第3回　肝臓移植の基準等に関する作業班

議事次第

日時：平成22年12月24日（木）
15：00～17：00
場所：厚生労働省　専用第14会議室

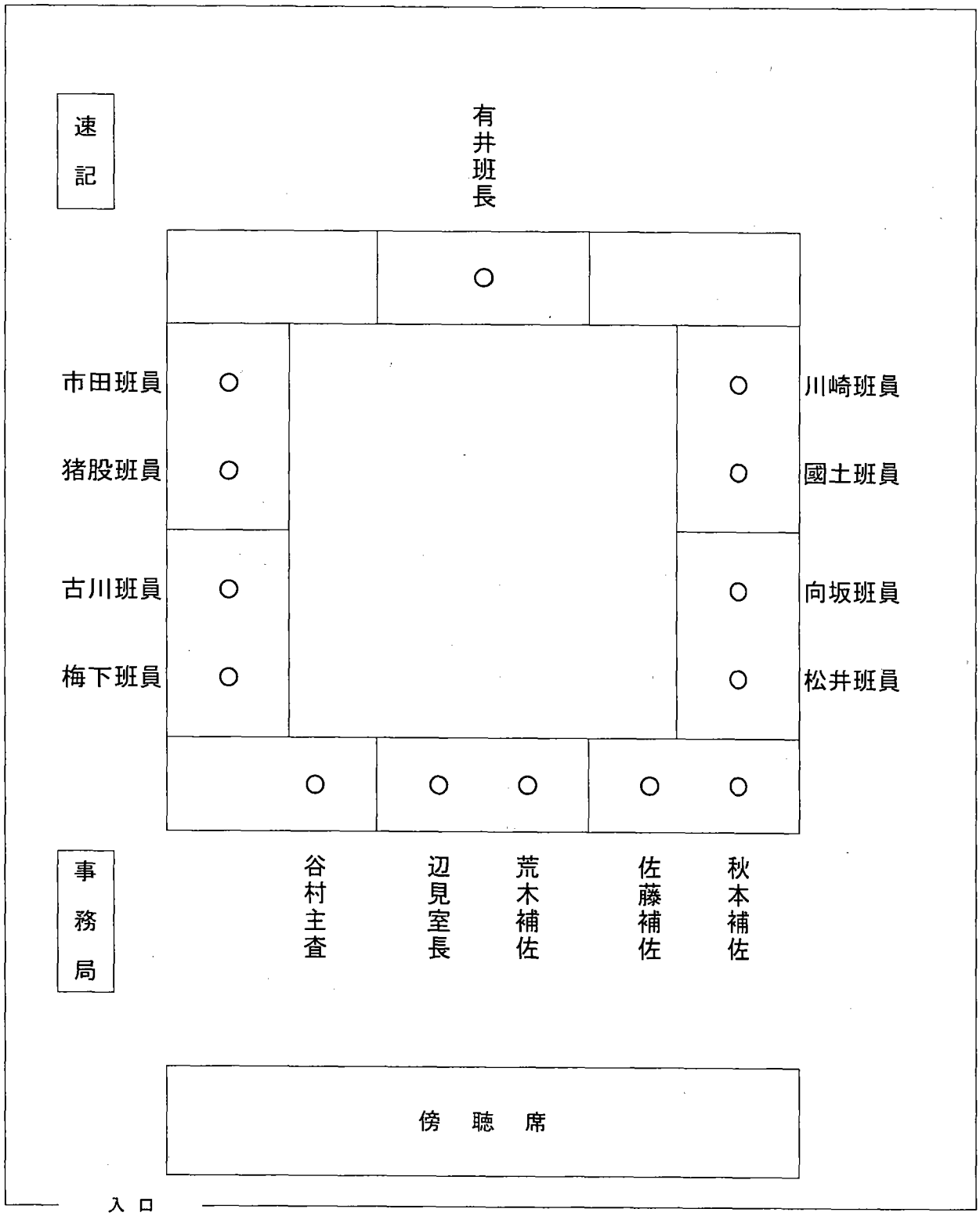
1．開　会
2．議　事
（1）　肝臓提供者（ドナー）適応基準について
（2）　レシピエント選択基準について
（3）　その他
3．閉　会

〈配布資料〉
資料1　　肝臓移植のドナー適応基準・レシピエント選択基準（案）
資料2　　小児ドナーから提供された肝臓の分配に関して

参考資料1　文献：Transplantation vol70(9) 1283-1291　（猪股班員提出）
参考資料2　文献：Liver Transplantation vol7(1) pp41-47（猪股班員提出）
参考資料3　文献：J Am Coll Surg vol208(5) 682-689
参考資料4　UNOS 小児ドナー分配システム（古川班員提出）
参考資料5　年齢別小児身長体重の幅と標準肝容積の幅（猪股班員提出）
参考資料6　肝臓移植希望者の転帰（古川班員提出）
参考資料7　法改正後提供事例一覧

第3回肝臓移植の基準等に関する作業班

日　時：平成22年12月24日（金）15：00～17：00
場　所：厚生労働省　専用第14会議室（12階）



資料１

肝臓移植のドナー適応基準・レシピエント選択基準の改正について（案）

1. ドナー適応基準の改正（別紙１）

慎重に適応を検討する対象として「ＨＢｃ抗体陽性」及び「先天性の代謝性肝疾患の保有の可能性がある者」を追加する。

また、重度の全身性疾患に関する項目を集約する。

2. レシピエント選択基準の改正（別紙２）

（１） 血液型の取り扱いについて

① 生後２４ヶ月未満の小児については血液型不適合の場合も一致･適合の場合と同等程度の生着率であり､臨床においても血液型不適合のための術前処置は不要とされていることに鑑み、移植を行う医学的緊急度の高い者に限り、レシピエント選択の対象とする。

② ①により対象となる者を含め､生後２４ヶ月未満の者については医学的緊急度９点とされている者は血液型の一致、適合、不適合にかかわらず、血液型の加点を１．５点とする。

【検討事項】

更に生後２４ヶ月以上の者であって､医学的緊急度が９点とされている者は一致、適合にかかわらず血液型の加点を１．５点とする

（２） 分割肝

分割肝にするか否かの判断については、現状通り、第１位候補のレシピエントに係る移植実施施設にゆだねることとし、今回はレシピエント選択基準に盛り込まないこととする。

（３） 肝臓小腸同時移植の位置づけ

肝小腸同時移植希望者が肝臓レシピエントリストで１位になった場合、小腸レシピエントリストでの順位にかかわらず、当該者に小腸を優先的に移植することとする。

一方、肝小腸同時移植希望者が小腸レシピエントリストで１位になったとしても肝臓を優先的に移植することにはしない。（この場合、肝臓は肝臓レシピエント１位の者に移植される。）

（４） 小児ドナーからの提供の場合のレシピエント選択

【資料２】

別紙１

＜肝臓＞臓器提供者（ドナー）適応基準（案）

１．以下の疾患又は状態を伴わないこととする。

（１）全身性の活動性感染症

（２）ＨＩＶ抗体、ＨＴＬＶ－１抗体、ＨＢｓ抗原などが陽性

（３）クロイツフェルト・ヤコブ病及びその疑い

（４）悪性腫瘍（原発性脳腫瘍及び治癒したと考えられるものを除く。）

２．以下の疾患又は状態を伴う場合は、慎重に適応を決定する。

（１）病理組織学的な肝臓の異常

（２）生化学的肝機能検査の異常

（３）１週間以内の腹部、消化管手術及び細菌感染を伴う腹部外傷

（４）胆道系手術の既往

~~（５）重度糖尿病~~

~~（６）過度の肥満~~

~~（７）重度の熱傷~~

（５）長期の低酸素状態

（６）高度の高血圧又は長期の低血圧

（７）ＨＣＶ抗体陽性

（８）ＨＢｃ抗体陽性

（９）先天性の代謝性肝疾患の保有の可能性がある者

（１０）重度糖尿病、過度の肥満、重症熱傷、その他の重度の全身性疾患

備考）摘出されたドナー肝については、移植前に肉眼的、組織学的に観察し、最終的に適応を検討することが望ましい(移植担当医の判断に委ねる)。

付記　上記の基準は適宜見直されること。

別紙２

肝臓移植希望者（レシピエント）選択基準（案）

１．適合条件

（１）ＡＢＯ式血液型

ＡＢＯ式血液型の一致（identical）だけでなく、適合（compatible）の待機者も候補者として考慮する。

ただし、移植時２歳（生後 24 ヶ月）未満の場合には医学的緊急性９点の場合に限り、不適合（imcompatible）の待機者も候補として考慮する。

（２）前感作抗体

当面、選択基準にしないが、必ず検査し、登録する。

（３）ＨＬＡ型

当面、選択基準にしないが、必ず検査し、登録する。

（４）搬送時間（虚血許容時間）

臓器提供者（ドナー）の肝臓を摘出してから１２時間以内に血流再開できることが望ましい。

２．優先順位

（１）医学的緊急性

予測余命が１ヶ月以内	９点
予測余命が１ヶ月～６ヶ月以内	６点
予測余命が６ヶ月～１年以内	３点
予測余命が１年を超えるもの	１点

ただし、先天性肝・胆道疾患及び先天性代謝異常症については、肝臓移植が治療的意義を持つ時期及び患者の日常生活に障害が発生している状態を考慮の上、上表に規定する点数のいずれかを用いることがある。

