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ORIGINAL ARTICLE

Adult-to-adult living donor liver transplantation for acute liver failure in China

Ding Yuan, Fei Liu, Yong-Gang Wei, Bo Li, Lv-Nan Yan, Tian-Fu Wen, Ji-Chun Zhao, Yong Zeng, Ke-Fei Chen

Ding Yuan, Fei Liu, Yong-Gang Wei, Bo Li, Lv-Nan Yan, Tian-Fu Wen, Ji-Chun Zhao, Ke-Fei Chen, Department of Liver and Vascular Surgery and Liver Transplantation Center of West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China
Yong Zeng, Department of Hepatopancreatobiliary Surgery of West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China
Author contributions: Yuan D and Liu F contributed equally to this work; Yuan D, Liu F and Wei YG designed the research; Li B, Yan LN, Wen TF, Zhao JC and Zeng Y performed the operations; Yuan D, Liu F, Wei YG and Chen KF took part in the operations; Yuan D and Liu F collected the data and performed the analysis; Yuan D, Liu F and Wei YG wrote the paper.
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Correspondence to: Bo Li, MD, Department of Liver and Vascular Surgery and Liver Transplantation Center of West China Hospital, Sichuan University, NO. 37, Guoxue Street, Chengdu 610041, Sichuan Province, China. cdlibo688@163.com
Telephone: +86-28-85422476 Fax: +86-28-85423724
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Abstract

AIM: To investigate the long-term outcome of recipients and donors of adult-to-adult living-donor liver transplantation (AALDLT) for acute liver failure (ALF).

METHODS: Between January 2005 and March 2010, 170 living donor liver transplantations were performed at West China Hospital of Sichuan University. All living liver donor was voluntary and provided informed consent. Twenty ALF patients underwent AALDLT for rapid deterioration of liver function. ALF was defined based on the criteria of the American Association for the Study of Liver Diseases, including evidence of coagulation abnormality [international normalized ratio (INR) $\geqslant$ 1.5] and degree of mental alteration without pre-existing cirrhosis and with an illness of < 26 wk duration. We reviewed the clinical indications, operative procedure and prognosis of AALDTL performed on patients with ALF and corresponding living donors. The potential factors of recipient with ALF and corresponding donor outcome were respectively investigated using multivariate analysis. Survival rates after operation were analyzed using the Kaplan-Meier method. Receiver operator characteristic (ROC) curve analysis was undertaken to identify the threshold of potential risk factors.

RESULTS: The causes of ALF were hepatitis B (n = 18), drug-induced (n = 1) and indeterminate (n = 1). The score of the model for end-stage liver disease was 37.1 ± 8.6, and the waiting duration of recipients was 5 ± 4 d. The graft types included right lobe (n = 17) and dual graft (n = 3). The mean graft weight was 623.3 ± 111.3 g, which corresponded to graft-to-recipient weight ratio of 0.95% ± 0.14%. The segment Ⅴor Ⅷ hepatic vein was reconstructed in 11 right-lobe grafts. The 1-year and 3-year recipient's survival and graft survival rates were 65% (13 of 20). Postoperative results of total bilirubin, INR and creatinine showed obvious improvements in the survived patients. However, the creatinine level of the deaths was increased postoperatively and became more aggravated compared with the level of the survived recipients. Multivariate analysis showed that waiting duration was independently correlated with increased mortality (P = 0.014). Furthermore, ROC curve revealed the cut-off value of waiting time was 5 d (P = 0.011, area under the curve = 0.791) for determining the mortality. The short-term creatinine level with different recipient's waiting duration was described. The recipients with waiting duration $\geqslant$ 5 d showed the worse renal function and higher mortality than those with waiting duration < 5 d (66.7% *vs* 9.1%, P = 0.017). In addition, all donors had no residual morbidity. Furthermore, univariate analysis did not show that short assessment time induced the high morbidity (P = 0.573).

CONCLUSION: Timely AALDLT for patients with ALF greatly improves the recipient survival. However, further systemic review is needed to investigate the optimal treatment strategy for ALF.

Key words: Acute liver failure; Adult-to-adult liver donor liver transplantation; Recipient; Donor; Risk factors

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INTRODUCTION

Acute liver failure (ALF) is a condition in which rapid deterioration of liver function results in hepatic encephalopathy and coagulopathy in individuals without pre-existing cirrhosis[1]. Because ALF progresses rapidly and recovers poorly, the emergency liver transplantation is recommended to treat ALF which has a high likelihood of death[1]. However, because the shortage of donor organ and the long waiting time for a suitable graft, the patients might deteriorate further and eventually die while waiting. Living donor liver transplantation (LDLT) is an effective option for this dilemma, which may reduce waiting time and provide more optimal timing for surgery and shorter cold ischemia time.

Adult-to-adult LDLT (AALDLT) for ALF has recently been reported, mostly in Asians[2-4], although it possibly increases the donor's risk because of large-sized graft removed and an evaluation of donor in an urgent scenario. In addition, an optimal graft might not be obtained because of a short assessment time for donors. The recent reports have described the optimal survival rate of recipients and the minimum rate of morbidity of the donors[2-6]. However, a small sample could not support AALDLT as a better solution for patients with ALF. Thus, the continued development of AALDLT treatment is necessary to determine treatment option for patients with ALF.

ALF caused by hepatitis B virus (HBV) infection has a lower spontaneous recovery rate than that induced by drugs[7]. In China, the most frequent cause of ALF is HBV, thus emergency AALDLT will be particularly significant for these patients with a high mortality and limited deceased organs. In this study, we reported the long-term outcome of recipients and donors of emergency AALDLT for ALF performed in our center.

