参考資料2

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Liver Transplantation, Vol 7, No 1 (January), 2001: pp 41-47

成人レシピエントで、小児（13歳未満）から(70例)と　19歳以上の成人から移植を受けた患者(1051例)の成績を比較した。肝動脈血栓症発症の率が、小児からの移植で12.9%と成人の3.8%より有意に高かった。特に、移植肝がレシピエント推定肝容積の40%未満の患者で発症率が高かった。よって、小児肝を成人に移植するにしても、40%以上が望ましい。

Safety and Risk of Using Pediatric Donor Livers in Adult Liver Transplantation

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Pediatric donor (PD) livers have been allocated to adult transplant recipients in certain situations despite size discrepancies. We compared data on adults (age ≥ 19 years) who underwent primary liver transplantation using livers from either PDs (age < 13 years; n = 70) or adult donors (ADs; age ≥ 19 years; n = 1,051). We also investigated the risk factors and effect of prolonged cholestasis on survival in the PD group. In an attempt to determine the minimal graft volume requirement, we divided the PD group into 2 subgroups based on the ratio of donor liver weight (DLW) to estimated recipient liver weight (ERLW) at 2 different cutoff values: less than 0.4 (n = 5) versus 0.4 or greater (n = 56) and less than 0.5 (n = 21) versus 0.5 or greater (n = 40). The incidence of hepatic artery thrombosis (HAT) was significantly greater in the PD group (12.9%) compared with the AD group (3.8%; $P = .0003$). Multivariate analysis showed that preoperative prothrombin time of 16 seconds or greater (relative risk, 3.206; $P = .0115$) and absence of FK506 use as a primary immunosuppressant (relative risk, 4.477; $P = .0078$) were independent risk factors affecting 1-year graft survival in the PD group. In the PD group, transplant recipients who developed cholestasis (total bilirubin level ≥ 5 mg/dL on postoperative day 7) had longer warm (WITs) and cold ischemic times (CITs). Transplant recipients with a DLW/ERLW less than 0.4 had a trend toward a greater incidence of HAT (40%; $P < .06$), septicemia (60%), and decreased 1- and 5-year graft survival rates (40% and 20%; $P = .08$ and .07 v DLW/ERLW of 0.4 or greater, respectively). In conclusion, the use of PD livers for adult recipients was associated with a greater risk for developing HAT. The outcome of small-for-size grafts is more likely to be adversely affected by longer WITs and CITs. The safe limit of graft volume appeared to be a DLW/ERLW of 0.4 or greater. (*Liver Transpl 2001;7:41-47.*)

Although pediatric donor (PD) livers are ideally used for pediatric recipients, they are occasionally allocated to adult recipients, e.g., when only a pediatric liver is available for a critically ill adult or when an adult patient is listed with the weight range for a PD. In these circumstances, it is important to know the risks of using a small-for-size liver in an adult.

The main risk with such grafts is that they will fail secondary to inadequate liver volume. Experience with living related liver transplantation (LT) in adults has shown that grafts as small as 25% to 30% of ideal liver volume can be tolerated.[1,2] However, Emond et al[3] reported early functional impairment with grafts less than 50% of the expected liver volume. In addition, Kiuchi et al[4] reported that small-for-size grafts (<1% of recipient body weight) were associated with lower graft survival, probably because of enhanced parenchymal cell injury and reduced metabolic and synthetic capacity. Thus, in living donor LT, it is now accepted that grafts must be greater than 0.8% of the recipient body weight (or >40% of expected liver volume).[5]

Similar data on small-for-size cadaveric liver grafts are not available. In this study, we reviewed our large experience with the transplantation of pediatric livers into adult recipients and attempted to identify risk factors for poor graft survival and determine minimal graft volume requirements.

Patients and Methods

Study Population and Design

Between September 1988 and March 1999, 1,121 adults (age ≥ 19 years) underwent primary LT using full-size (whole) allografts from either PDs (age < 13 years; n = 70) or adult donors (ADs; age ≥ 19 years; n = 1,051). Patients who received primary transplants from donors aged between 13 and 18 years were excluded from analysis.

Mean post-LT follow-up was 1,830 days (median, 1,738 days; range, 78 to 3,664 days) in the PD group and 1,591 days (median, 1,477 days; range, 5 to 3,840 days) in the AD group. Donor liver weight (DLW) was measured at the end of the back-table procedure. Based on data from the first thousand LTs performed at our institution, estimated recipient liver weight (ERLW) was calculated using a formula developed at our center[6]:

$$\text{ERLW (cubic centimeters)} = 6 \times \text{weight (lb)} + 4 \times \text{age (years)} + 350$$

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Presented in part at the 50th Annual Meeting of the American Association of the Study of Liver Disease, November 5-9, 1999, Dallas, TX.