（２）ＡＢＯ式血液型

ＡＢＯ式血液型が一致	１．５点
ＡＢＯ式血液型が適合	１．０点

（案１）　ただし、選択時に２歳（生後 24 ヶ月）未満かつ医学的緊急性９点の待機者

は、血液型を問わず、１．５点を加点する。

（案２）

	年齢（選択時）	血液型	加点
医学的緊急性	２歳未満	問わない	1.5点
９点の者	２歳以上	一致・適合	1.5点
上記以外の者	全年齢	一致	1.5点
		適合	1.0点

３．具体的選択方法

適合条件に合致する移植希望者（レシピエント）が複数存在する場合には、優先順位は、以下の順に勘案して決定する。

（１）優先すべき親族を優先する。

（２）２．の（１）、（２）の合計点数が高い順とする。ただし、これらの条件が同一の移植希望者（レシピエント）が複数存在した場合は、待機期間の長い者を優先する。

（３）（１）又は（２）で選ばれた移植希望者（レシピエント）が肝腎同時移植の待機者である場合であって、かつ、臓器提供者（ドナー）から肝臓及び腎臓の提供があった場合には、当該待機者に優先的に肝臓及び腎臓を同時に配分する。なお、選ばれた肝腎同時移植の待機者が優先すべき親族でない場合であって、腎臓移植希望者（レシピエント）が優先すべき親族であるときは、当該腎臓移植希望者（レシピエント）が優先される。

（４）（３）により、肝腎同時移植希望者（レシピエント）が選定されたものの、肝臓が移植に適さないことが判明した場合には、腎臓移植希望者（レシピエント）選択基準で選ばれた腎臓移植希望者（レシピエント）に腎臓を配分する。

（５）（１）又は（２）で選ばれた移植希望者（レシピエント）が肝小腸同時移植の希望者である場合であって、かつ、臓器提供者（ドナー）から肝臓及び小腸の提供があった場合には当該待機者に優先的に肝臓及び小腸を同時に配分する。なお、選ばれた肝小腸同時移植の待機者が優先すべき親族でない場合であって、小腸移植希望者（レシピエント）が優先すべき親族であるときには、当該小腸移植希望者（レシピエント）が優先される。

（6）（5）により、肝小腸同時移植希望者（レシピエント）が選定されたものの、肝臓が移植に適さないことが判明した場合には、小腸移植希望者（レシピエント）選択基準で選ばれた小腸移植希望者（レシピエント）に小腸を配分する。

4．その他

ＡＢＯ式血液型の取扱いや優先順位の点数付け等、当基準全般については、今後の移植医療の定着及び移植実績の評価を踏まえ、適宜見直すこととする。

また、将来ネットワークが整備され、組織的にも機能的にも十分機能した場合は、改めてブロックを考慮した優先順位を検討することが必要である。

資料２

小児ドナーからの提供された肝臓の分配について（案）

１．改正案

・　18 歳未満のドナーからの提供があった場合には、移植時 18 歳未満のレシピエントに一定の加点を行うこととする。

・ 加点の点数は医学的緊急度に逆転を生じない程度とし、１点とする。

２．考え方

①　18 歳未満の小児レシピエントは 18 歳未満の小児から提供を受けた場合、大人から提供を受けた場合と比較して顕著に長期成績が良いことが示されている。（参考資料１）

②　大人のレシピエントは 13 歳未満のドナーから提供を受けた場合、肝動脈血栓症の発生する率が高いことが示されている。特に移植肝の容積がレシピエント推定肝容積の 40%未満であると、その発生率は高率であった。（参考資料２）

以上の２点からドナーが小児の場合、小児レシピエントに優先的に配分することとする。

参考資料１

TRANSPLANTATION Vol. 70, 1283–1291, No. 9, November 15, 2000

IMPROVED GRAFT SURVIVAL OF PEDIATRIC LIVER RECIPIENTS TRANSPLANTED WITH PEDIATRIC-AGED LIVER DONORS

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UNOS data 1992-1997の分析　(18歳未満を小児と定義)

小児ドナー中　35.6%が小児レシピエントに使用(1998年の小児、成人別登録後死亡率は小児7.4%、成人7.3%)

小児レシピ (n=2668)で、小児ドナーからと成人ドナーからの移植を比べると、３生率が81%対63%と有意に小児ドナーからの成績が良かった。成人レシピ (n=18525) で比べるとこのような差は見られなかった。

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IMPROVED GRAFT SURVIVAL OF PEDIATRIC LIVER RECIPIENTS TRANSPLANTED WITH PEDIATRIC-AGED LIVER DONORS

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Background. **Improving graft survival after liver transplantation is an important goal for the transplant community, particularly given the increasing donor shortage. We have examined graft survivals of livers procured from pediatric donors compared to adult donors.**

Methods. **The effect of donor age (<18 years or ≥18 years) on graft survivals for both pediatric and adult liver recipients was analyzed using data reported to the UNOS Scientific Registry from January 1, 1992 through December 31, 1997. Graft survival, stratified by age, status at listing, and type of transplant was computed using the Kaplan-Meier method. In addition, odds ratios of graft failure at 3 months, 1 year, and 3 years posttransplant were calculated using a multivariate logistic regression analysis controlling for several donor and recipient factors. Modeling, using the UNOS Liver Allocation Model investigated the impact of a proposed policy giving pediatric patients preference to pediatric donors.**

Results. **Between 1992 and 1997 pediatric recipients received 35.6% of pediatric aged donor livers. In 1998 the percent of children dying on the list was 7.4%, compared with 7.3% of adults. Kaplan-Meier graft survivals showed that pediatric patients receiving livers from pediatric aged donors had an 81% 3-year graft survival compared with 63% if children received livers from donors ≥18 years ($P<0.001$). In contrast, adult recipients had similar 3-year graft survivals irrespective of donor age. In the multivariate analysis, the odds of graft failure were reduced to 0.66 if pediatric recipients received livers from pediatric aged donors ($P<0.01$). The odds of graft failure were not affected at any time point for adults whether they received an adult or pediatric- aged donor. The modeling results showed that the number of pediatric patients trans-**

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planted increased by at most 59 transplants per year. This had no significant effect on the probability of pretransplant death for adults on the waiting list. Waiting time for children at status 2B was reduced by as much as 160 days whereas adult waiting time at status 2B was increased by at most 20 days.

Conclusion. **A policy that would direct some livers procured from pediatric- aged donors to children improves the graft survival of children after liver transplantation. The effect of this policy does not increase mortality of adults waiting. Such a policy should increase the practice of split liver transplantation, which remains an important method to increase the cadaveric donor supply.**

The nationwide donor shortage has forced scrutiny of our practices of organ allocation. In particular, liver allocation policies have been the subject of intense debate extending beyond the medical profession to the pages of the lay press and the corridors of the federal government (*1–4*).The issues of waiting time and mortality while waiting are amplified for liver transplant candidates (*5*) (and heart transplant candidates) because unlike kidney transplant candidates, no sustainable form of artificial organ support exists. In such patients allocation policies therefore take on a new urgency. If there were unlimited numbers of organs the justice of the argument "sickest first" is undisputed. However, given the limited organ supply, consideration must also be given to the question of how a scarce resource should be best utilized (*6*). In effect, which patients are likely to have the best graft survival?

Several investigators have identified factors that affect outcome after pediatric liver transplantation. Not surprisingly, as in adult liver recipients, the most important predictor is medical urgency (*7*). Although the technical challenges are considerable, young age itself is not a predictor of poor outcome in experienced centers (*8–11*). To date, donor factors considered have focused on whether the use of partial liver grafts affects the outcome of pediatric liver recipients. The use of split livers (one cadaveric donor divided to provide two transplantable segments), reduced livers (a cadaveric donor liver reduced in size to produce one transplantable segment), and living donor grafts, have already been shown to decrease the mortality of pediatric patients awaiting liver transplantation without decreasing patient and graft survivals (*12–14*). However, the effect of pediatric versus adult donor age on outcome has not been well studied. Our preliminary data showed that the majority of livers procured from pediatric-aged donors (<18 years of age) were transplanted into adults, although proportionately the same number of children die on the list as adults. This information caused to us question whether the outcome of pediatric or adult recipients was affected by the age of the donor. We postulated that if the results of this investigation showed that pediatric liver recipients benefited from receiving a donor of a pediatric age, as measured by improved graft and patient survival, without causing a negative impact on the adult population, then both utility and justice would suggest that pediatric recipients should receive at least some preference in receiving organs from pediatric donors.

METHODS

These analyses of posttransplant outcome were based on liver transplants reported to UNOS Scientific registry from January 1, 1992 through December 31, 1997. Odds ratios were calculated using a multivariate logistic regression analysis. This analysis controlled for several donor and recipient risk factors (e.g. donor race, donor cause of death, recipient race, diagnosis at time of transplant, previous transplant, medical condition at time of transplant, cold ischemia time, serum creatinine level and year of transplant). The outcome of interest was the odds of graft failure within 3 months, 1 year and 3 years posttransplant. PROC LOGISTIC, SAS version 6.3, was used to perform the logistic regression analysis. A stepwise regression technique, was used to determine the factors to be included in the final logistic regression model. Missing values for continuous variables were set to the mean, and for categorical variables, were set to the baseline value.

