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Factors affecting survival after living-related liver transplantation

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Abstract The purpose of this study was to determine the perioperative factors that influence patient and graft outcome in living-related liver transplantation (LRLT). Between April 1995 and October 1998, we performed a series of 46 LRLT procedures, including 11 adult cased, at our institute. Mean age and weight of the recipients were 12.0 ± 2.3 years and 23.7 ± 2.6 kg, respectively. Seven out of the 46 patients had renal failure and received hemodialysis therapy before and after LRLT or kidney transplantation. The recipients were divided into two groups: those who survived for 7–48 months after LRLT (group 1, $n = 36$), and those who died within 4 months after surgery (group 2, $n = 10$). Factors analyzed included recipient age and weight, graft/recipient body weight ratio (G/R ratio), emergent vs elective surgery, United Network for Organ Sharing (UNOS) status, presence of preoperative plasmapheresis (PEX) and renal failure, and so on. Recipients in group 1 compared with group 2 had less advanced liver disease (i.e., a lower rate of emergent surgery, 14% vs 50%, and fewer patients with UNOS status 1, 14% versus 70%; $P < 0.05$ and $P < 0.001$, respectively). Group 1 recipients also had a lower percentage of preoperative treatment with plasmapheresis (22% vs 70%, $P < 0.01$). However, neither the G/R ratio nor the presence of renal failure affected the patient survival rate. In conclusion, factors independently associated with reduced patient survival after LRLT include emergent surgery, Child-Pugh class, UNOS status 1, and preoperative plasmapheresis.

Key words Living-related liver transplantation · Outcome · Risk factors

Introduction

Living-related liver transplantation (LRLT) has become a well-recognized treatment modality for patients with end-stage liver disease. Refinement of the surgical techniques and improved postoperative management in the treatment of rejection and complications have contributed to improving the success rate of the procedure [1–3]. The purpose of this study was to analyze, retrospectively, donor and recipient factors that influence patient and graft outcome after LRLT.

Patients and methods

Between April 1995 and October 1998 46 LRLTs were performed on 46 recipients (35 children and 11 adults) at Tokyo Women's Medical University Hospital after approval was obtained from the hospital ethics committee. The age of the recipients ranged from 6 months to 53 years (mean 12.0 ± 2.3 years) and weight from 6 to 59 kg (mean 23.7 ± 2.6 kg). The donor age ranged from 23 to 57 years (mean 37.0 ± 1.2 years) and weight from 42 to 90 kg (mean 59.5 ± 1.6 kg). The minimum follow-up was 7 months. The 46 recipients included 22 with biliary atresia, 9 with fulminant hepatitis, 4 with primary biliary cirrhosis, 2 with oxalosis, 2 with cryptogenic hepatitis, 2 with primary sclerosing cholangitis, and 1 each with hepatoblastoma, extrahepatic phlebosclerosis, hepatic fibro-

Table 1 Profiles of recipients and indications for living-related liver transplantation (LRLT)

	Group 1	Group 2	*P* value
No. of patients	36	10	
No. of adults (%)	8 (22)	3 (30)	NS
Sex (M : F)	20 : 16	5 : 5	NS
Age (years) (± SE; range)	10.6 ± 2.5 (0.5–51)	17.1 ± 5.9 (0.6–53)	NS
Body weight (kg) (± SE; range)	22.1 ± 2.9 (5.9–55)	29.6 ± 5.8 (6.7–59)	NS
No. of ABO incompatible transplantations	2	1	NS
Indications[a]			
Biliary atresia (%)	18 (50)	4 (40)	
Fulminant hepatitis (%)	5 (14)	4 (40)	
Biliary cirrhosis (%)	4 (11)	1 (10)	
Others (%)	9 (25)	1 (10)	

[a] No formal statistical analysis was performed because the number of patients was too small

Table 2 Demographic and preoperative laboratory features of the patients in each group (*aPTT* activated partial thromboplastin time, *PT* prothrombin time)

	Group 1	Group 2	*P* value
UNOS status (%)			< 0.001
1	5 (14)	7 (70)	
2	28 (78)	3 (30)	
3 or 4	3 (8)	0 (0)	
Child-Pugh classification (%)			< 0.05
A	10 (28)	1 (10)	
B	19 (53)	3 (30)	
C	7 (19)	6 (60)	
Renal failure (%)	6 (17)	1 (10)	NS
Plasmapheresis (%)	8 (22)	7(70)	< 0.01
Ammonia (μg/dl)	125 ± 13	157 ± 18	< 0.05
PT (s) (range)	16.4 ± 0.8	18.1 ± 2.1	NS
aPTT (s) (range)	45.3 ± 2.6	49.8 ± 7.1	NS
Platelets (~ 10^4/μl) (range)	11.1 ± 1.3	7.9 ± 2.1	NS
Fibrinogen (g/dl) (range)	191 ± 14.2	188 ± 28.2	NS