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1527-6465/01/0701-0014$5.00/0

doi:10.1053/jlts.2001.20940

In this study, DLW/ERLW ratio was used as an indicator of graft size matching.

Part 1: Comparison of outcomes in PD and AD groups. We compared the following factors between groups: recipient and donor age and sex, DLW/ERLW ratio, indication for LT, United Network for Organ Sharing (UNOS) status, and preoperative values for total bilirubin (TBil), prothrombin time (PT), and creatinine. Surgical data analyzed included cold (CIT) and warm ischemic time (WIT), total operative time, bypass use, type of caval reconstruction, and use of packed red blood cells and fresh frozen plasma. CIT was defined as the period from donor cross-clamping to the start of anastomosis in the recipient, and WIT was defined as the period from the start of anastomosis to allograft reperfusion. One- and 5-year patient and graft survival were also compared between groups, as was the incidence of postoperative complications, including primary nonfunction (PNF), hepatic artery thrombosis (HAT), portal vein thrombosis, bile leak, intrahepatic and extrahepatic bile duct stricture, septicemia, acute rejection, and post-LT ascites.

Part 2: Univariate and multivariate analysis. Univariate and multivariate analyses were performed in the PD group to determine the independent risk factors that adversely affected 1- and 5-year patient and graft survival. Continuous variables were dichotomized at clinically established cutoff points and presented as categorical. Diagnoses at primary LT were categorized into acute or chronic for statistical convenience. Variables found to predict 1-year graft survival on univariate analysis were further entered into multivariate analysis.

Part 3: Risk factors for prolonged cholestasis. To identify factors that predict and/or increase the risk for prolonged cholestasis in adults who receive small-for-size cadaveric livers, we compared PD recipients with and without prolonged cholestasis (TBil ≥ 5.0 mg/dL on postoperative day [POD] 7). Eighteen patients were excluded because of either graft loss within 7 days or inadequate data. Of the 52 patients remaining, TBil level was less than 5.0 mg/dL in 41 patients and 5.0 mg/dL or greater in 11 patients. Recipient and donor age, UNOS status, DLW/ERLW, CIT, WIT, use of packed red blood cells and fresh frozen plasma, and 1- and 5-year patient and graft survival were compared between the subgroups.

Part 4. To clarify minimal liver volume requirements, PD patients were divided on the basis of 2 different DLW/ERLW cutoff values (<0.4 or ≥0.4 and <0.5 or ≥0.5). Nine patients were excluded for lack of data on either DLW (n = 4) or recipient body weight (RBW) (n = 5); 61 patients were included in the analysis, as follows: DLW/ERLW less than 0.4 (n = 5) versus 0.4 or greater (n = 56) and DLW/ERLW less than 0.5 (n = 21) versus 0.5 or greater (n = 40).

Postoperative complications, including the incidence of PNF, HAT, portal vein thrombosis, bile leak, septicemia, and acute rejection, were compared at each cutoff point, as were 1- and 5-year patient and graft survival. TBil, glutamic-oxaloacetic transaminase, and PT values for PODs 2, 7, and 14 were also compared between the groups.

Statistical Analysis

Survival analysis was performed using the Kaplan-Meier method, and the groups were compared by means of the log-rank test. Continuous variables were compared using a 2-tailed, unpaired *t*-test for independent samples. Categorical data were compared using chi-squared test. For survival analysis, continuous variables were dichotomized at a clinically relevant cutoff point. Variables found to impact significantly on 1-year graft survival were analyzed by multivariate analysis. Multivariate analysis was performed using stepwise forward and backward Cox proportional-hazards models. *P* less than .05 is considered significant. All statistical analyses were performed with the StatView7 4.5 software for Macintosh (Abacus Concepts Inc, Berkeley, CA).

Results

Part 1

Groups were similar in terms of recipient age, cause of liver disease, UNOS status, and pre-LT liver function test results. There was also no difference between groups in terms of WIT or total ischemic time, bypass use, arterial anastomosis technique, blood product use, and initial immunosuppression. Preoperative demographics and surgical data, including initial immunosuppressive therapy, are listed in Table 1.

One- and 5-year patient survival rates were 82.9% and 70.0% in the PD group and 82.5% and 73.2% in the AD group (*P* = not significant). One- and 5-year graft survival rates tended to be less in the PD group than the AD group (68.6% *v* 75.0% for 1-year survival; *P* = .17; 52.6% *v* 65.8% for 5-year survival; *P* = .051), but did not reach statistical significance (Fig. 1).

Table 2 lists the incidence of postoperative complications and length of hospital and intensive care unit stays. The rate of HAT was 12.9% in the PD group compared with 3.8% in the AD group (*P* = .0003).