Acturial graft survival was computed using Kaplan-Meier method. These survival curves were stratified by age, status at transplant, type of transplant, and ICU group. A log-rank statistic was used to test the hypothesis of no difference in survival between groups.

For the median waiting times analyses, the cohort of patients included all registrations added to the UNOS Liver Waiting List between January 1, 1995 and December 31, 1997. Kaplan-Meier waiting times where calculated using PROC LIFETEST, SAS version 6.3. The actual probabilities on the waiting list of death, transplant, removed (not for reason of death or transplant), and still waiting, were computed using a competing risk method.

In April 1994 the UNOS liver data collection forms were amended. Among the information added to the forms was whether the transplanted liver was split or otherwise reduced in size. Therefore any information that specifies whole or split livers covers only the time period from April 1994 through December 31, 1997.

Modeling methods. Modeling results were generated by ULAM, the UNOS Liver Allocation Model. ULAM is a PC-based software package that simulates the current national and alternative liver allocation policies. Details of the construction of ULAM have been

TABLE 1. Distribution of pediatric and adult donor livers into pediatric and adult recipients, divided by age ranges: 1/1/92–12/31/97

Recipient age (yr)	Donor age (yr)				Total
	0–17		18+		
0–17	1786		882		2668
18+	3225		15300		18525
Total	5011		16182		21193
Recipient age	0–5	6–17	18–49	50+	
0–2	531	459	324	25	1339
3–17	263	533	449	84	1329
18–49	15	1712	5917	1989	9633
50+	13	1485	5224	2170	8892
Total	822	4189	11914	4268	21193

TABLE 2. Median waiting times for liver transplantation: by age and UNOS status: 1/1/92–12/31/97

Age group	Num Added	Status 1 95%			Status 2 95%			Status 3,4,7 95%	
		MWT	Conf limits	Num added	MWT	Conf limits	Num added	MWT	Conf limits
0–2 yr	295	23	(12,50)	178	51	(29,73)	815	189	(173,213)
3–5	75	10	(5,47)	36	35	(17,130)	211	231	(207,300)
6–10 yr	74	12	(5,40)	57	53	(22,246)	241	328	(235,428)
11–17 yr	153	10	(7,16)	77	46	(18,80)	382	409	(347,520)
18–49 yr	1236	9	(8,11)	834	28	(22,34)	8929	495	(472,517)
50+ yr	753	10	(8,12)	690	27	(22,32)	8757	460	(434,486)

TABLE 3. Mortality of patients on the UNOS liver waiting list for 1998 (Source UNOS OPTN Waiting List and Removal Files as of 9/7/1999)

Age (yr)	<1	1–5	6–10	11–17	18–34	35–49	50–64	65+
Patients	286	549	295	411	1143	6358	7411	1530
Deaths	50	34	15	16	84	445	556	117
Rate[a]	827.5	119.6	87.2	70.9	131.8	123.2	128.8	123.7
%	17.5	6.2	5.1	3.9	7.3	7.0	7.5	7.6

[a] Annual death rate per 1000 patient years at risk.

published elsewhere (*15*). In brief, ULAM is a discrete event simulation that matches individual donors and recipients using the same general algorithm as the UNOS match system. All statistical components of ULAM were derived from historical OPTN/SR data and the model has been validated against actual data from 1998–1999.

In our analysis, ULAM results were generated for the current national policy and the proposed policy giving pediatric patients preference to pediatric donors. For each policy, four independent simulations of 1998–2003 were generated with statistics collected from 1999–2003. A 1-year transition period allows the effects of the current policy to dissipate so that the impact of the proposed policy can be assessed more accurately. Output measures from the model represent the average of the four simulations of 1999–2003.

RESULTS

Current allocation of livers procured from donors <18 years. The first analysis determined how many livers procured from donors less than 18 years of age were transplanted into children (<18 years) compared to adults (18+ years). As seen in Table 1, which includes all cadaveric organs procured between 1/1/92 and 12/31/97 (including reduced and split grafts) pediatric recipients received 1786 of the total of 5011 (35.6% of pediatric-aged donor livers).

Analyzing these data further by dividing recipient and donor ages into subgroups, it can be seen that it is predominantly donors in the 6–17 age group that are transplanted into adults. Of donors aged 6–17 years, 1712 were transplanted into recipients aged 18–49, and 1485 into recipients aged greater than 50 years. Taken together, 3197 of 4189 (76.3%) 6- to 17-year-old donors were placed into adult recipients of which 46.4% were older than 50 years of age. In contrast, children received 882 of 16,182 adult liver donors (5.4%); this includes split and reduced size grafts (Table 2).

Current pediatric and adult mortality and waiting times on liver transplant list. The next questions examined were whether waiting time and mortality on the list differed between children and adults. Table 2 shows median waiting times for cadaveric liver transplants for pediatric and adult patients added to the liver waiting list between 1/1/95 to 12/31/97, divided according to age and UNOS status at time of listing. (Summary of Definitions of UNOS status codes: Up to and including 1997: status 1=In intensive care unit (ICU); status 2=hospitalized not in ICU; status 3=at home. 1998: status 1 adults=acute liver failure and in ICU; status 1 pediatrics=in ICU; status 2A (adults only)=chronic liver failure in ICU; status 2B=moderately urgent, defined by specific criteria; status 3=least urgent. Full definitions of status codes used can be found in the 1996 and 1998 UNOS Annual Reports.)

It can be seen that children 0–2 years waited longer in status 1 and status 2 than any other age range apart from status 2, 6- to 10-year-olds with an initial listing of status 2. At status 3, 4, and 7, adults waited longer than children. When this analysis was divided into years before and after split and reduced graft data were collected, i.e., 1/1/92 to 12/31/94 compared to 1/1/95 to 12/31/97 the same trends persisted (data not shown).

Mortality on the liver waiting list was also considered for different age ranges. For all patients on the liver waiting list during calendar year 1998 the number and percentage of patients dying is shown in Table 3. Note these numbers

TABLE 4. Patients listed on the liver waiting list between 1/1/95–12/31/97 (first 6 months after listing: probability of events)

Group	Initial status	Removed	Waiting	Transplanted	Died
Adult	1	0.151	0.082	0.448	0.319
	2	0.088	0.145	0.510	0.257
	3	0.032	0.690	0.197	0.082
Pediatric	1	0.179	0.118	0.433	0.270
	2	0.152	0.237	0.488	0.124
	3	0.088	0.573	0.283	0.056

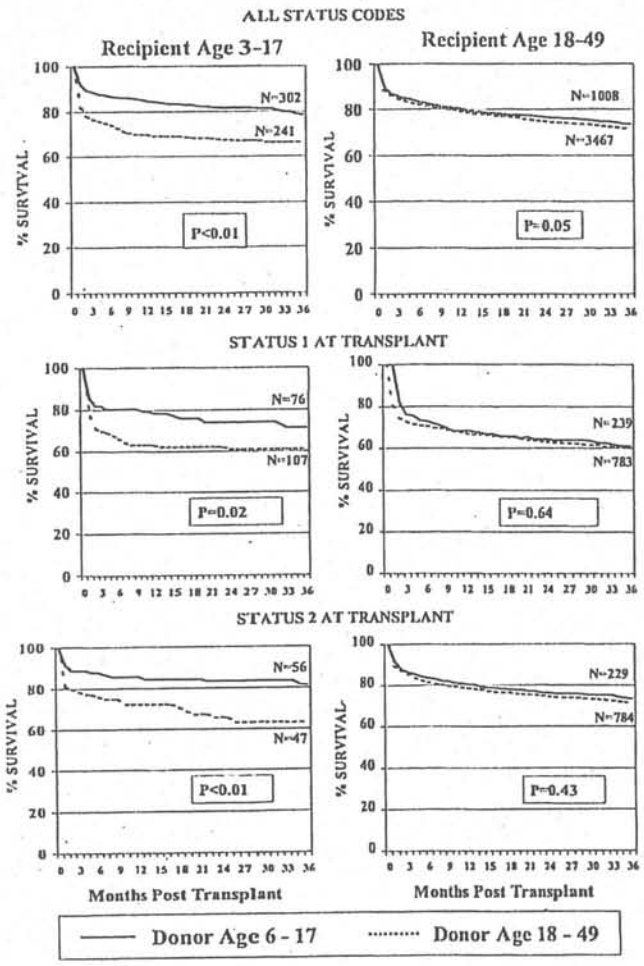

FIGURE 1. The unadjusted Kaplan-Meier 3-year survivals are shown for pediatric recipients (3–17 years) receiving livers from pediatric-aged donors (6–17 years) compared to adult donors (18–49 years) and adult recipients (18–49 years) receiving livers from pediatric aged donors (6–17 years). Results shown include retransplants, all UNOS statuses, and analyses for status 1 and status 2. Graphs on the left show the pediatric recipient data, graphs on the right show the adult recipient data.

exclude patients removed from the list because they became too ill to transplant. The percentage of patients dying was highest in the less than 1-year age range. Combining the <1 and 1- to 5-age groups, the percentage of patients dying is 10%, still higher than any other age range. From this data, the overall percent of children and adults dying in 1998 on the liver list was almost identical, 7.4%, the children (115 of 1541) and 7.3% adults.(1202 of 16,442)

We also analyzed the probability of death on the waiting list, divided by status at time of listing and adjusted for race, ABO match, and repeat listing. For adult and pediatric liver recipients added to the waiting list between 1/1/95 and 12/31/97, four possible events could occur: 1) the patient was removed from the waiting list for reasons other than death or transplant, 2) the patient continued to wait, 3) the patient received a cadaveric organ, (living related transplants excluded, reduced and split grafts included), 4) the patient died before transplantation. Patients removed from the list because they were too ill to receive a transplant were counted as pretransplant deaths. Table 4 shows the estimates for the probability of these four possible outcomes in the first 6 months after listing for patients added to the list between 1/1/95 and 12/31/97. Both adult and pediatric patients at status 1 and 3 had similar probabilities of dying on the list. A total of 31% of adults and 27% of children initially listed in status 1, died waiting. In status 2, pediatric patients had a lower probability of dying but a longer waiting time compared to adults. A total of 25.7% of adults at status 2 died compared with 12.4% of children, whereas 14.5% of adults originally listed were still waiting at the end of 6 months compared to 23.7% of children at status 2. In the second 6 months after listing the probability for all four outcomes was similar between adults and children (data not shown).