Table 3 Surgical data

	Group 1	Group 2	*P* value
Emergency (%)	5 (14)	5 (50)	< 0.05
Graft weight (g)	284 ± 15	276 ± 32	NS
Graft/recipient Body weight ratio (%)	2.13 ± 0.24	1.39 ± 0.32	NS
Surgical duration (h)	12.6 ± 3.2	11.2 ± 1.6	NS
Blood loss (g)	1576 ± 339	4271 ± 2344	NS

sis, secondary biliary cirrhosis due to a choledochal cyst, and Caroli's disease. Candidates for LRLT were assigned according to their medical condition to one of the following United Network for Organ Sharing (UNOS) categories: status 1, in intensive care unit with expected survival of less than 7 days; status 2, continuously hospitalized; status 3, at home, but requiring continuous medical care; and status 4, at home and relatively functional [4]. Seven out of the 46 patients had renal failure and received hemodialysis therapy before and after LRLT or kidney transplantation. LRLT was performed on the basis of the recipientís body weight and the estimated graft size. Ten of the 11 adult recipients, in contrast to 3 of the 35 children, received a left lobe graft. Of the 46 patients, 10 died within 4 months after LRLT (range 4 days–4 months). All recipients were divided into two groups: those who survived between 7 and 49 months after LRLT (group 1, $n = 36$), and those who died within 4 months after surgery (group 2, $n = 10$).

Factors analyzed included recipient age and weight, graft/recipient body weight ratio (G/R ratio), emergent vs elective surgery, UNOS status [4], Child-Pugh classification [5, 6], preoperative ammonia level, presence of preoperative plasmapheresis (PEX), renal failure, and features of the surgery.

Continuous variables are expressed as mean ± SEM. The Mann-Whitney nonparametric test was used to test for differences in factors between the two groups. Dichotomous variables were analyzed using the chi-square test for independence and, when applicable, Fisher's exact probability test. Factors that differed between the two groups in univariate tests ($P < 0.05$) were considered in a multiple logistic regression model. The STATISTICA package for Macintosh (StatSoft, Tulsa, OK) was used to perform the logistic regression analysis.

Table 4 Cause of death and original disease (*BA* biliary atresia)

Cause of death	Original disease
Fungal sepsis	BA (child)
Cerebral hemorrhage	BA (child)
Aplastic anemia, fungal sepsis	Fulminant hepatitis (child)
Sepsis	BA (child)
Sepsis	Fulminant hepatitis (adult)
Portal thrombus	BA (child)
Abdominal bleeding	Secondary sclerosing cholangitis (adult)
Recurrence of hepatitis	Fulminant hepatitis (child)
Sepsis	Cryptogenic hepatitis (child)
Sepsis	Fulminant hepatitis (adult)

Table 5 Factors affecting survival after LRLT

Variable	Univariate analysis (*P* value)	Logistic regression (*P* value)
UNOS status	< 0.001	< 0.001
Child-Pugh classification	< 0.05	< 0.05
Plasmapheresis	< 0.01	< 0.01
Ammonia level	< 0.05	NS
Emergent surgery	< 0.05	< 0.05

Results

The profiles of the recipients and indications for LRLT in each group are summarized in Table 1. There was no significant difference in the age and body weight between groups 1 and 2. An equal distribution of adult and child recipients and of male and female recipients was noted in both groups. The disease severity, as defined by the UNOS status and Child-Pugh classification at the time of LRLT, was less advanced in group 1 compared with group 2 ($P < 0.001$ and $P < 0.05$, respectively) (Table 2). No difference was noted in the incidence of renal failure which required renal support between the two groups (17% in group 1 versus 10% in group 2, NS). However, a lower frequency of preoperative plasmapheresis was noted in group 1 (22% vs 70% in group 2, $P < 0.01$). The blood ammonia level immediately before LRLT was significantly lower in group 1 than in group 2 ($P < 0.05$). Table 3 summarizes the features of surgery. A significant difference was noted in the distribution of emergent LRLT in the two groups (14% in group 1 vs 50% in group 2, $P < 0.05$). No significant difference was noted in the graft weight, G/R ratio, surgical duration or blood loss, although an adult recipient who received the smallest graft for G/R ratio died after the surgery. Table 4 shows the causes of death. Infectious complications, including fungal infection and generalized sepsis, were responsible for 60% of the deaths. Univariate analysis in this study showed the following five factors to be significantly associated with mortality after LRLT: UNOS status, Child-Pugh classification, requirement for preoperative plasmapheresis, ammonia level, and emergent surgery. When a logistic regression analysis was performed, UNOS status, Child-Pugh classification, preoperative plasmapheresis, and emergent surgery remained independently associated with mortality after LRLT (Table 5).

