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• *BRIEF REPORTS* •

Personal experience with the procurement of 32 liver allografts

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Abstract

AIM: To introduce the American Pittsburgh's method of rapid liver procurement under the condition of brain death and factors influencing the quality of donor liver.

METHODS: To analyze 32 cases of allograft liver procurement retrospectively and observe the clinical outcome of orthotopic liver transplantation.

RESULTS: Average age of donors was 38.24±12.78 years, with a male:female ratio of 23:9. The causes of brain death included 21 cases of trauma (65.63%) and nine cases of cerebrovascular accident (28.13%). Fourteen grafts (43.75%) had hepatic arterial anomalies, seven cases only right hepatic arterial anomalies (21.88%), five cases only left hepatic arterial anomalies (15.63%) and two cases of both right and left hepatic arterial anomalies (6.25%) among them. Eight cases (57.14%) of hepatic arterial anomalies required arterial reconstruction prior to transplantation. Of the 32 grafts evaluated for early function, 27 (84.38%) functioned well, whereas three (9.38%) functioned poorly and two (6.25%) failed to function at all. Only one recipient died after transplantation and thirty-one recipients recovered. Four recipients needed retransplantation. The variables associated with less than optimal function of the graft consisted of donor age (35.6±12.9 years *vs* 54.1±4.3 years, $P<0.05$), duration of donor's stay in the intensive care unit (ICU) (3.5±2.4 d *vs* 7.4±2.1 d, $P<0.005$), abnormal graft appearance (19.0% *vs* 100%, $P<0.05$), and such recipient problems as vascular thromboses during or immediately following transplantation (89.3% *vs* 50.0%, $P<0.005$).

CONCLUSION: During liver procurement, complete heparization, perfusion *in situ* with localized low temperature and standard technique procedures are the basis ensuring the quality of the graft. The hepatic arterial anomalies should be taken care of to avoid injury. The donor age, duration of donor's staying in ICU, abnormal graft appearance and recipient problem are important factors influencing the quality of the liver graft.

INTRODUCTION

Enormous progress including surgical techniques has been achieved since the first orthotopic liver transplantation (OLTx) was performed in humans in 1963 and OLTx has established its role as a therapeutic option for patients with end-stage liver disease. Primary graft nonfunction (PGN) remains a dreadful complication of OLTx, one that is associated with a high mortality and morbidity, and therefore liver allograft with good function is the most important point for ensuring the success of liver transplantation. A single donor surgeon's experience procuring the livers from 32 donors in Pittsburgh Transplant Center is analyzed in order to identify the role of a number of variables pertinent to the clinical outcome of OLTx.

MATERIALS AND METHODS

Donor data

The author performed 32 allograft hepatectomies at the University of Pittsburgh Transplant Center. All donors were brain dead and the age of the donors varied from 12 to 63 years with the average of 38.24±12.78 years. Among them, there were 23 male donors and 9 female donors. Table 1 lists the causes of death of the donors.

Table 1 Causes of brain death among 32 liver donors

Cause	*n* (%)
Trauma	21 (65.63)
Motor vehicle accident	16
Gunshot wound	1
Fall	2
Other	2
Cerebrovascular accident	9 (28.13)
Cerebral infarct	6
Subarachnoid hemorrhage	3
Others	2 (6.24)
Total	32 (100)

Donor selection criteria

In general, donors were selected who were less than 65 years

of age, had no history of liver disease such as hepatitis or alcoholism, and a total serum bilirubin less than 34 μmol/L, normal or near-normal alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (AKP), γ-glutathione transferase (γ-GT) and prothrombin time (PT), and adequate arterial blood gas. Elevations of ALT, AST, AKP and γ-GT, with a tendency to decline, were not regarded as a contraindication for donation of the liver.

Donor maintenance

Donors were fluid-resuscitated once they had been pronounced brain dead in order to maintain a central venous pressure of 8-10 cm H_2O and urine output over 1 mL/(kg • h) as a guide. For donors receiving vasopressin for diabetes insipidus, the vasopressin was discontinued as soon as possible to avoid liver ischemia secondary to a decreased splanchnic blood flow. Urine output was replaced vigorously with intravenous fluids, usually one-half or quarter normal saline solution with potassium chloride. Electrolytes were checked frequently, especially to correct hypokalemia. Normothermia was maintained with a thermoblanket. Blood was transfused to maintain the hematocrit above 30% in order to maintain adequate oxygen delivery to the tissues.