MATERIALS AND METHODS

Patients

Between January 2005 and March 2010, 170 LDLTs were performed at West China Hospital of Sichuan University. Twenty ALF patients underwent AALDLT for rapid deterioration of liver function. ALF was defined based on the criteria of the American Association for the Study of Liver Diseases (AASLD)[1], including evidence of coagulation abnormality [international normalized ratio (INR) $\geqslant$ 1.5] and any degree of mental alteration without pre-existing cirrhosis and with an illness of < 26 wk duration. Patients with underlying chronic diseases such as chronic hepatitis B and autoimmune hepatitis were included if their disease has only been recognized for < 26 wk. Patients with cirrhosis identified by histologic examination of the liver explants were excluded. Informed consent was obtained from the patients and their families.

Donor evaluation

The primary selection criteria for a living liver donor were: being voluntary and providing informed consent which clearly stated that living liver donation can lead to donor risk. Each donation was approved by the Ethics Committee of West China Hospital of Sichuan University. The first essentiality of donor medical evaluation included ABO blood type identity or compatibility and age < 65 or > 18 years. Donors with known medical disorder that significantly increased a perioperative risk or contraindicated donation were excluded. Liver biochemistry, hepatitis serological tests, and complete blood cell count, coagulation test, cardio-pulmonary function tests to exclude chronic liver disease or potential contraindication were routinely performed in donors. Computed tomography (CT) scan for volumetric size measurement was performed to evaluate graft size and the size of the future remnant donor liver. The donors' remnant liver volume should be greater than 30% of the total liver volume (TLV) by CT volumetry. Dual graft liver transplantation with two left hemiliver or a combination of a right hemiliver and left hemiliver was adopted when the suitability of single graft transplant was in doubt in view of donor safety [remnant liver volume (RLV) < 30% of TLV] or small-for-size graft for recipients [graft volume to recipient standard liver volume (GV/SLV) ratio < 40%]. The donor assessment was usually completed within 24-48 h to shorten the waiting time of recipients.

For minimizing the risks and complications of definitive donors, the typical preoperative invasive diagnostic procedures, including hepatic angiography, liver biopsy, and cholangiography, were abolished and the following managements were adopted: (1) hepatic angiography was substituted with CT arteriography to study the tracks and variations of the hepatic artery, but hepatic angiography will further be performed if hepatic artery was not visualized; (2) preoperative endoscopic retrograde

choledochopancreatography was routinely substituted by magnetic resonance cholangiopancreatography and intraoperative cholangiography[8].

Donor and recipient operations

The donor and recipient operation was performed according to the previously published technique[8]. Intraoperative liver biopsy was routinely performed to exclude donors with severe hepatic steatosis. We emphasized the following practices, including identifying hepatic incision line with intraoperative ultrasonography, hepatectomy using an ultrasonic dissector without inflow occlusion, identifying biliary duct anatomy by intraoperative cholangiography and leaving middle hepatic vein (MHV) in the donor side. Recipients' great saphenous vein or cryopreserved vessels were anastomosed between the crassitude tributaries of the graft MHV (> 5 mm in diameter) and inferior vena cava to avoid graft (segment V and Ⅷ) congestion and to provide sufficient functioning liver mass. Weight and volume of the grafts were respectively measured using the balance and water replacement method in the back table, and graft-to-recipient weight ratio (GRWR) and GV/SLV ratio were calculated. In addition, the rate of donor RLV was calculated as follows: [(TLV - GV)/TLV] × 100%.

Postoperative treatment and follow-up

Each donor and recipient were routinely cared in the intensive care unit of liver transplantation after operation, and transferred to the regular ward when their conditions became stable. Liver biochemical tests, blood routine examination, hepatic vascular status and remnant liver volume regeneration were monitored during hospital stay and follow-up. The Clavien classification system for liver transplantation was used to respectively define postoperative recipient[9] and donor complications[10]. Standard immunosuppression regimen is triads of ciclosporin or tacrolimus, mycophenolate mofetil and prednisone. Lamivudine was given orally to recipients with hepatitis B once the decision to perform liver transplantation was made, and was continued throughout and after the operation. Hepatitis B immunoglobulin was used for the prevention of hepatitis B relapse. Discharge donors and recipients were regularly followed up with an endpoint of September 30, 2010.

Statistical analysis

Data were expressed as mean and standard deviations or as median and range depending on the distribution. Continuous variables of two groups were compared by the Student *t* test or the Mann-Whitney test as appropriate. Survival rates after operation were analyzed using the Kaplan-Meier method. Multivariate Cox regression further analyzed the independently related factors of mortality. Receiver operator characteristic (ROC) curve analysis was undertaken to identify the threshold of potential risk factors. Statistical significance was defined as $P < 0.05$. All statistical analysis were performed using SPSS for Windows 13.0.

Table 1 The characteristics of recipients with acute liver failure

Parameters	Recipients (n = 20)
Preoperative	
Age (yr)	39.5 ± 7.3
Gender (male/female)	17/3
BMI (kg/m^2)	23.4 ± 3.4
SLV (cm^3)	1339.7 ± 147.5
Etiologies (n)	
Hepatitis B	18
Drug induced	1
Indeterminate	1
MELD scores	37.1 ± 8.6
Total bilirubin (μmol/L)	456.1 ± 207.3
Creatinine (μmol/L)	136.7 ± 102.1
INR	4.18 ± 3.42
Hepatorenal syndrome (n)	4
Waiting duration (d)	5 ± 4
Intraoperative	
Graft volume (cm^3)	618.3 ± 111.0
Graft weight(g)	623.3 ± 111.3
GV/SLV	46.2% ± 7.2%
GRWR	0.95% ± 0.14%
Graft type (n)	
Right lobe	17
Dual graft	3
Cold ischemia time (min)	131 ± 24
Anhepatic phase time (min)	95.3 ± 24.9
Operation time (h)	11.5 ± 3.1
Blood loss (mL)	2700 (1000-7000)
Postoperative	
Hospital stay (d)	33.7 ± 18.5
Death in hospital (n)	7
Follow-up (d)	425 (1-1654)

BMI: Body mass index; GRWR: Graft-to-recipient weight ratio; GV/SLV: Graft volume to recipient standard liver volume; MELD: Model for end-stage liver disease; INR: International normalized ratio.