Kaplan-Meier patient and graft survivals: effect of donor age on outcome of pediatric and adult liver recipients. Our first analysis attempted to answer this question by subdividing donor and recipient ages into several age ranges. However, the numbers in each subgroup became too small to allow for a meaningful statistical analysis. It was decided to eliminate several subdivisions of age ranges as well as extremes of donor and recipient age that might bias the results. Therefore, for the first analysis, the 0–5 age range for donors and the 0–2 age range for recipients was eliminated and the 3- to 5-year and 6- to 17-year age range for recipients was combined into one group, i.e., 3–17 years. It was also reasoned that pediatric recipients less than 3 years generally received whole organs from similar age donors based on size considerations. The upper limit of donor and recipient age was set at less than 50 years to exclude the possible negative effects of older donors and recipients. Figure 1, shows the unadjusted Kaplan-Meier 3-year graft survivals for pediatric recipients (3–17 years) receiving livers from pediatric-aged donors (6–17 years) compared to adult donors (18–49 years), and adult recipients receiving livers from pediatric aged donors. Results shown include retransplants, all UNOS statuses and a further analysis for status 1 and status 2. Excluded are reduced, split or living donor transplants. Pediatric recipients receiving livers from younger donors had a significantly improved graft survival, 81% compared with

TABLE 5. The odds of graft survival compared for adult and pediatric donors and recipient: whole grafts only

Recip age (yr)	Donor age (yr)	Num txd	Time points					
			3 Mo post-Tx		1-Yr post-Tx		3 Yr post-Tx	
			Odds ratio	*P*	Odds ratio	*P*	Odds ratio	*P*
3–17	6–17	496	0.62	0.02	0.50	<0.01	0.58	0.03
3–17	18–49	362	1.00	Ref.	1.00	Ref.	1.00	Ref.
18–49	6–17	1699	0.82	0.20	0.77	0.07	0.84	0.36
18–49	18–49	5879	0.78	0.08	0.77	.05	0.84	0.26

TABLE 6. Transplants performed 4/1/94–12/31/97, numbers of whole, reduced, split, and living donors by year 1994–1997

Yr	Type of transplant				
	Whole	Reduced	Split	Live	Total
1994	2669	108	26	45	2848
1995	3771	87	21	45	3924
1996	3865	84	62	46	4057
1997	3935	79	84	60	4158
Total	14240	358	193	196	14987

TABLE 7. Numbers of whole, reduced, split and living donors by age of recipient: 1994–1997

Age	Type of transplant				
	Whole	Reduced	Split	Live	Total
<1	254	131	39	106	530
1–2	304	102	35	47	488
3–5	192	42	13	15	262
6–10	223	35	13	14	285
11–17	375	21	13	7	416
18+	12892	27	80	7	13006
Total	14240	358	193	196	14987

63%, $P<0.001$. In contrast, adult recipients had similar graft survivals irrespective of donor age. These differences remained significant when status at time of listing was considered.

Multivariate analyses: effect of donor age or outcome of pediatric and adult liver recipients. The Kaplan-Meier survival curves were unadjusted for risk. Therefore a further multivariate regression analysis was performed to determine if placing younger donor livers into younger recipients reduced the odds of graft failure. As before, this analysis excluded living related donors and split and reduced grafts. Donor and recipient risk factors controlled for were: donor and recipient race, donor cause of death, recipient diagnosis at transplant, medical condition (UNOS status) at transplant, cold ischemia time, ABO match, donor creatinine level, and year of transplant. The odds of graft failure at three months, 1 and 3 years posttransplant were determined (Table 5). At all three time points, the odds of graft failure were significantly less if pediatric recipients (3–17 years) received livers from younger donors (6–17 years). In contrast the odds of graft failure at each time point for adult recipients were similar whether or not the donor was younger or older.

The same multivariate regression analysis was repeated but now applied to all pediatric and adult recipients, with no age exclusions and inclusive of split and reduced grafts. Table 6 shows the number of reduced and split organ transplants performed during the period of this analysis, and Table 7 the type of transplant according to age. During this time period 66 pediatric-aged donors were split, of which 24 segments were placed in adults.

The results of the unrestricted analysis (Table 8) remained very similar to the restricted analysis: pediatric patients have significantly reduced odds of graft failure if receiving a graft from a pediatric-aged donor whereas the age of the donor had little impact on the odds of graft failure to adult recipients.

An expected outcome of a policy that would direct more livers from pediatric donors to pediatric recipients would be an increased number of relatively large organs being directed to smaller recipients. This would encourage split liver transplantation whereby two recipients benefit from one organ. As well, reduced size transplantation, where part of the liver is discarded, might also occur. Therefore, we investigated the graft survivals of reduced and split size livers. For the time period 4/1/94–12/31/97 the Kaplan-Meier 3-year graft survival estimates for pediatric recipients of primary liver transplants subdivided by the type of organ received are shown (Fig. 2). It can be seen that reduced size grafts had a significantly lower 3-year graft survival compared to all other graft types. In comparison, split liver grafts had an overall 70% 3-year graft survival, not significantly different from either whole or living donor grafts. We were also interested in whether a split liver from a pediatric donor had a different patient and graft survival compared to that from an adult donor. Although the numbers were small, Kaplan-Meier three year adjusted patient survivals for split livers were not different if the liver was from an adult donor (n=51, patient survival 87%) or a pediatric donor (n=32, patient survival 89%). However, in comparison, the 3-year Kaplan-Meier graft survival was worse if the split liver was from an adult donor, 62%, as compared to a pediatric donor, 83%.

For all the above analyses of graft survivals, patient survivals were also examined (data not shown), and similar results were observed. Because of the complexity of the analyses derived from data accrued over several years, we did attempt to detect any possible center effects.

UNOS liver allocation model (ULAM) results. ULAM was used to investigate whether the proposal to allocate livers from pediatric donors preferentially to pediatric recipients, within urgency status and geographic areas, would have a detrimental impact on adult patients waiting on the list. In particular we believed it was important to investigate whether the number of adults dying either pretransplant or posttransplant would be effected by the proposed new policy. The proposed allocation sequence used in the model is shown in Table 9.

Two models were developed; the first defined a pediatric

TABLE 8. Odds of graft survival compared for pediatric and adult aged donors and recipients; including reduced and split grafts

Recip age (yr)	Donor age (yr)	Num txd	Time points					
			3 Mo post-Tx		1 Yr post-Tx		3 Yr post-Tx	
			Odds ratio	P	Odds ratio	P	Odds ratio	P
0–17	0 –17	1786	0.66	<0.01	0.62	<0.01	0.65	<0.01
0–17	18+	882	1.00	Ref.	1.00	Ref.	1.00	Ref.
18+	0 –17	3225	0.62	<0.01	0.84	0.29	1.06	0.75
18+	18+	15300	0.66	<0.01	0.86	0.33	1.06	0.75

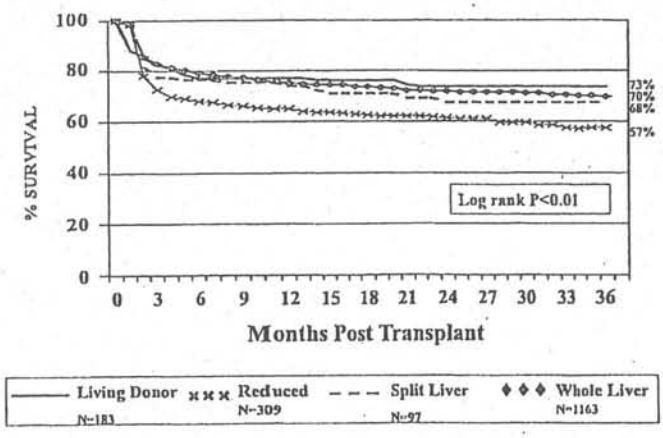

FIGURE 2. The Kaplan-Meier 3-year graft survivals are shown for pediatric recipients of primary liver transplants subdivided by type of organ received.

donor as <18 years, and the second defined a pediatric donor as <18 years and less than a specified weight range. Three weight ranges were investigated, <40, <45, and <50 kg. The second model was developed in response to concerns that small adult recipients might be disadvantaged by the proposed pediatric definition of <18 years without weight restrictions.

Neither model takes into account the data presented above which shows improved patient and graft survivals for children receiving livers from pediatric aged donors. Further, split liver transplant and outcomes were not considered.