Operative technique

The technique of allograft hepatectomy involved both rapid perfusion and modified rapid perfusion[1-3]. Rapid perfusion technique is as follows. Briefly, both the terminal aorta and the inferior mesenteric vein were dissected to insert aortic and portal perfusion cannulae. The supraceliac abdominal aorta was encircled and crossclamped. Following cardiectomy, dissection of liver hilum was performed in a bloodless field[4,5]. Following identification of whether or not an aberrant right hepatic artery (HA) originating from superior mesenteric artery (SMA) in the retropancreatic portion, the right side of the SMA was dissected toward the aorta. A Carrel patch of aorta was excised, with care not to injure the origin of the renal arteries. This has been our preferred method of hepatectomy in unstable donors, or in cases of extreme urgency when the recipient is in fulminant liver failure due to fulminant hepatitis or graft nonfunction following OLTx. Modified rapid perfusion technique differs from the rapid perfusion technique in that dissection of the liver hilum occurs prior to crossclamping of the aorta and cannulation of the distal splenic vein with a larger caliber catheter for a quicker portal perfusion. This preliminary dissection allows more selective and rapid cooling of the liver than does the rapid perfusion technique. These additional preparatory steps required 30-45 min. This technique has been our choice for stable donors and for donors whose livers are of a questionable quality. During the preparatory dissection, changes in the color or consistency of the allograft were observed in response to diuresis, or better oxygenation.

Technique of vascular reconstruction for arterial anomalies

Arterial reconstruction of the liver graft is required prior to transplantation and is very pivotal if a common arterial channel is absent due to an anomaly. The most common arterial anomaly requiring reconstruction was the aberrant right HA arising from the SMA, for which an end-to-end anastomosis was performed between the distal donor splenic artery and the proximal aberrant right HA. This was achieved with a Carrel patch of the SMA, obviating a small caliber anastomosis[6]. Care was taken to avoid an inadvertent anastomosis with rotation. The continuous suture technique with 8-0 monofilament polypropylene (Prolene) was used for the reconstruction. Just before the sutures were tied, the reconstructed HA was allowed to distend by pulsatile infusion of cold solution. With the application of "growth factor" principle to the *ex vivo* condition, this method facilitated migration of Prolene sutures into the anastomosis and allowed secure anastomosis without leakage or stricture.

Classification of early graft function

Early graft function was divided into four grades as good, fair, poor and PGN. Good meant AST<1 500 IU/L, ALT <1 000 IU/L and fresh frozen plasma (FFP) was not necessary. Fair meant AST 1 500-3 500 IU/L, ALT 1 000-2 500 IU/L and FFP was not required. Poor meant AST> 3 500 IU/L, ALT>2 500 IU/L and FFP was required. PGN was defined as the inability of graft to sustain the metabolic homeostasis of the recipient during the first postoperative week, presenting with the clinical manifestations of grade III or IV coma, coagulopathy with prothrombin time over 20 s, high ALT and AST values, renal failure, and progressive or persistent hyperbilirubinemia, resulting in retransplantation of the graft or death of the recipient.

Statistical analysis

Student's *t* and χ^2 tests were used for the statistical evaluation of the data.

RESULTS

Vascular anomalies

Table 2 lists the incidence of hepatic arterial anomalies and various methods of arterial reconstruction. Hepatic arterial anomalies were present in 14 grafts (43.75%): the aberrant right HA in seven (21.88%), the aberrant left HA in five (15.63%), and both aberrant right and left hepatic arteries in two grafts (6.25%). Of these, eight grafts (57.14%) required vascular reconstruction at the back table in order to construct a common arterial channel, and one of the anastomoses constructed at the back table required the revision due to rotation.

Table 2 Vascular reconstruction for hepatic arterial anomalies

Anomaly	*n* (%)	Method of reconstruction (*n*)
Aberrant RHA	7 (21.88)	
From SMA	6	Donor SpA to aberrant RHA (4)
From aorta	1	Donor SpA to aberrant RHA (1)
Aberrant LHA	5 (15.63)	
From CA	3	
From aorta	2	Donor SpA to PHA (1)
Aberrant RHA and LHA	2 (6.25)	
RHA from SMA	1	Donor SpA to RHA (1)
LHA from CA	1	CA to distal SMA (1)
Total	14 (43.75)	

RHA: right hepatic artery; SMA: superior mesenteric artery; SpA: splenic artery; LHA: left hepatic artery; CA: celiac axis, PHA: proper hepatic artery.