RESULTS

Recipient characteristics

Patients included 17 men and 3 women, with mean age of 39.5 ± 7.3 years (range, 29-63 years). The causes of ALF were hepatitis B (n = 18, including 10 patients with acute hepatitis B and 8 patients with acute-on-chronic hepatitis B), drug-induced (n = 1) and indeterminate (n = 1). The parameters of the recipients are summarized in Table 1. The average score of the model for end-stage liver disease (MELD) was 37.1 ± 8.6, ranging from 24 to 55. Hepatorenal syndrome was present in four patients, but none required preoperative hemodialysis. Three patients received dual grafts transplantation with right hemiliver and left hemiliver, and their accumulated grafts weight was 800 g, 754 g and 680 g, respectively. The overall graft weight was 623.3 ± 111.3 g (range, 400-850 g) and the graft volume was 618.3 ± 111.0 cm^3 (range, 400-870 cm^3) , which corresponded to the GRWR of 0.95% ± 0.14% (range, 0.75%-1.31%) and GV/SLV of 46.2% ± 7.2% (range, 37%-68%). The segment V or Ⅷ hepatic vein, which was 8.5 ± 2.5 mm (range, 5-13 mm), were reconstructed in 11 right-lobe grafts. The methods

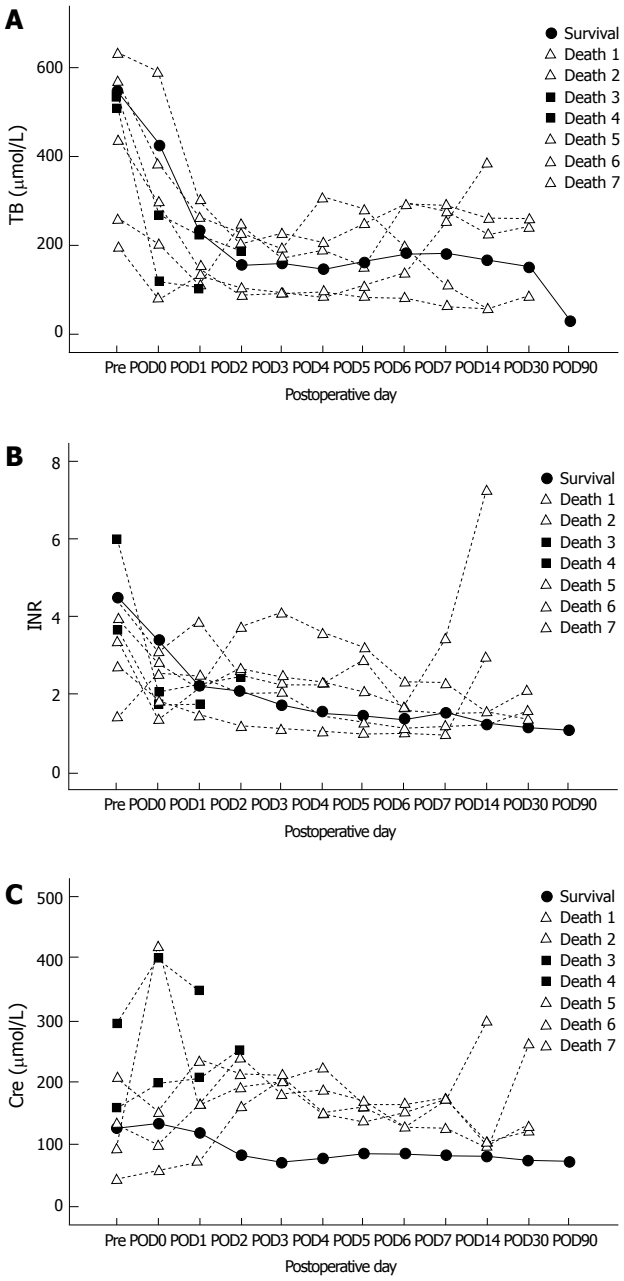

Figure 1 Hepatic and renal function change of all recipients with acute liver failure. The solid line displays the mean of values level in survived recipients (n = 17). The dashed line displays the values level of seven dead recipients. The triangles show the dead recipients with survival time > 7 d, and the black boxs show the dead recipients with survival time < 2 d. A: Total bilirubin(TB) tendency; B: INR: International normalized ratio tendency; C: Creatinine (Cre) tendency.

of biliary reconstruction included duct-to-duct manner without T-tube (n = 17) and with T-tube (n = 1), Roux-en-Y anastomosis (n = 1) and combined duct-to-duct and Roux-en-Y anstomosis (n = 1).

Recipient outcomes

The respiratory tube was extubated at median postoperative 10 h (range, 5-95 h) in all patients. Hospital stay was 33.7 ± 18.5 d (range, 1-84 d) and seven recipients died in hospital. Postoperative liver and renal function

Table 2 Classification of common complications of the recipients

Clavien grade	Complications	*n*
Grade Ⅰ (n = 2)	Pleural effusion (mild)	1
	Anastomotic stoma stenosis of right hepatic vein without treatment	1
Grade Ⅱ (n = 10)		
Ⅱa	Pleural effusion (server) using pleurocentesis	1
	Transfusion 4 foreign blood units and pleural effusion (mild)	2
	A persistent elevated prothrombin time > 20 over 3 d	1
	Transient increase in creatinine levels (> twice the pretransplantation level) for one month	1
Ⅱb	Bile duct stricture corrected by endoscopic therapy, and pulmonary infection	1
	Hepatic artery thrombus requiring surgery, and bile leakage requiring endoscopic procedure	1
	Postoperative bleeding requiring laparotomy	1
Grade Ⅲ (n = 0)	None	0
Grade Ⅳ (n = 7)	Renal failure and/or hepatic function failure	5
	Pulmonary infection	1
	Abdominal infection from bile leakage	1
Total		17

are shown in Figure 1. Postoperative results of total bilirubin, INR and creatinine showed obvious improvement in survived patients. However, the creatinine level of dead cases was increased postoperatively and was more aggravated than the level of survived recipients.