Table 10 summarizes the most relevent data from the simulations comparing the current allocation policy to the four proposed pediatric donor definitions: 1) <18 years, 2) <18 years and <40 kg, 3) <18 years and <45 kg, 4) <18 years and <50 kg (Table 11).

The data presented in Table 12 represents the average of each measure for 5 years (1999–2003) and over four simulation runs. The data address: 1) the number of pediatric and adult patients transplanted by age (pediatric recipients divided 0 to 5 years, 6–11 years, 11–17 years) and by status, 2) median waiting time by status, and 3) probability of pretransplant death within 6 months of listing. The number of repeat transplants, and patient life years under the different proposals is not shown because the model did not account for expected improvements in pediatric graft survival should pediatrics recipients receive livers from pediatric aged donors.

In all of the proposed policies, slightly more pediatric patients were transplanted over the 5-year period. The increase over the current policy ranged from 151 over 5 years (30 per year) for the most restrictive policy with donors defined as <18 years and <40 kg, to 297 over 5 years (59 per year) the least restrictive policy defining a pediatric donor as <18 years. Consequently, each of the policies resulted in a corresponding decrease in the number of adult patients receiving transplants.

Investigating the change in the number of transplants by age and status showed that among pediatric patients fewer were transplanted in status 1 under the proposed policies. This is because more pediatric patients were transplanted at less urgent statuses under the proposed policies. In contrast about the same or slightly higher numbers of adult patients

TABLE 9. Proposed order of allocation for a liver from a pediatric donor

1. Local
   Pediatric status 1
   Adult status 1
2. Regional
   Pediatric status 1
   Adult status 1
3. Local
   Adult status 2a
   Pediatric status 2b
   Adult status 2b
   Pediatric status 3
   Adult status 3
4. Regional
   Adult status 2a
   Pediatric status 2b
5. National
   Pediatric status 1
   Adult status 1
   Adult status 2a
   Adult status 2b
   Pediatric status 3
   Adult status 3

were transplanted in status 1 because there were fewer pediatric patients competing for organs while in status 1. This is reflected in the increased numbers of children transplanted at status 2B. This was most evident in the policy defining pediatric donors <18 years without weight restriction. The increase in pediatric status 2B patients transplanted was 304 over 5 years compared to current policies. This benefit was diluted as the more restrictive pediatric donor definitions by weight were applied. In contrast, the more stable pediatric patients at status 3 showed only a modest increase, approximately 4–10 more children per year. In examining the data by status for adults, it is also important to note that all of the proposed policies slightly increased the number of adult patients transplanted at status 2A. This effect ranged among 18 to 78 patients over 5 years.

Of all pediatric donor livers, the percent that went into adults was 68.8% under the current policy. Under the least restrictive proposed policy the percentage of adults still receiving pediatric donors was 59.2%, and ranged between 63–64% under the other pediatric donor proposals divided by weight. There was also a decrease in the percentage of adult livers that were transplanted into pediatric patients. This was most pronounced, 3.9%, in the policy defining pediatric donors <18 years, without weight restriction. Only a negligible increase in the percentage of adult livers that were transplanted into adults was demonstrated.

The percentage of local, regional, and national transplants was essentially unchanged as was the average and median distance the organ traveled. The percentage of organs that traveled greater than 1000 miles increased from 1.6 to 1.7%.

Deaths pretransplant and posttransplant and total deaths for the proposed policies was examined and no significant changes were noted with all four policies proposed as compared to the current policy.

When the probability of pre transplant death within 6 months of listing was analyzed, there were minimal differences, none of which was statistically significant, between

TABLE 10. ULAM comparison of current liver allocation policy to four proposed pediatric donor definitions: <18 yr and <40 kg; <18 yr and <50 kg; the model simulates 5 yr of transplant activity under the various definitions

	Current policy	<18 Yr	<40 kg	<45 kg	<50 kg
No. ped. txs	2132	2429	2283	2299	2307
Change from current policy		+297	+151	+167	+175
No. ped. txs by age					
0–5	1238	1417	1336	1339	1353
6–11	367	413	387	391	397
11–17	528	600	560	569	558
Txs by age and status					
Adult 1	4061	4085	4056	4100	4087
Adults 2A	4713	4731	4729	4733	4781
Ped 1	764	711	755	733	731
Ped 2B	1069	1372	1206	1246	1256
% of total/ped donor to adult recipient	69%	59%	64%	64%	63%
Med wait time					
Ped. 2B:2B	340.8	179.0	264.5	252.3	243.0
Ped. 3:2B	776.5	624.3	685.5	699.5	674.0
Adult 2A:2A	11.3	12.3	11.3	11.3	11.5
Adult 2B:2B	553.0	573.0	550.8	572.3	569.0
Adult 3:2B	947.5	968.5	958.5	963.0	965.5
Probability of pre-Tx death w/in 6 mo of listing					
Adult 1	11.8%	11.4%	11.7%	11.9%	11.6%
Ped 1	16.4%	15.5%	15.3%	15.4%	15.1%
Adult 2A	23.4%	22.2%	22.0%	21.9%	22.9%
Adult 2B	13.7%	14.0%	13.9%	13.6%	13.6%
Ped 2B	13.5%	12.3%	12.8%	12.0%	12.5%

the current and proposed policies among adult and pediatric recipients. Among pediatric patients, death rates decreased for patients listed initially in status 2B and status 3. Waiting time as measured by Kaplan-Meier estimates for most categories were reduced for pediatric patients and increased slightly for adult patients. Of importance, both pediatric and adult patients at status 1 had essentially no change in waiting time at status 1 although on average pediatric patients waited 2 days longer for transplant at status regardless of the policy. Of importance, children in status 2B had the most benefit from the policy defining pediatric <18 years without weight restriction, with median waiting time reduced by 160 days. In that same simulation adult waiting time at 2B was increased by only 20 days. When pediatric donors were further restricted by weight, the beneficial effect of decreased waiting time at status 2B for children continued to be evident but much less important ranging between 76 and 97 days, whereas the waiting time for adults was effected only slightly 2–16 days. Among adults waiting times increased the most for patients listed initially in status 3 with an ending status of 2B from 947 to 966 days and under the least restrictive policy.

DISCUSSION

We have shown that there is a significant beneficial effect on liver graft survival if pediatric recipients receive livers from pediatric-aged donors, whereas graft survival of adult recipients is not advantaged or disadvantaged by the age of the liver donor. This effect is seen at 3 months after liver transplantation, when donor factors are likely to have the strongest influence on outcome, but also persists at 3 years posttransplant. These findings hold true whether using a univariate or multivariate method of analysis or unadjusted Kaplan-Meier estimates of graft survival. Importantly, whether the analysis is performed on a restricted population of donor and recipients to decrease the potential impact of the extremes of donor and recipient age, and the possible influence of partial liver grafts, or the entire population of adult and pediatric recipients and donors, including partial liver grafts, the same benefit to pediatric patients receiving livers from younger donors persists. The improvement in graft survival for pediatric patients who receive younger donors compared to adults receiving younger donors, will have the greatest impact on the most medically urgent children, who we have shown wait longer to receive a donor, especially if aged less than 5 years, compared with adults of equivalent status.

We can only postulate why pediatric recipients have an improved survival if they receive a liver from a pediatric-aged donor. Donor quality, which is usually excellent in pediatric-aged donors, is a likely explanation. The recent research impetus studying the process of senescence at the cellular level, may provide new insights in the future.

Should these results be utilized to change allocation policies to give children awaiting liver transplantation some preference in receiving younger donors? To answer this important question several related issues must first be considered. 1) Do children already hold an advantage over adults waiting liver transplantation, reflected either by shorter waiting times or a decreased mortality on the list? 2) Would redirecting some pediatric donors away from adults awaiting liver transplantation have a significant negative effect on the outcome of adults undergoing liver transplantation? 3) Could directing some adolescent donor livers to small children encourage split liver transplantation, which would increase the donor supply?

It has been argued that children already have an advantage over adult candidates awaiting liver transplantation because they have three possible options for receiving a liver:

a whole cadaveric graft, a partial cadaveric graft or a living donor organ (*16*). Despite this, an analysis of the last 3 years of the UNOS database show that children have similar mortalities and waiting times compared to adults on the transplant list. In fact, it is children less than 2 years of age at status 1 who waited significantly longer than any other age group. As well, in 1998, children less than 1 year had the highest mortality rate waiting for any age group, followed only by children in the 1- to 5-year age range. Therefore the data suggest that the availability of living related donors and partial liver grafts, which would most likely have benefited small children on the list, has not yet had a significant impact on pediatric mortality or waiting time as compared with adults. Furthermore, given that the results of liver transplantation in small pediatric patients in experienced centers are comparable to those of older children, there can be no justification for not providing young children with at least equal access to liver donors.

Although living related donation for children has been properly advocated as one means of alleviating the donor shortage for children (*17*), this modality should not be viewed as an excuse to divert cadaveric donors away from children (*18*). Because of the risk to the otherwise healthy donor, most often a parent (*18*), the ethically correct position is that living related donation should continue to be seen as last resort to try and alleviate the donor supply problem. Conversely, the split liver donor technique should become the first consideration for every suitable donor (*19*). The most recent reported results are comparable to whole graft transplantation (*20*). As well, a recent report suggests graft survival is better in infants who receive a split compared to a whole graft (*21*). However, reduced graft transplantation should be actively discouraged: not only are the results inferior, but a whole liver is diverted away from a more appropriately sized recipient.