Discussion

It is well-known that survival after cadaveric liver transplantation depends on many pre- and posttransplant conditions [7–9]. To our knowledge, however, no multivariate analysis of these factors has been reported up to now in LRLT. In this study, four independent significant pretransplant predictors of survival after LRLT could be identified. The severity of liver disease, as assessed by UNOS status and the Child-Pugh classification, was significantly greater in the group 2 patients who died within 4 months after LRLT, implying that disease severity is a factor predictive of mortality after LRLT, as well as after cadaveric liver transplantation. In addition, the requirement for preoperative plasmapheresis, which also reflects the preoperative status of the patients, was a significant factor affecting the short-term outcome of LRLT. Furthermore, the proportion of emergent LRLT was significantly higher in group 2. These results emphasize that the preoperative condition of the patient plays a crucial role in the outcome after LRLT. On the other hand, no significant difference was noted in the graft weight, G/R ratio, surgical duration, and blood loss, although an adult patient who received the smallest graft for G/R ratio (0.42) died after the surgery.

In our series, patients who needed renal support did not have a significantly higher mortality rate, in contrast to a report on cadaveric liver transplantation by Baliga et al. [7]. Renal failure is one of the more frustrating complications in the LRLT recipient and is caused by acute tubular necrosis, hepatorenal syndrome, drug nephrotoxicity, or allergic interstitial nephritis [7, 8]. Although it has been accepted that renal dysfunction in advanced cirrhosis is associated with a poor post-transplant prognosis, appropriate and intensive renal sup-

port, including hemodialysis, continuous hemofiltration, or hemodiafiltration, may improve the prognosis.

Infectious complications as a cause of significant morbidity and mortality after cadaveric liver transplantation have been well-described [10]. Similar to these reports, mortality due to infectious complications, including bacterial sepsis in 4 and fungal infection in 2 patients, was high in our series (Table 4).

In conclusion, the preoperative condition – i.e., UNOS status, Child-Pugh classification, and an urgent situation such as the need for plasmapheresis – are the most influential factors in the outcome after LRLT. Further investigation is needed to refine the risk factors and devise strategies to decrease morbidity and mortality after LRLT.

References

1. Broelsch CE, Whitington PF, Emond JC, Heffron TG, Thistelethwaite JR, Stevens L, Piper J, Whitington SH, Lichter JL (1991) Liver transplantation in children from living related donors. Surgical techniques and results. Ann Surg 214: 428–439
2. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, Sawada H, Shirahase I, Kim HJ, Yamaoka Y, Ozawa K (1993) Surgical techniques and innovations in living related liver transplantation. Ann Surg 217: 82–91
3. Makuuchi M, Kawasaki S, Noguchi T, Hashikura Y, Matsunami H, Hayashi K, Harada H, Kakazu T, Takayama T, Kawarasaki H (1993) Donor hepatectomy for living related partial liver transplantation. Surgery 113: 395–402
4. Memsic L, Makowka L (1996) Donor selection and management. In: Busuttil RW, Klintmalm GB (eds) Liver transplantation. WB Saunders, Philadelphia, pp 386–391
5. Child CG, Turcotte JG (1964) Surgery and portal hypertension. In: Child CG (ed) The liver and portal hypertension. WB Saunders, Philadelphia, pp 1–85
6. Pugh RNH, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R (1973) Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60: 646–649
7. Baliga P, Merion RM, Turcotte JG, Ham JM, Henley KS, Lucey MR, Schork A, Shyr Y, Campbell DA (1992) Preoperative risk factor assessment in liver transplantation. Surgery 112: 704–711
8. McCauley J, Van Thiel DH, Starzl TE, Puschett JB (1990) Acute and chronic renal failure in liver transplantation. Nephron 55: 121–128
9. Clavien PA, Argemiro de Camargo C Jr, Croxford R, Langer B, Levy GA, Greig PD (1994) Definition and classification of negative outcomes in organ transplantation. Ann Surg 220: 109–120
10. Colonna JO, Winston DJ, Brill JE, Goldstein LI, Hoff MP, Hiatt JR, Quinones-Baldrich W, Ramming KP, Busuttil RW (1988) Infectious complications in liver transplantation. Arch Surg 123: 360–364