A total of 17 (85%) recipients suffered from different grades of complications (Table 2). One biliary anastomotic stricture occurred, which was successfully treated by an endoscopic procedure. One patient required surgical revision for hepatic artery thrombosis and endoscopic procedure for bile leakage. One case required laparotomy for intraperitoneal hemorrhage. Seven recipients (35%) died in hospital, and the others were still alive. The 1-year and 3-year recipient survival and graft survival rates were 65%. One patient died from the acute rejection after one month. One case developed severe pulmonary mixed infection (*Burkholderia cepacia*, and *Acinetobacter baumanii*/*Acinetobacter haemolytius*) and died three weeks later. Two patients died from severe pulmonary infection (*Pseudomonas aeruginosa* and *Klebsiella pneumonia*) after one month. One case required surgical procedure for bile leakage on POD14, but died of abdominal infection on the second postoperative day 5. Two patients died from the continuing severe hepatic function failure on POD1 and POD2.

The patient 1-year and 3-year survival rates were 65%, and 13 patients were still alive (Figure 2). No significant related factors for a recipient mortality were observed using univariate analysis, including MELD scores, preoperative total bilirubin, pre-creatinine, pre-INR, GV/SLV and reconstruction of segment hepatic vein outflow as shown in Table 3 (all $P > 0.05$). And the similar operative liver and renal functions were observed in group with and without segment hepatic vein outflow (all $P > 0.05$). However, gender (P = 0.037), the longer duration of waiting (P = 0.014) and higher creatinine level on POD1 (P = 0.021) were associated with the mortality. Furthermore,

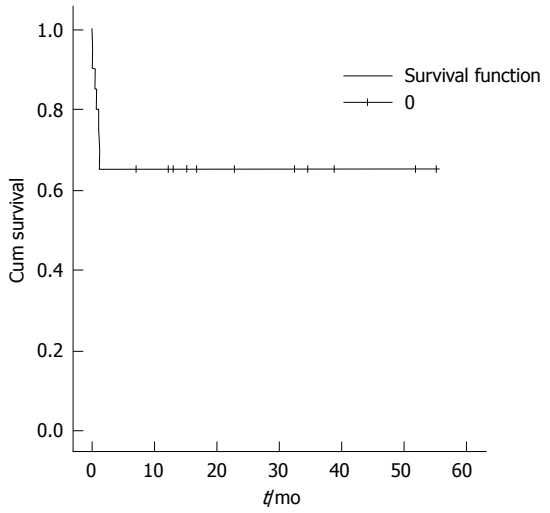

Figure 2 Survival curve of patients with acute liver failure. The patient 1-year and 3-year survival rates in the present study were 65%.

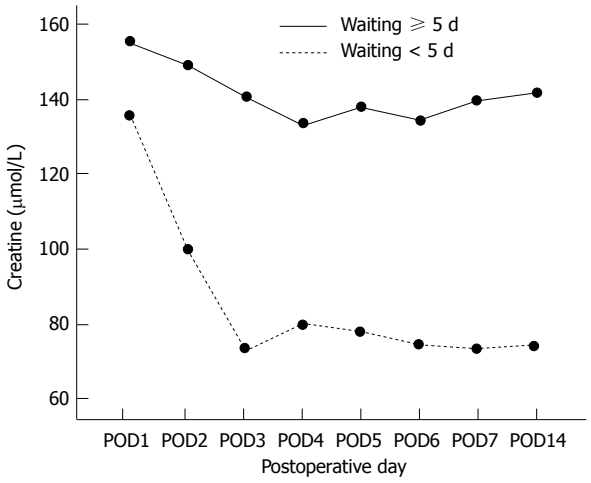

Figure 3 Short-term creatinine level change with different recipient waiting time. The recipients with waiting time ⩾ 5 d (the solid line) showed a higher creatinine level than those with waiting time < 5 d (the dashed line).

multivariate analysis showed that waiting time was only independently correlated with the increased mortality (P = 0.016), but the clinical significance was likely not accepted because of a low odds ratio (OR = 1.19, 95%CI = 1.033-1.385). Furthermore, ROC curve revealed the cut-off value of waiting time was 5 d (P = 0.011, area under the curve = 0.791) for determining the mortality. The short-term creatinine levels and recipient's waiting duration are shown in Figure 3. We found that recipients with waiting duration ⩾ 5 d showed the worse renal function and higher mortality than with waiting duration < 5 d (66.7% *vs* 9.1%, P = 0.017).

Donor results

The mean age of the 23 living donors was 37.7 ± 10.2 years (range, 19-58 years). The preoperative parameters of donors are shown in Table 3. The mean donor assessment was 2.1 ± 1.3 d (range, 1-5 d). The assessment time was more than 3 d in five donors, including 3 d (n = 2), 4 d (n = 1) and 5 d (n = 2). The assessment time was prolonged because some excluded potential donors resulted in re-evaluating another donor, whose causes included viral hepatitis, blood type incompatibility, obesity or graft size mismatch. Five donors with mild steatosis were observed by biopsy and their macrosteatosis was less than 30% (maximum 25%), and three of the five cases developed mild hepatic function impairment and recovered within one week. The RLV/TLV was 56.6% ± 12.1% (range, 26%-79%). It was less than 30% in only one case, but the total bilirubin (60-90.8 μmo/L) was high within postoperative three days.