The next question was more complex: would adults be disadvantaged by diversion of some pediatric donors to pediatric recipients? Fairness and balancing the conflicting notions of transplanting the most urgent first regardless of age versus best utilization of a scarce resource, would require that pediatric-aged donors should not always be placed in pediatric recipients. For example, it would seem inappropriate and unjust, either on a local or regional level that a status 1 adult should be bypassed for a status 2B child. For this reason, ULAM was programed to assign priority so that within each medical urgency status and within each geographic distribution level (local, regional, and national) pediatric candidates are prioritized.

The most important result of the modeling was that none of the proposed policies allocating livers from pediatric donors to pediatric recipients increased the probability of death for adults waiting on the transplant list. Although more children were transplanted per year (at most 59, less than 1 additional child per pediatric transplant center), and therefore proportionately less adults, the impact for the adults was on waiting time at the less urgent statuses, 2B and 3. Even then, the average wait was at most increased by 20 days. Importantly, the waiting time for the most medically urgent adults at status 2A and 1 was not affected by any of the proposed policies. In fact adults waited an average of 2 days less at status 1 compared to children, because more children were transplanted at status 2B. As well slightly more status 1 adult patients were transplanted under the proposed policies.

The decrease in waiting time for children at 2B was as much as 160 days. Clinically this is important as one of the most common criteria for listing children at status 2B is a growth failure, i.e., weight or height less than 5th percentile. The impact of decreasing waiting time by as much as half a year for the young, cholestatic, malnourished child is clinically highly relevant to the unique issues of growth and development in chronically ill children (*22, 23*). It has already been shown that malnutrition has a negative effect on both pre- and posttransplant survival (*24, 25*), and that age at transplant of <2 years in children is an important independent predictor of improved growth after transplantation (*26*). It should still be noted that even under the most liberal of the proposed policies, the majority of livers procured from pediatric aged donors will still be transplanted into adult recipients. As well, the percentage of transplants performed locally, regionally, and nationally would be affected only minimally.

The third question to be considered is how might a proposal to direct some livers from pediatric donors best encourage split liver transplantation. Our data show that split liver graft survival is significantly improved if the donor is in the pediatric age range. This result is most likely a reflection of the usually excellent quality of the adolescent donor and highlights the need for very careful donor selection if the split procedure is performed on adult-aged donors.

In comparing the four pediatric allocation proposals, with the least restrictive being any pediatric donor <18 years, and the most restrictive being <18 years as well as <40 kg, the data showed that the most positive effect occurred for the pediatric patients when the pediatric donor was defined <18 years. When the pediatric donor was further subdivided by weight, the potential benefit to pediatric patient was diminished without a substantial increase in benefit to adult patients. If the definition of the pediatric donor was restricted to weight <40 kg, the advantage of directing some of the larger pediatric donors to smaller pediatric recipients, which would promote split liver transplantation, would be lost. As can be seen from the data, most pediatric donor livers exported to adult recipients are in the donor age range of 11–17 years, are generally of excellent quality and ideal for splitting. In fact, UNOS recently approved a proposal that requires all participating centers to split suitable donor livers. If adolescent liver donors are preferentially offered to children waiting, many of whom would be too small to accept a whole graft, the center accepting such a liver should split the graft so that an adult patient would not be deprived of an organ. If the center was unwilling to split the donor liver, it should be returned to the donor pool for reassignment to the next eligible recipient. Such a policy could then be seen as a reason to improve the utilization of these excellent quality younger donors. The success of this concept will depend on centers being prepared to "share" split grafts. A recent report shows that "shipped" segments have an equivalent graft survival compared to locally procured segments (*27*). Given the demonstrated excellent results achievable both for the right and left split liver grafts (*28*), and the ongoing organ shortage, urgent priority should be assigned to any allocation policy that will encourage split liver transplantation (*29*). The onus will lie on the surgical transplant community to not

accept such livers for reduced size transplantation, a technique now in disrepute given the proven success of split livers, and the increasing donor shortage.

We have shown that an allocation policy giving some priority to children to receive livers from pediatric donors can improve the outcomes after liver transplantation, without a negative impact on adults. As well, such a policy would encourage split transplantation, the only method currently available to increase the cadaveric donor supply. Furthermore, this proposal strikes a balance between justice and utility; the sickest patients, whether adult or pediatric are still transplanted first, more grafts are made available by encouraging split transplantation, and patient and graft survival for children are improved without detriment to adult recipients outcome. As such this proposal is worthy of serious consideration by the community of transplant physicians, surgeons, and their patients.

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

Sukru Emre, Yuji Soejima, Gulum Altaca, Marcelo Facciuto, Thomas M. Fishbein, Patricia A. Sheiner, Myron E. Schwartz, and Charles M. Miller

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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

Sukru Emre, Yuji Soejima, Gulum Altaca, Marcelo Facciuto, Thomas M. Fishbein, Patricia A. Sheiner, Myron E. Schwartz, and Charles M. Miller

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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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 $\geq$ 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 PD (n = 70)	AD (n = 1,051)	*P*
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

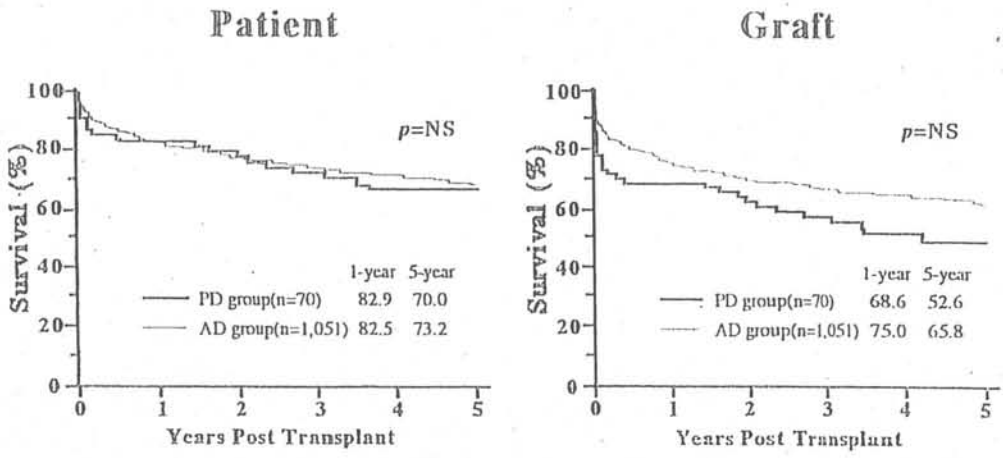

Figure 1. Comparison of patient and graft survival between the PD (n = 70) and AD groups (n = 1,051).

Table 2. Postoperative Complications

Variables	PD (n = 70)	AD (n = 1,051)	*P*
PNF (%)	7.1	6.3	NS
HAT (%)	12.9	3.8	.0003
Portal vein thrombosis (%)	2.1	1.5	NS
Bile leak (%)	5.7	3.8	NS
Bile duct stricture (%)*	5.7	5.8	NS
Septicemia (%)	28.6	19.8	NS
Acute rejection (%)	42.9	50.1	NS
Posttransplantation ascites (%)	7.1	10.5	NS

Abbreviation: NS, not significant.
* Intrahepatic and extrahepatic stricture.

Table 3. Independent Predictors of Inferior 1-Year Graft Survival in Recipients of PD Livers

Variables	Graft Survival (%)	Coefficient	Relative Risk	*P*
PT (s)				
<16	80.5	1		
≥16	51.7	1.165	3.206	.0115
FK506 use				
Yes	86.2	1		
No	57.5	1.499	4.477	.0078

group were only 40% and 20% compared with 73.2% and 57.1% in patients with a DLW/ERLW of 0.4 or greater. Although there was no statistical significance, probably because of the small sample size, diminished graft survival in this group of patients should be noted. When divided at a cutoff value of 0.5 for DLW/ERLW, postoperative complications and patient and graft survival were similar between the groups, except for a greater incidence of bile leak in patients with a DLW/ERLW less than 0.5.

Regarding chronological changes in serum TBil, glutamic-oxaloacetic transaminase, and PT values early after LT, we found that serum bilirubin levels tended to be greater in the group with a DLW/ERLW less than 0.4 at all points, but this did not reach statistical significance. PT POD 2 was significantly greater in the group with a DLW/ERLW less than 0.4 compared with the group with a DLW/ERLW of 0.4 or greater ($P < .05$).

Although females accounted for 39.8% of AD recipients, 78.6% of PD recipients were female. Primary biliary cirrhosis (21.4%) was a relatively frequent indication in the PD group compared with AD group (10.4%).

Table 1 lists surgical data. Mean CIT was significantly longer in PD recipients ($P < .04$). A piggyback procedure was used in 51.4% of PD recipients in contrast to only 4.6% of AD recipients ($P < .0001$). Patients in the PD group were significantly more likely to require Roux-en-Y hepaticojejunostomy than patients in the AD group because of the size discrepancy between donor and recipient ducts (26.7% *v* 12.7%).

