequent Doppler ultrasound screening could be considered for the possible prevention or early detection of HAT after liver transplantation.

REFERENCES

1. Todo S, Makowka L, Tzakis AG, et al. Hepatic artery in liver transplantation. Transplant Proc 1987; 19: 2406.
2. Langnas AN, Marujo W, Stratta RJ, Wood RP, Shaw BW. Vascular complication after orthotopic liver transplantation. Am J Surg 1991; 161: 76.
3. Tzakis AG, Gordon RD, Shaw BW, Iwatsuki S, Starzl TE. Clinical presentation of hepatic artery thrombosis after liver transplantation in the cyclosporine era. Transplantation 1985; 40: 667.
4. Hesselink EJ, Klompmaker IJ, Prium J, Van Schilfgaarde R, Slooff MJH. Hepatic artery thrombosis after orthotopic liver transplantation- a fatal complication or an asymptomatic event. Transplant Proc 1989; 21: 2462.
5. Esquivel CO, Koneru B, Karrer F, et al. Liver transplantation before 1 year of age. J Pediatr 1987; 110: 545.
6. Bell R, Sheil AGR, Thompson JF, et al. Vascular complications following orthotopic liver transplantation. Aust NZ Surg 1990; 60: 193.
7. Tzakis AG. The dearterialized liverallograft. Semin Liver Dis 1985; 5: 375.
8. Valente JF, Alonso MH, Weber FL, Hanto DW. Late hepatic artery thrombosis in liver allograft recipients is associated with intrahepatic biliary necrosis. Transplantation 1996; 61: 61.
9. Wellings RM, Olliff SP, Olliff JFC, Deakin M, Alton H. Duplex doppler detection of hepatic artery thrombosis following liver transplantation. Clin Radiol 1993; 47: 180.
10. Kubota K, Billing H, Ericzon BG, Kelter U, Groth CG. Duplex doppler ultrasonography for monitoring liver transplants. Acta Radiol 1990; 31: 279.
11. Segel MC, Zajko AB, Bowen A, et al. Doppler ultrasound as a screen for hepatic artery thrombosis after liver transplantation. Transplantation 1986; 41: 539.
12. Zajko AB, Bron KM, Starzl TE, et al. Angiography of liver transplantation patients. Radiology 1985; 157: 305.
13. Yanaga K, Lebeau G, Marsh JW, et al. Hepatic artery reconstruction for hepatic artery thrombosis after orthotopic liver transplantation. Arch Surg 1990; 125: 628.
14. Sheiner PA, Varma CV, Guarrera JV, et al. Selective revascularization of hepatic artery thromboses after liver transplantation improves patient andallograft survival. Transplantation 1997; 64: 1295.
15. Langnas AN, Marujo W, Stratta RJ, Wood RP, Li S, Shaw BW. Hepatic artery allograft rescue following arterial thrombosis: role of urgent revascularization. Transplantation 1991; 51: 86.
16. Hoffer FA, Teele RL, Lillehei CW, Vacanti JP. Infected bilomas and hepatic artery thrombosis in infant recipients of liver transplants: interventional radiology and medical therapy as an alternative to retransplantation. Radiology 1988; 169: 435.
17. D'Alessandro AM, Ploeg RJ, Knechtle SJ, et al. Retransplantation of the liver-a seven-year experience. Transplantation 1993; 55: 1083.
18. Shaw BW, Gordon RD, Iwatsuki S, et al. Hepatic retransplantation. Transplant Proc 1985; 17: 264.
19. Stevens LH, Emond JC, Piper JB, et al. Hepatic artery thrombosis in infants: a comparison of whole livers, reduced-size allograft and allograft from living-related donors. Transplantation 1992; 53: 396.
20. DeBakey ME, Lawrie GM, Glaeser DH. Patterns of atherosclerosis and their surgical significance. Ann Surg 1985; 201; 115.
21. Samuel D, Gillet D, Castaing D, Reynes M, Bismuth H. Portal and arterial thrombosis in liver transplantation: a frequent event in severe rejection. Transplant Proc 1989; 21: 2225.
22. Demetris AJ, Lasky S, Van Thiel DH, Starzl TE, Dekker A. A pathology of hepatic transplantation: a review of 62 adult allograft recipients immunosuppressed with a cyclosporine/steroid regimen. Am J Pathol 1985; 118: 151.
23. Madalosso C, de Souza NF Jr, Ilstrup DM, Wiesner RH, Krom RA. Cytomegalovirus and its association with hepatic artery thrombosis after liver transplantation. Transplantation 1998; 66: 294.
24. Van Geelen AGM, Slobbe-van Drunen MEP, Muller AD, Bruggeman CA, Van Dam-Mieras MCE. Membrane related effects in endothelial cells induced by human cytomegalovirus. Arch Virol 1995; 140: 1601.
25. Abbasoglu O, Levy MF, Testa G, et al. Does intraoperative hepatic artery flow predict arterial complications after liver transplantation? Transplantation 1998; 66: 598.
26. Feliciano DV. Surgery for liver trauma. Surg Clin North Am 1989; 69: 273.
27. Madariaga J, Tzakis A, Zajko AB, et al. Hepatic artery pseudoaneurysm ligation after orthotopic liver transplantation- a report of 7 cases. Transplantation 1992; 54: 824.
28. Wachsberg RH, Koneru B, Levine CD. Transcapsular arterial collateralization of a liver allograft after hepatic artery occlusion in an adult: color Doppler ultrasonographic diagnosis. J Ultrasound Med 1995; 14: 859.
29. Myerson D, Hackman RC, Nelson JA, Ward DC, McDougall JK. Widespread presence of histologically occult cytomegalovirus. Hum Pathol 1984; 15: 430.
30. Sedmak DD, Knight DA, Vook NC, Waldman JW. Divergent patterns of ELAM-1, ICAM-1 and VCAM-1 expression on cytomegalovirus-infected endothelial cells. Transplantation 1994; 58: 1379.
31. Span AHM, Van Dam-Mieras MCE, Mullers W, Endert J, Muller AD, Bruggeman CA. The effect of virus infection on the adherence of leukocytes or platelets to endothelial cells. Eur J Clin Invest 1991; 21: 331.
32. Van Dam-Mieras MCE, Muller AD, Van Hinsbergh VWM, Mullers WJHA, Bomans PHH, Bruggeman CA. The procoagulant response of cytomegalovirus infected endothelial cells. Thromb Haemost 1992; 68: 364.
33. Brooks BK, Levy MF, Jennings LW, et al. Influence of donor and recipient gender on the outcome of liver transplantation. Transplantation 1996; 62: 1784.
34. Rosen HR, O'Reilly PM, Shackleton CR, et al. allograft loss following liver transplantation in patients with chronic hepatitis C. Transplantation 1996; 62: 1773.
35. Ghobrial RM, Farmer DG, Baquerizo A, et al. Orthotopic liver transplantation for hepatitis C: outcome, effect of immunosuppression, and causes of retransplantation during an 8-year single center experience. Ann Surg 1999; 229: 824.
36. Dosquet C, Weill D, Wautier JL. Cytokines and thrombosis. J Cardiovasc Pharmacol 1995; 25 (suppl. 2): S13.
37. Andus T, Bauer J, Gerok W. Effect of cytokines on the liver. Hepatology 1991; 13: 364.

Received 21 January 2000.
Provisionally accepted 26 February 2000. Accepted 24 July 2000.