Injury of hepatic artery

A total of four complications (6.25%) occurred during or after allograft hepatectomy due to aberrant HA: inadvertent transection of the aberrant right HA, once originating directly from the aorta and once from the left side of the SMA. The transected aberrant right hepatic arteries were reconstructed using end-to-end anastomosis with the donor splenic artery with interrupted 8-0 Prolene sutures. Overall, none of the complications affected the outcome of the liver or other organ recipients.

Early graft function

Table 3 lists the early graft function of the 32 allografts after OLTx. Graft function was good or fair in 25 out of 28 (89.3%) of the grafts without recipient problems, whereas as many as two out of four (50%) of the grafts with recipient problems during or immediately following OLTx exhibited poor or nonfunction ($P<0.005$; $\chi^2 = 12.96$). This was due to HA thrombosis and multi-organ failure and meanwhile HA thrombosis was caused not by HA anomaly during allograft procurement but by HA reconstruction. Table 4 shows the correlation between the donor or graft variables and the early graft function of the 28 grafts that survived the operation and did not develop the aforementioned recipient complications during or immediately following OLTx. A statistically significant difference was noticed in the duration of patient's stay in ICU, requirement of cardiopulmonary resuscitation and the presence of abnormal graft appearance ($P<0.05$).The donors of grafts with fair or poor function stayed in ICU longer than those with good function ($P<0.005$), and the grafts with abnormal appearance were associated with a higher incidence of fair or poor graft function in recipients ($P<0.05$; $\chi^2 = 6.21$). The donors of graft with poor or nonfunction were significantly older than those with good or fair function and there was no significant difference between good and fair groups. On the other hand, no definitive correlation with early graft function was observed in sex, results of liver function tests, infusion of high-dose vasopressors and cold ischemia time.

Table 3 Early graft function after orthotopic liver transplantation

Early graft function	Number of recipient problems		Total (%)
	No (%)	Yes[1] (%)	
Good	21 (75)	1 (25)	22 (68.75)
Fair	4 (14.29)	1 (25)	5 (14.29)
Poor	2 (7.14)	1 (25)	3 (9.38)
PGN	1 (3.57)	1 (25)	2 (6.25)
Total	28 (100)	4 (100)	32 (100)

[1]Including hepatic artery thrombosis in one patient, intraoperative incidence from severe hemorrhage in two patients, and multi-organ failure in one patient.

Table 4 Correlation between donor or graft variables and early graft function

Variable	Good (n = 21)	Fair (n = 4)	Poor (n = 2)	PGN (n = 1)
Age (yr)	35.6±12.9	43.5±13.8	54.1±4.3	63
Sex (M:F)	15:6	2:2	2:0	1:0
AST(IU/L)	76.4±23.6	63.3±37.1	89.2±42.1	151
ALT(IU/L)	43.2±26.1	69.8±34.9	68.1±31.2	78.1
T. Bil (μmol/L)	12.5±3.4	14.5±7.4	11.8±7.9	20.5
PT(s)	15.2±1.4	14.8±1.2	14.2±1.6	15.5
CPR	4 (19.0%)	2 (50%)		
ICU stay (d)	3.5±2.4	6.2±3.3	7.4±2.1	12
High dose vasopressors	8 (38.1%)	2 (50%)	1 (50%)	0
Abnormal graft appearance	4 (19.0%)	1 (25%)	2 (100%)	1 (100%)
CIT (min)	379±128	421±183	389±214	402±103

CIT: cold ischemia time; T. Bil: total bilirubin; CPR: cardiopulmonary resuscitation.

Recipient survival

Of the 32 patients who received liver allografts, 27 patients recovered and remained alive and well after first liver transplantation, four patients needed retransplantation and all were discharged. One patient died of multi-organ failure in one month after transplantation due to primary graft nonfunction.