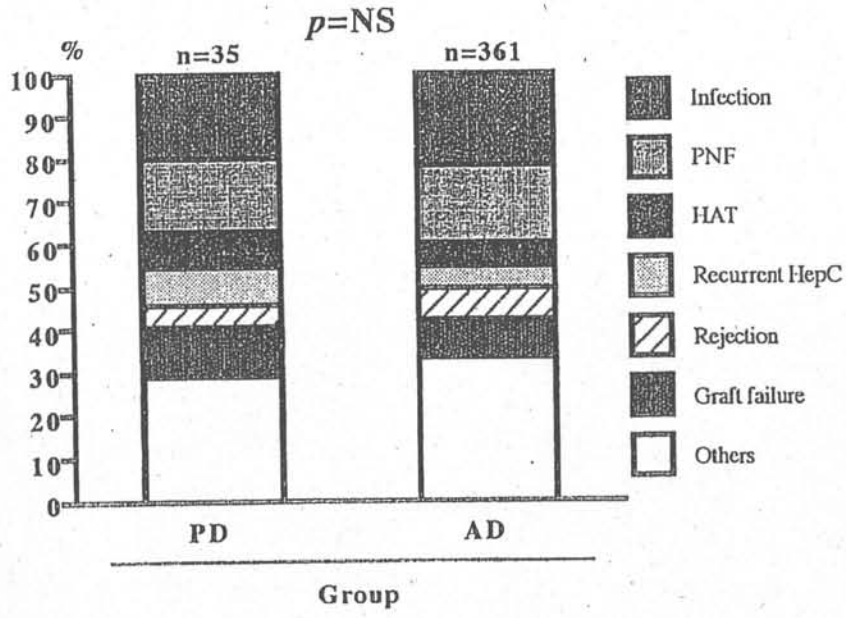

Figure 2. Comparison of causes of graft loss between the PD (n = 70) and AD groups (n = 1,051). (HepC, hepatitis C; NS, not significant.)

Table 4. Delayed Cholestasis After LT

Variables	TBil (mg/dL) POD 7 <5.0 (n = 41)	TBil (mg/dL) POD 7 ≥5.0 (n = 11)	*P*
Recipient age (yr)	51.1 ± 14.3	51.0 ± 14.5	NS
UNOS status (%)			NS
1	11.1	27.2	
2	36.1	18.2	
3	52.8	54.6	
Donor age (yr)	8.7 ± 2.1	9.7 ± 1.3	NS
DLW (kg)	855 ± 385	784 ± 147	NS
DLW/ERLW	0.63 ± 0.23	0.67 ± 0.49	NS
CIT (h)	10.5 ± 3.0	13.1 ± 4.3	.02
WIT (min)	45.5 ± 9.0	57.2 ± 13.0	.001
Intraoperative transfusions			
PRBCs (units)	10.9 ± 7.2	15.7 ± 14.9	NS
FFP (units)	17.9 ± 14.3	11.8 ± 8.7	NS
Patient/graft survival (%)			
1-yr	92.7*/80.5†	54.5*/36.4†	*†<.001
5-yr	80.5‡/65.9§	36.4‡/18.2§	‡§<.0001

NOTE. Values expressed as mean ± SD unless noted otherwise.
Abbreviations: PRBC, packed red blood cells; FFP, fresh frozen plasma; NS, not significant.
* 1-year patient survival.
† 1-year graft survival.
‡ 5-year patient survival.
§ 5-year graft survival.

Table 5. Preoperative Demographics and Postoperative Complications in the PD Group With Special Reference to DLW/ERLW at 2 Cutoff Points

Variables	DLW/ERLW <0.4 (n = 5)	DLW/ERLW ≥0.4 (n = 56)	*P*	DLW/ERLW <0.5 (n = 21)	DLW/ERLW ≥0.5 (n = 40)	*P*
Mean preoperative variables						
Recipient age (yr)	51.4	50.7	NS	51.5	50.4	NS
RBW (kg)	78.0	64.2	.04	69.0	63.4	NS
Donor age (yr)	8.6	8.7	NS	8.0	9.1	.06
Donor body weight (kg)	26.0	32.9	NS	26.6	35.2	.003
DLW (g)	555.6	883.2	.007	619.4	980.8	<.0001
DLW/ERLW	0.35	0.63	.001	0.42	0.71	NS
Postoperative complications						
PNF (%)	20.0	7.1	NS	5.8	10.0	NS
HAT (%)	40.0	10.7	.06	14.3	12.5	NS
Portal vein thrombosis (%)	0.0	3.6	NS	0.0	5.0	NS
Bile leak (%)	0.0	7.1	NS	19.0	0.0	.004
Septicemia (%)	60.0	25.0	NS	38.1	22.5	NS
Acute rejection (%)	40.0	44.6	NS	47.6	42.5	NS
Patient/graft survival (%)						
1-yr	80.0/40.0	85.7/73.2	NS	85.7/71.4	85.0/70.0	NS
5-yr	60.0/20.0	73.2/57.1	NS	66.7/52.4	75.0/55.0	NS

Abbreviation: NS, not significant.

Discussion

Currently, more than 14,000 patients are on the waiting list for liver transplants in the United States, with an expected supply of 4,500 donors per year.[7] The gap between the demand and supply of donor organs has been constantly increasing. As a result, centers have been expanding their donor acceptance criteria, including the use of small-for-size livers under certain conditions.

The use and allocation of pediatric livers in adult recipients is controversial. According to UNOS data,[7] approximately 20% of liver donors in the United States in 1997 were aged younger than 18 years, and 8.7% were aged younger than 10 years. Approximately 150 livers per year procured from PDs (defined as age < 13 years) were transplanted into adults (≥19 years; UNOS data request, 1999). According to Wight,[8] 28 pediatric livers were transplanted into adults in the United Kingdom in 1989, whereas 64 pediatric livers were transplanted into pediatric patients.

Because there was no UNOS policy for allocating PD livers to pediatric recipients during this study period, the use of pediatric livers in adult recipients was justified under certain urgent conditions. Recently, UNOS adopted a policy to allocate PD livers preferentially to pediatric recipients in the same region.

Our study showed that results with the use of pediatric livers in adults was similar to results with adult-to-adult combinations, although graft survival tended to be less in the former group. Of note, the incidence of HAT was significantly greater in the PD group compared with the AD group (12.9% *v* 3.8%). The incidence of HAT after primary LT varies from 1.6% to 8% in adults[9-13] and 5% to 38% in children.[14-16] Numerous factors have been implicated in HAT, including a prolonged CIT.[13,17-19] Not surprisingly, an increased incidence has been reported in pediatric recipients, in whom vessels are small.[14] It is also reported that size mismatching in vascular components could be problematic in LT using small-for-size grafts.[20] In our present study, CIT was longer in the PDs, and this may partly explain the high incidence of HAT. Furthermore, we believe the small size of the donor artery and inevitable size discrepancy between donor and recipient arteries might facilitate development of HAT. It is our policy to administer anticoagulation therapy with heparin to the recipient in this setting to prevent HAT.

Adam et al[21] reviewed their use of small donor livers in adult recipients and found that a very small graft size (<600 g), DRW ratio less than 0.5, and preservation time exceeding 12 hours were risk factors for complications. We did not confirm these findings in our patients (data not shown). Our multivariate analysis showed 2 independent risk factors for poor graft survival: preoperative PT greater than 16 seconds and no use of FK506 for primary immunosuppression. Patients with a preoperative PT less than 16 seconds who were administered FK506 had a 1-year graft survival rate of 94.1% (n = 17) versus a 37.5% (n = 16) 1-year graft survival rate in patients with a PT greater than 16 seconds preoperatively who were not administered FK506. The effect of a high preoperative PT on negative outcome can be explained by poor pre-LT patient condition and intraoperative blood loss (data not shown). These results suggest that restricting the use of small PD livers to relatively healthy adults may be the key to better graft and patient survivals. However, possibly because a cyclosporine-based immunosuppressive regimen was used earlier in our program, the improved graft survival in the FK506 era may reflect our learning curve related to increased surgical experience.

It is important to know the expected (or ideal) recipient liver weight before accepting a donor liver, especially when there is a size discrepancy between the donor and recipient. Urata et al[22] proposed a simple formula for predicting standard (or ideal) liver volume:

$$\text{Liver volume (milliliters)} = 706.2 \times \text{body surface area (square meters)} + 2.4$$

Since it was published in 1995, this formula has been widely used. However, we found that this formula tended to underestimate liver volume when we applied it to our donor population (data not shown). Heinemann et al[23] recently reported the same observation. The reason is not clear but is probably caused by the racial difference on which the formula was based. Thus, we adopted the formula developed at our institution:

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

Among 5 grafts with a DLW/ERLW less than 0.4, 1 graft (DLW/ERLW = 0.35) was lost to PNF, which was attributed to a small-for-size graft. The 2 smallest grafts (0.29 and 0.34) developed HAT on PODs 12 and 1. One graft (DLW/ERLW = 0.39) was lost to an unknown cause on POD 982. Thus, the 3 smallest of these 5 grafts were lost to causes attributable to the graft itself. Considering the high incidence of complications, including HAT (40%) and septicemia (60%), and the low graft survival, we currently believe we should not use grafts with a DLW/ERLW less than 0.4 in cadaveric LT.