Table 3 Univariate analysis of the mortality in the acute liver failure cases

Variables	*P* value	Variables	*P* value
Gender	0.037	Outflow reconstruction	0.924
Age	0.442	Urine volume	0.291
BMI	0.914	Blood loss	0.608
Child-Pugh scoring	0.963	Operation duration	0.536
MELD scoring	0.727	Re-warm ischemia	0.394
MELD scoring grade (> 30)	0.306	Pre_TB	0.878
Waiting duration	0.014	Pre_Cre	0.563
GV/SLV	0.396	Pre_INR	0.670
GW/BW	0.385	POD1_TB	0.622
Anhepatic phase	0.620	POD1_Cre	0.021
Cold ischemia	0.767	POD1_INR	0.930

GV/SLV: Graft volume to recipient standard liver volume; GW/BW: Graft weight to recipient body weight; MELD: Model for end-stage liver disease; BMI: Body mass index; Pre: Preoperative; POD1: One of postoperative day one; TB: Total bilirubin; INR: International normalized ratio.

The complications of donors are shown in Table 4. There was no death and grade Ⅳ morbidity. Surgical morbidity was found in 11 patients (47.8%) in this series. However, the major complication only occurred in one donor, which was severe pleural effusion with pleurocentesis and classified as grade Ⅲa. Pleural effusion was the most frequent morbidity for living donor, and occurred in 8 cases (34.8%). Four donors developed mild hepatic function impairment, but spontaneously recovered within one week. One case with pulmonary infection had hyperbilirubinemia more than 3 wk, and the hepatic function was recovered with Transmetil treatment. The mean hospital stay was 13.4 ± 3.5 d (range, 6-22 d).The similar morbidity and postoperative hepatic function were found between donors with short (< 3 d) and with long (⩾ 3 d) assessment time (all P > 0.1).With a median follow-up of 29 mo, all donors had no residual morbidity and resumed normal preoperative activities with normal liver function. Furthermore, univariate analysis did not show that short assessment time induced the high morbidity (P = 0.573) and the correlation between RLV/TLV and the morbidity (P = 0.268).

DISCUSSION

Initially LDLT for ALF was only performed in children.

Table 4 The characteristics of living donors

Parameters	Donors (n = 23)
Preoperative	
Age (yr)	37.7 ± 10.2
Gender (male/female)	8/15
BMI (kg/m^2)	23.8 ± 3.5
Relationship with recipient (n)	
Siblings	12
Daughter	4
Wives	5
Father	1
Uncle	1
Assessment time (d)	2.1 ± 1.3
Intraoperative	
Graft steatosis (normal/mild)	18/5
Graft type (right lobe/left lobe)	20/3
RLV/TLV (%)	56.5 ± 12.1
Operation time (h)	6.9 ± 1.4
Blood lost (mL)	665.2 ± 480.9
Postoperative	
Hospital stay (d)	13.4 ± 3.5
Peak of TB (μmol/L)	53.4 ± 22.7
Peak of INR	1.71 ± 0.36
Complications (n)	11
Grade Ⅰ (n = 7)	
Pleural effusion (mild)	4
Hepatic function impairment (mild)	2
Hepatic cut-section local fluid collection	1
Grade Ⅱ (n = 3)	
Pleural effusion (moderate) leading to partial compression atelectasis and hepatic function impairment (mild)	1
Pleural effusion (moderate) and pericardial effusion	1
Pulmonary infection undergone antibiotic therapy and hepatic function impairment (moderate)	1
Grade Ⅲa (n = 1)	
Pleural effusion (server) using pleurocentesis	1

Hepatic function impairment: Mild, hyperbilirubinemia (TB being 51-85 μmol/L for more than 3 d or 34-51 μmol/L on POD7) and/or PT prolongation (6-8 s for more than 3 d or 4-6 s on POD7); Moderate, hyperbilirubinemia (TB > 85 μmol/L for more than 3 d or exceeding 51 μmol/L on POD7) and/or PT prolongation (> 8 s for more than 3 d or exceeding 6 s on POD7). BMI: Body mass index; RLV: Remanet live volume; TLV: Total liver volume; TB: Total bilirubin; INR: International normalized ratio; PT: Prothrombin time.

Since the first report of successful AALDLT using right-lobe graft for adult ALF patients by Lo *et al*[11], AALDLT has been gradually accepted as an alternative treatment for adult ALF patients. Most cases came from Asian countries[2-4,6], whereas a few cases were reported from Western countries[5]. Experiences of AALDLT in ALF are summarized in Table 5[2-6,12-17]. The mean waiting time was mostly less than five days and 1-year survival rate (> 70%) was satisfactory in the recipients. Zero mortality and low morbidity (< 40%) were achieved in all donors. Thus, it is rational to conclude that AALDLT is a safe treatment for patients with ALF.

This study demonstrated that AALDLT was an efficient treatment for patients with ALF. Patients who survived postoperatively (n = 13, 65%) were still alive at the postoperative 1-year and 3-year. This result was worse than those reported in literature (> 70%), the possible explanations include worse preoperative patient condition, increased waiting time, inadequate venous draining resulting from right-lobe graft without MHV.