DISCUSSION

Early graft function is very closely associated with donor age, duration of patient's stay in ICU and the presence of abnormal graft appearance. The effect of increased donor age on the outcome of OLTx remains controversial[7,8]. Previously the upper limit of donor age was 50 years. As gradual accumulation of experience of clinical OLTx, now some transplant centers elevate the upper limit of donor age to 65 years. But we suggest that the donor age should be limited to below 60 years, or allograft dysfunction or non-function would easily appear and increase mortality[9]. When the appearance of the liver has changes in color, blunt edge and anomalous nodulae, it is necessary for frozen pathological examination before transplantation. Steatosis is the most important cause of PGN. The comparatively simple differentiating method is that white four-by being put into the container will turn into pale yellowish after several minutes and this will suggest that the degree of fat infiltrating liver tissue will be over 30%, however, pathological examination to evaluate the degree of fatty infiltration is the most reliable method. As to the hemodynamic stability of the donor, hypotension or the requirement of high-dose dopamine has been associated with nonfunction or delayed function, respectively. Although no obvious harmful effects of cardiopulmonary resuscitation on the early function of the liver allograft were demonstrated in this study, suboptimal perfusion of the liver and warm ischemic injury were strongly suggested. As to the abnormal appearance of the graft, little is known about the correlation between gross appearance and quality of the graft. Livers from donors with diabetes insipidus, who have been on vasopressin for a prolonged period of time, are often firm and suggest the presence of ischemic injury and liver allograft will be harder to touch. Since the use of vasopressin has been associated with a marked reduction in the blood flow to the

liver, donors scheduled for liver procurement should stop vasopressin as soon as possible in order to minimize ischemic damage. Overhydration can distend the liver by an increase in central venous pressure and give a false impression as to the consistency of the liver. If the liver is distended from overhydration, the administration of intravenous diuretics can be used immediately.

As far as now, there have been two methods for procurement of liver allografts including aortic perfusion only (APO)[10] and aortic and portal perfusion (APP). Due to shortage of donors, most American transplantation centers adopt multi-organ procurement, which means APO is the sole choice. The experience of Pittsburgh is that APO has no harm to allograft liver and its advantage is simple surgical procedure compared with APP[11], meanwhile, superior mesenteric vein need not be exposed and therefore it reduces the separation and division of tissue. If RHA originates from superior mesenteric artery, the unexposition of superior mesenteric vein might avoid injuring aberrant right hepatic artery and ischemic injury of splenic organ due to arterial spasm by surgical procedure[12-14].

The aberrant hepatic artery is very common; the aberrant rate was as high as 43.75% in our group. The right hepatic artery originating from SMA is the most common[15]. In order to avoid injuring hepatic artery, it is very important to decide by touch whether or not there are pulses behind hepatoduodenal ligament before the abdominal aorta is clamped in the process of procurement of allograft liver. Even if there is no pulse, it could not exclude aberrant right hepatic artery. So routinary division of the right side of SMA can often protect aberrant right hepatic artery before dissection of hepatoduodenal ligament. Once there exist the injuries of aberrant hepatic arteries, several aspects should be noticed in the process of the reconstruction of hepatic arteries as follows: (1) the inner membrane of hepatic artery should not be dragged; (2) it is achieved with Carrel patch of the SMA to obviate a small caliber anastomosis; (3) whether the continuous suture will be used depends on operator's mastering of the technique of vascular anastomosis; (4) just before the sutures were tied, the reconstructed HA was allowed to distend by pulsatile infusion of cold solution while the distal HA was occluded digitally and such method can identify whether the reconstructed anastomosis has leakage and stricture, or thrombosis of HA will occur which could cause biliary tract complication[16-19].

Although division of third hepatic hilum caused severe bleeding for two recipients in our group, this would not affect the early function of allograft liver. Hepatic artery thrombosis and multi-organ failure in earlier stage after transplantation caused poor and non-function for another two patients. Pittsburgh Transplant Center adopts the anastomosis between hepatic artery at the level of gastroduodenal artery in recipient and hepatic artery in donor, hepatic artery thrombosis in earlier stage after transplantation is associated with the technique of anastomosis. The simple differentiating method is to observe the pulse of hepatic artery after anastomosis, Doppler for hepatic artery the first day after liver transplantation is the optimal for finding thrombosis as soon as possible. Multi-organ failure often accompanies the instability of systemic hemodynamics and the liver is much easier to be affected by ischemic-reperfusion injury, while the injury of the liver also worsens the multi-organ failure and this pernicious recycle can cause patients to die.

For the assessment of allograft viability in clinical OLTx, there is, to date, no practical and simple technique available that is discriminately predictive of allograft function before the actual transplant procedure. Primary graft non-function remains a major cause of mortality, and although the shortage of donor organs remains a major limiting factor in clinical liver transplantation[20], still we should have a careful attitude toward the choice of liver allograft and take into serious account several predictive factors. If so, better therapeutic effect will be achieved.

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