Figure 2 shows the causes of graft loss in the 2 groups. Thirty-five grafts were lost in the PD group and 361 grafts were lost in the AD group. Overall, causes of graft loss were similar between the groups.

Part 2

On univariate analysis, diagnosis at primary LT (*P* = .01), UNOS status (*P* < .05), pre-LT PT (*P* = .005), creatinine level (*P* = .01), DLW/RBW (*P* = .01), and primary immunosuppressive therapy (*P* = .03) reached statistical significance regarding 1-year graft survival in PD recipients. These variables were further evaluated in forward and backward stepwise Cox regression models. Independent risk factors were a high pre-LT PT and not using FK506 as primary immunosuppressive therapy (Table 3).

Table 1. Preoperative Demographics

Variables	Group		*P*
	PD (n = 70)	AD (n = 1,051)	
Recipient variables			
Sex (% female)	78.6	39.8	<.0001
RBW (kg)	65.3 ± 14.3	75.6 ± 16.9	<.0001
ERLW (g)	1,346 ± 319	1,511 ± 319	<.0001
Donor variables			
Donor age (yr)	8.9 ± 2.1	45.3 ± 17.3	<.0001
Sex (% female)	35.7	41.3	NS
Donor body weight (kg)	33.4 ± 11.7	72.9 ± 15.4	<.0001
DLW (g)	865 ± 267	1,477 ± 308	<.0001
DLW/ERLW	0.69 ± 0.44	1.05 ± 0.50	<.0001
CIT (h)	10.9 ± 3.4	10.0 ± 3.3	.04
Piggyback (%)	51.4	4.6	<.0001
Bile duct reconstruction (%)			.0006
Duct-to-duct with T-tube	49.3	44.5	
Duct-to-duct without T-tube	24.0	42.7	
Roux-en-Y	26.7	12.8	
ICU stay (d)	10.0 ± 11.7	8.9 ± 13.4	NS
Hospital stay (d)	36.7 ± 33.9	35.5 ± 32.8	NS

NOTE. Values expressed as mean ± SD unless otherwise noted.
Abbreviations: ICU, intensive care unit; NS, not significant.

Part 3

Table 4 shows the effect of post-LT cholestasis on patient and graft survival. One- and 5-year patient and graft survival were significantly worse in patients with a TBil level ≥5.0 mg/dL on POD 7. In these patients, WIT and CIT were significantly longer than those in patients with TBil levels less than 5 mg/dL on POD 7 (57.2 ± 13.0 *v* 45.5 ± 9.0 minutes; 13.1 ± 4.3 *v* 10.5 ± 3.0 hours, respectively).

Part 4

Table 5 lists postoperative complication rates and 1- and 5-year patient and graft survival rates, with special reference to DLW/ERLW. There was no statistical difference in diagnosis, UNOS status, or surgical variables (data not shown). Patients with a DLW/ERLW less than 0.4 had a trend toward a greater rate of HAT (40% *v* 10.7%; $P < .06$) and septicemia (60% *v* 25.0%). Furthermore, 1- and 5-year graft survival rates in this

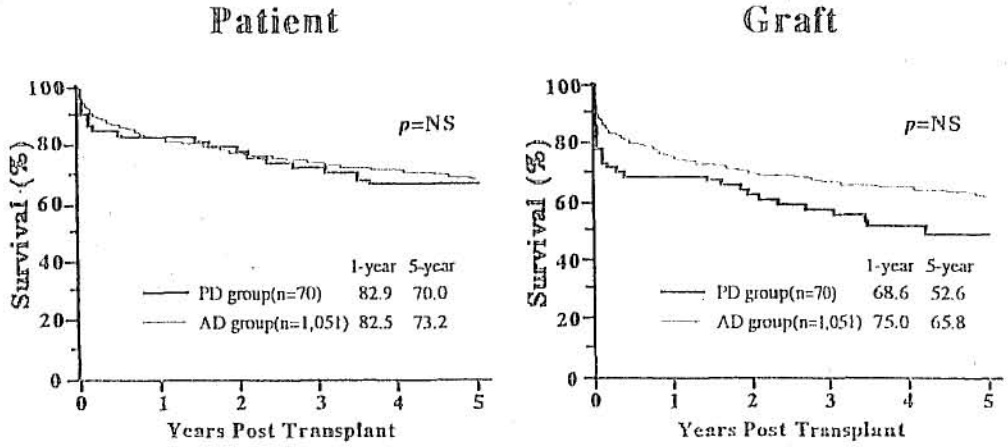

Figure 1. Comparison of patient and graft survival between the PD (n = 70) and AD groups (n = 1,051).