The MELD score was used to allocate cadaveric liver grafts among patients with end-stage liver disease[18], and was also considered to be a useful indicator of LDLT in ALF patients[19-21]. Several authors suggested that MELD scores greater than 25 should be considered as a relative contraindication for transplantation because of the poor outcomes[22]. Yantorno *et al*[20] advocated the MELD score cut-off value for determining whether a transplantation was indicated should be 30. In our series, the mean MELD was 37.1 ± 8.6, which was higher than that reported from all other centers (Table 5). The mortality of recipients with MELD > 30 (7 of 15, 46.7%) was higher than those with MELD ≤ 30 (0 of 5), but not statistically significant (P = 0.306). The increased MELD score may account for an increased mortality (65%) in our reports. However, Matsui *et al*[13] considered that MELD score has little clinical significance for ALF patients who received plasma exchange.

In the present study, multivariate analysis identified waiting duration as the sole independent prognostic factor for 1-year mortality. The duration of waiting time for liver transplantation can significantly affect patient survival, especially for patients with ALF[2,6,23]. Prolonged waiting time means increased risk of severe complications, including deterioration of hepatic or/ and renal function, intracranial bleedings or sepsis[6,24], which contributed to increased mortality in our series. The mean waiting time in this study was slightly longer than that in other centers (5 d *vs* 3.7 d). Recipients with waiting duration ≥ 5 d correlated with worse outcome. This was possibly due to the following causes, such as delayed donor evaluation or/and the hesitancy for LDLT from the patient's family. This result was possibly of defective clinical significance because of the low odds ratio of waiting duration (OR = 1.19) for a recipient mortality and the small sample size of our study. However, this data showed that timely LDLT for ALF patients greatly improved the recipient survival.

On one hand, the graft volume is positively correlated with the recipient outcome in LDLT[16,25,26]. To meet the demand of patients with ALF, a safety margin of a smaller graft was GV/SLV > 30%-35%[4,12,27]. Despite acceptable survival with GV/SLV < 30%[28] was reported, small graft should be avoided if possible[4,11]. Based on recent reports (Table 4), satisfactory survival resulted from right-lobe graft with a GV/SLV more than 30%. In this study, the mortality of recipients was not associated with GV/SLV because of the GV/SLV > 37%. On the other hand, right liver graft without middle hepatic vein may lead to venous congestion of right anterior segments[16,29-31]. The functional graft volume relies on a perfect outflow[32,33], thus it is necessary to reconstruct the crassitude hepatic vein outflow to avoid graft congestion. Our data can not provide evidence to answer whether a graft with or without MHV correlates to recipient mor-

Table 5 Adult-to-adult living donor liver transplantation for acute liver failure between 2000 and 2010

Study	Recipient									Donor complications			
	Cases	MELD	Waiting time (d)	Graft type			GV/SLV (%)	Mortality	Survival rate, *n* (%)	Cases	Minor	Major	Morbidity
				Right	Left	Dual							
Park *et al*[2]	40	36	2.5	35	0	6	ND	6	1 (85)	45	11	0	24.40%
Shi-Chun *et al*[3]	10	34.5 ± 2.1	3	10	0	0	56.7 (47.7-66.9)	2	2 (80)	10	4	0	40%
Ikegami *et al*[4,12]	44	24 ± 6	8 ± 6	12	32	10	22.8-56.8	10	1 (78.3); 3 (71.6)	44	15	0	34%
Campsen *et al*[5]	10	> 21	2.7	10	0	0	ND	3	1-5 (70)	10	5	0	50%
Matsui *et al*[13]	36 (4)[1]	22 ± 6	ND	18	16	0	46 (22-75)	4	1 (94); 5 (87)	36	1	1	5.60%
Rajekar *et al*[14]	15	32	ND		ND		ND	3	4 (80)	ND	ND	ND	ND
Lee *et al*[15]	57	32	2.4	33	9	15	27-81	10	1-5 (82)	72	ND	ND	ND
Liu *et al*[16]	32	36 ± 1.8	2.5	32	0	0	52 (33-87)	4	2 (88)	32	8	2	31.30%
Nishizaki *et al*[17]	15	ND	5	0	15	0	36.7 (23-54)	3	1 (80)	15	ND	ND	ND

[1]Four pediatric recipients were not clarified from 36 cases in this report. Major complications of donors were defined as the Clavine grade Ⅲ-Ⅳ. MELD: Model for end-stage liver disease; GV/SLV: Graft volume to recipient standard liver volume; ND: Not described. The latest report was as the summarized standard if multiple reports were from the same center and author.

tality because all grafts were without middle hepatic vein. However, comparable patient outcome was achieved in our series which warrants that the reconstruction of a crassitude hepatic vein outflow is necessary.

Some scholars concerned that the expedited donor assessment may incur poor donor outcome. However, there was no mortality or reoperation among donors in our series. Although 34.8% of donors suffered from complications, all improved spontaneously or with conservative management except one pleural effusion with pleurocentesis. This morbidity was slightly higher than that reported by other centers because of the variation of defining and reporting complications[34,35]. Postoperative complications of donors is usually underestimated even using the Clavien classification (1992 version)[13,36]. Thus, this morbidity in our center was acceptable using the new Clavien classification. In addition, our results also indicated that transitory assessment for donors had no negative effect on the donor outcome. Similarly, the small sample size in our study is still insufficient to determine a potential correlation between expedited donor assessment and donor outcome. In our experience, a rapid evaluation process did not bring any negative effect to donors.

In summary, this study demonstrated that AALDL should be performed as early as possible in patients with ALF for a satisfactory survival rate. There are few studies with a large sample size to support AALDLT as a better treatment for patients with ALF. Thus, a systemic review and continued development of AALDLT are important to determine treatment option for patients with ALF.

COMMENTS

Background

Acute liver failure (ALF) is a condition with rapid deterioration of liver function. Because ALF progresses rapidly and recovers poorly, the emergency liver transplantation is recommended as the effective treatment for ALF which has a high likelihood of death. Adult-to-adult living-donor liver transplantation (AALDLT) would help address the shortage of available organs for patients with ALF.

Research frontiers

AALDLT for ALF has recently been mostly reported in Asia and there were also cases reported in Western countries. The recent reports have described the optimal survival rate of recipients and the minimum rate of morbidity of the donor. However, a small sample could not support AALDLT as a better solution for patients with ALF. Thus, the continued development of AALDLT treatment is necessary to determine the treatment option for patients with ALF.

Innovations and breakthroughs

This study evaluated the outcome of recipients with ALF and living donor in detail. Based on the Clavien classification, the outcome of recipients and donors were first objectively evaluated. The authors indicated that the duration of waiting was an independent risk factor for a recipient's mortality. In addition, sample size is still small among studies of AALDLT for ALF in the world. Thus, this study presented some experience for further system reviews.

Applications

This study indicated that patients with ALF should receive AALDL as early as possible for satisfactory survival rate. And the model for end-stage liver disease score may not be related to the outcome of recipient's outcome.

Terminology

ALF is a condition in which rapid deterioration of liver function results in altered mentality and coagulopathy in individuals without preexisting cirrhosis.

Peer review

The manuscript provided information about LTx for ALF in China. This is a very interesting analysis of a series of 20 patients who underwent LDLT for ALF. From the "west-countries" point of view, these series are important as we may consider increasing our rate of LDLT for several etiologies, including ALF.

REFERENCES

1 **Polson J**, Lee WM. AASLD position paper: the management of acute liver failure. *Hepatology* 2005; **41**: 1179-1197

2 **Park SJ**, Lim YS, Hwang S, Heo NY, Lee HC, Suh DJ, Yu E, Lee SG. Emergency adult-to-adult living-donor liver transplantation for acute liver failure in a hepatitis B virus endemic area. *Hepatology* 2010; **51**: 903-911

3 **Shi-Chun L**, Meng-Long W, Ning L, Wei L, Ping C, Jin-Ning L, Jun D, Zhen Z, Ju-Shan W, Dong-Dong L, Qing-Liang G, Yue Z. Emergent right lobe adult-to-adult living-donor liver transplantation for high model for end-stage liver disease score severe hepatitis. *Transpl Int* 2010; **23**: 23-30

4 **Ikegami T**, Taketomi A, Soejima Y, Yoshizumi T, Sanefuji K, Kayashima H, Shimada M, Maehara Y. Living donor liver transplantation for acute liver failure: a 10-year experience in a single center. *J Am Coll Surg* 2008; **206**: 412-418

5 **Campsen J**, Blei AT, Emond JC, Everhart JE, Freise CE, Lok AS, Saab S, Wisniewski KA, Trotter JF. Outcomes of living donor liver transplantation for acute liver failure: the adult-to-adult living donor liver transplantation cohort study. *Liver Transpl* 2008; **14**: 1273-1280

6 **Liu CL**, Fan ST, Lo CM, Wei WI, Yong BH, Lai CL, Wong J.

Live-donor liver transplantation for acute-on-chronic hepatitis B liver failure. *Transplantation* 2003; **76**: 1174-1179
7 **Ostapowicz G**, Fontana RJ, Schiødt FV, Larson A, Davern TJ, Han SH, McCashland TM, Shakil AO, Hay JE, Hynan L, Crippin JS, Blei AT, Samuel G, Reisch J, Lee WM. Results of a prospective study of acute liver failure at 17 tertiary care centers in the United States. *Ann Intern Med* 2002; **137**: 947-954
8 **Yan LN**, Li B, Zeng Y, Wen TF, Wang WT, Yang JY, Xu MQ, Chen ZY, Zhao JC, Ma YK, Wu H. Analysis of fifty adult to adult living donor liver transplantation. *Sichuan Daxue Xuebao Yixueban* 2007; **38**: 513-517
9 **Clavien PA**, Camargo CA, Croxford R, Langer B, Levy GA, Greig PD. Definition and classification of negative outcomes in solid organ transplantation. Application in liver transplantation. *Ann Surg* 1994; **220**: 109-120
10 **Dindo D**, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205-213
11 **Lo CM**, Fan ST, Liu CL, Wei WI, Lo RJ, Lai CL, Chan JK, Ng IO, Fung A, Wong J. Adult-to-adult living donor liver transplantation using extended right lobe grafts. *Ann Surg* 1997; **226**: 261-269; discussion 269-270
12 **Ikegami T**, Taketomi A, Soejima Y, Maehara Y. Feasibility of adult-to-adult living donor liver transplantation for acute liver failure. *Liver Transpl* 2009; **15**: 117-118
13 **Matsui Y**, Sugawara Y, Yamashiki N, Kaneko J, Tamura S, Togashi J, Makuuchi M, Kokudo N. Living donor liver transplantation for fulminant hepatic failure. *Hepatol Res* 2008; **38**: 987-996
14 **Rajekar H**, Wai CT, Majeed TA, Lee KH, Wong SY, Leong SO, Singh R, Tay KH, Soosaynathan C, Tan KC. Prognostic factors in patients with acute liver failure undergoing live donor liver transplantation. *Transplant Proc* 2008; **40**: 2492-2493
15 **Lee SG**, Ahn CS, Kim KH. Which types of graft to use in patients with acute liver failure? (A) Auxiliary liver transplant (B) Living donor liver transplantation (C) The whole liver. (B) I prefer living donor liver transplantation. *J Hepatol* 2007; **46**: 574-578
16 **Liu CL**, Fan ST, Lo CM, Yong BH, Fung AS, Wong J. Right-lobe live donor liver transplantation improves survival of patients with acute liver failure. *Br J Surg* 2002; **89**: 317-322
17 **Nishizaki T**, Hiroshige S, Ikegami T, Uchiyama H, Hashimoto K, Soejima Y, Shimada M. Living-donor liver transplantation for fulminant hepatic failure in adult patients with a left-lobe graft. *Surgery* 2002; **131**: S182-S189
18 **Habib S**, Berk B, Chang CC, Demetris AJ, Fontes P, Dvorchik I, Eghtesad B, Marcos A, Shakil AO. MELD and prediction of post-liver transplantation survival. *Liver Transpl* 2006; **12**: 440-447
19 **Kremers WK**, van IJperen M, Kim WR, Freeman RB, Harper AM, Kamath PS, Wiesner RH. MELD score as a predictor of pretransplant and posttransplant survival in OPTN/UNOS status 1 patients. *Hepatology* 2004; **39**: 764-769
20 **Yantorno SE**, Kremers WK, Ruf AE, Trentadue JJ, Podestá LG, Villamil FG. MELD is superior to King's college and Clichy's criteria to assess prognosis in fulminant hepatic failure. *Liver Transpl* 2007; **13**: 822-828
21 **Dhiman RK**, Jain S, Maheshwari U, Bhalla A, Sharma N, Ahluwalia J, Duseja A, Chawla Y. Early indicators of prognosis in fulminant hepatic failure: an assessment of the Model for End-Stage Liver Disease (MELD) and King's College Hospital criteria. *Liver Transpl* 2007; **13**: 814-821
22 **Yu JW**, Wang GQ, Zhao YH, Sun LJ, Wang SQ, Li SC. The MELD scoring system for predicting prognosis in patients with severe hepatitis after plasma exchange treatment. *Hepatobiliary Pancreat Dis Int* 2007; **6**: 492-496
23 **Everhart JE**, Lombardero M, Detre KM, Zetterman RK, Wiesner RH, Lake JR, Hoofnagle JH. Increased waiting time for liver transplantation results in higher mortality. *Transplantation* 1997; **64**: 1300-1306
24 **Testa G**, Malagó M, Nadalin S, Hertl M, Lang H, Frilling A, Broelsch CE. Right-liver living donor transplantation for decompensated end-stage liver disease. *Liver Transpl* 2002; **8**: 340-346
25 **Zhang F**, Wang XH, Li XC, Kong LB, Sun BC, Li GQ, Qian XF, Cheng F, Lu S, Lü L. Adult living donor liver transplantation using right lobe for severe hepatitis in emergency: a report of 9 cases. *Zhonghua Waike Zazhi* 2007; **45**: 1019-1022
26 **Soejima Y**, Taketomi A, Yoshizumi T, Uchiyama H, Harada N, Ijichi H, Yonemura Y, Shimada M, Maehara Y. Feasibility of left lobe living donor liver transplantation between adults: an 8-year, single-center experience of 107 cases. *Am J Transplant* 2006; **6**: 1004-1011
27 **Cho JY**, Suh KS, Kwon CH, Yi NJ, Lee HH, Park JW, Lee KW, Joh JW, Lee SK, Lee KU. Outcome of donors with a remnant liver volume of less than 35% after right hepatectomy. *Liver Transpl* 2006; **12**: 201-206
28 **Lo CM**, Fan ST, Chan JK, Wei W, Lo RJ, Lai CL. Minimum graft volume for successful adult-to-adult living donor liver transplantation for fulminant hepatic failure. *Transplantation* 1996; **62**: 696-698
29 **Hwang HJ**, Kim KW, Jeong WK, Kim SY, Song GW, Hwang S, Lee SG. Hepatic outflow obstruction at middle hepatic vein tributaries or inferior right hepatic veins after living donor liver transplantation with modified right lobe graft: comparison of CT and Doppler ultrasound. *AJR Am J Roentgenol* 2009; **193**: 745-751
30 **Fan ST**, Lo CM, Liu CL, Wang WX, Wong J. Safety and necessity of including the middle hepatic vein in the right lobe graft in adult-to-adult live donor liver transplantation. *Ann Surg* 2003; **238**: 137-148
31 **Sugawara Y**, Makuuchi M, Takayama T, Imamura H, Kaneko J, Ohkubo T. Safe donor hepatectomy for living related liver transplantation. *Liver Transpl* 2002; **8**: 58-62
32 **Konishi N**, Ishizaki Y, Sugo H, Yoshimoto J, Miwa K, Kawasaki S. Impact of a left-lobe graft without modulation of portal flow in adult-to-adult living donor liver transplantation. *Am J Transplant* 2008; **8**: 170-174
33 **Radtke A**, Nadalin S, Sotiropoulos GC, Molmenti EP, Schroeder T, Valentin-Gamazo C, Lang H, Bockhorn M, Peitgen HO, Broelsch CE, Malagó M. Computer-assisted operative planning in adult living donor liver transplantation: a new way to resolve the dilemma of the middle hepatic vein. *World J Surg* 2007; **31**: 175-185
34 **Umeshita K**, Fujiwara K, Kiyosawa K, Makuuchi M, Satomi S, Sugimachi K, Tanaka K, Monden M. Operative morbidity of living liver donors in Japan. *Lancet* 2003; **362**: 687-690
35 **Grewal HP**, Thistlewaite JR, Loss GE, Fisher JS, Cronin DC, Siegel CT, Newell KA, Bruce DS, Woodle ES, Brady L, Kelly S, Boone P, Oswald K, Millis JM. Complications in 100 living-liver donors. *Ann Surg* 1998; **228**: 214-219
36 **Broering DC**, Wilms C, Bok P, Fischer L, Mueller L, Hillert C, Lenk C, Kim JS, Sterneck M, Schulz KH, Krupski G, Nierhaus A, Ameis D, Burdelski M, Rogiers X. Evolution of donor morbidity in living related liver transplantation: a single-center analysis of 165 cases. *Ann Surg* 2004; **240**: 1013-1024; discussions 1024-1026

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