In living related LT, small-for-size grafts are report-

edly associated with impaired graft function, indicated by prolonged hyperbilirubinemia, profuse ascites, and high PTs.[3] In our study, TBil levels in patients with a DLW/ERLW less than 0.4 tended to be greater, but the difference did not reach statistical significance. PT on POD 2 was significantly higher in patients with a DLW/ERLW less than 0.4. The incidence of post-LT ascites was similar between the PD and AD groups. In living related donor LTs, the development of increased ascites related to small-for-size livers may be caused by the large cut surface on the donor liver. This theory may explain why increased ascites was not seen in our transplant recipients, in whom the small-for-size livers were whole organs.

When we divided the PD liver recipients into 2 groups based on TBil level on POD 7, we found that graft volume (DLW/ERLW) was not associated with prolonged cholestasis (defined as TBil $\geq$ 5 mg/dL on POD 7). Conversely, grafts with long WITs and CITs developed cholestasis, suggesting that small-for-size livers were more vulnerable to ischemic insult. Furthermore, we found that graft and patient survival in patients who developed prolonged cholestasis were markedly inferior to those who did not.

In conclusion, the use of PD livers in adults was associated with a greater incidence of HAT, probably attributable to smaller donor vessel size and the inadequate capacity of the donor vessel for accommodating high arterial flow velocity in the recipient. Post-LT anticoagulation therapy is warranted when using PD livers in adults. The outcome of small-for-size grafts is more likely to be adversely affected by longer WITs and CITs. Grafts with a DLW/ERLW of 0.4 or greater (or $\geq$40% of ideal liver volume) can be used safely.

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参考資料3

Longterm Outcomes for Whole and Segmental Liver Grafts in Adult and Pediatric Liver Transplant Recipients: A 10-Year Comparative Analysis of 2,988 Cases

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BACKGROUND: Data on longterm outcomes after liver transplantation with partial grafts are limited. We compared 10-year outcomes for liver transplant patients who received whole grafts (WLT), split grafts from deceased donors (SLT), and partial grafts from living donors (LDLT).

STUDY DESIGN: We conducted a single-center analysis of 2,988 liver transplantations performed between August 1993 and May 2006 with median followup of 5 years. Graft types included 2,717 whole-liver, 181 split-liver, and 90 living-donor partial livers. Split-liver grafts included 109 left lateral and 72 extended right partial livers. Living-donor grafts included 49 left lateral and 41 right partial livers.

RESULTS: The 10-year patient survivals for WLT, SLT, and LDLT were 72%, 69%, and 83%, respectively ($p = 0.11$), and those for graft survival were 62%, 55%, and 65%, respectively ($p = 0.088$). There were differences in outcomes between adults and children when compared separately by graft types. In adults, 10-year patient survival was significantly lower for split extended right liver graft compared with adult whole liver and living-donor right liver graft (57% versus 72% versus 75%, respectively, $p = 0.03$). Graft survival for adults was similar for all graft types. Retransplantation, recipient age older than 60 years, donor age older than 45 years, split extended right liver graft, and cold ischemia time > 10 hours were predictors of diminished patient survival outcomes. In children, the 10-year patient and graft survivals were similar for all graft types.

CONCLUSIONS: Longterm graft survival rates in both adults and children for segmental grafts from deceased and living donors are comparable with those in whole organ liver transplantation. In adults, patient survival was lower for split compared with whole grafts when used in retransplantations and in critically ill recipients. Split graft-to-recipient matching is crucial for optimal organ allocation and best use of a scarce and precious resource. (J Am Coll Surg 2009;208:682–691. © 2009 by the American College of Surgeons)

Donor availability is the principal limiting factor for expansion of liver transplantation (LT). In 2007, there were 17,000 candidates on the waiting list; only 6,400 patients received transplants and more than 2,300 patients died for lack of donor organs (2008 Organ Procurement and Transplantation Network/Scientific Resistry of Transplant Recipients). With the scarcity of whole organ grafts, particularly in small children, innovative procedures using partial liver grafts from deceased and living donors have improved the availability of donor organs and lowered mortality on the transplant waiting list.

The ability to use partial hepatic grafts is dependent on the segmental hepatic anatomy (as shown in Figure 1), and regeneration potential of the transplanted graft and the remnant liver. Table 1 summarizes various functional grafts used in liver transplantations for both adults and children. Deceased-donor grafts are of whole organ and split types. Whole organs are used for both pediatric and adult recipients; the conventional split types produce smaller segment

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Abbreviations and Acronyms

LDLT = living-donor segmental graft liver transplantation
LT = liver transplantation
MELD = Model for End-Stage Liver Disease
SL-ER = split extended right liver graft
SLT = split-graft liver transplantation
WLT = whole-organ liver transplantation

II to III grafts for children and larger extended-right grafts for adults. Splitting the liver can also yield functional grafts for two small adults. The full left-right splitting remains experimental because of its inferior outcomes compared with whole-organ LT (WLT).[1,2] There are two methods of splitting the liver. In the ex vivo technique, the whole organ is retrieved and preserved and then divided into two functional grafts on the back table.[3] The in situ method divides the hepatic parenchyma in the heart-beating brain-dead donor before aortic cross-clamping and cold perfusion.[4,5] Ex vivo grafts are subjected to a longer cold ischemia time and graft rewarming, which may have a deleterious effect on graft function after transplantation. Advantages of the in situ method include shorter cold ischemia time, minimal graft rewarming, and easier identification of biliary and arterial systems. Living donors provide segmental grafts including left lateral for pediatric recipients and right or left partial hepatic grafts for adults.

Deceased and living donors have been complementary in providing grafts for small children and have resulted in a significant decline in mortality in patients on the pediatric waiting list. For adults, the use of segmental grafts from both deceased and living donors has not gained wide application. Split-graft liver transplantation (SLT) in adults is controversial; proponents report outcomes comparable with those with WLT,[6-8] but others argue that the procedure converts an otherwise optimal whole organ to a marginal segmental graft.[9,10] For living-donor segmental graft liver transplantation (LDLT), the risk to the living donor remains a subject of ethical debate, and the annual volume of LDLT in the US has continued to decline for 7 consecutive years, from a total of 520 in 2001 to 266 in 2007.

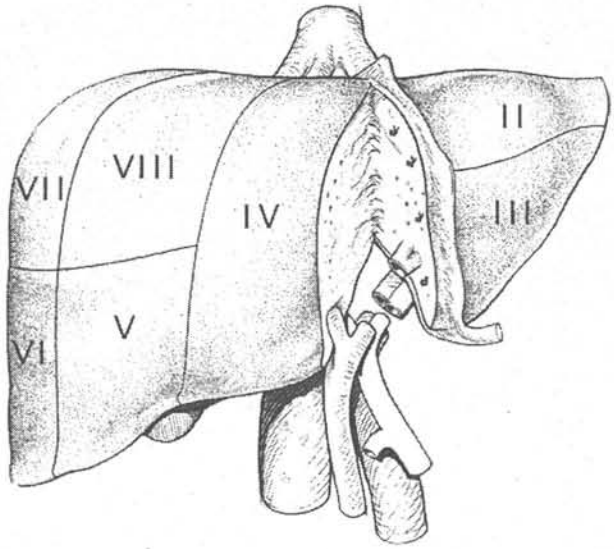

Figure 1. Conventional in situ split technique. The conventional in situ split technique separates the hepatic parenchyma to the right of the falciform ligament and yields a smaller left lateral graft (segments II and III) for a child and a larger extended-right graft (segments I, IV to VIII) for an adult recipient. (From: Yersiz H, Renz JF, Hisatake GM, et al. The conventional technique of in situ split-liver transplantation. J Hepatobiliary Pancreat Surg 2003;10:11–15, Fig. 2, with kind permission of Springer Science & Business Media.)

Although short-term outcomes for segmental grafts have been comparable with those with WLT, few longterm data are reported.[6,7,11] In addition, when data were analyzed separately for pediatric and adult recipients, there were distinct differences in outcomes based on graft types.[10,12] This single center study was undertaken to compare longterm outcomes for whole and segmental liver grafts in adult and pedi-

Table 1. Organ Grafts Used in Liver Transplantation

Donor	Graft	Segments	Common name	Recipient	Abbreviation
Deceased	Whole	I–VIII		Adult	Adult-WL
				Pediatric	Ped-WL
	Split	II–III	Left lateral	Pediatric	SL-LL
		I, IV–VIII	Extended right	Adult	SL-ER
		I–IV	Full left	Adult	SL-FL
		V–VIII	Full right	Adult	SL-FR
Living	Segmental	II–III	Left lateral	Pediatric	LD-LL
		I–IV	Left	Adult	LD-L
		V–VIII	Right	Adult	LD-R

Adult-WL, adult deceased donor whole liver graft; LD-L, living donor left liver graft; LD-LL, living donor left lateral liver graft; LD-R, living donor right liver graft; Ped-WL, pediatric deceased donor whole liver graft; SL-ER, split extended right liver graft; SL-FL, split-extended full left liver graft; SL-FR, split extended full right liver graft; SL-LL, split extended left lateral liver graft.

Table 2. Patient and Donor Characteristics by Graft Type

Characteristic	Adult				Children			
	Adult-WL (n = 2,433)	SL-ER (n = 72)	LD-R (n = 41)	p Value	Ped-WL (n = 284)	SL-LL (n = 109)	LD-LL (n = 49)	p Value
Recipient								
Median age, y	52	51	52	0.5019	3.4	1	0.9	<0.0001
Female gender, n (%)	968 (40)	14 (19)	14 (34)	<0.0001	156 (55)	60 (55)	28 (57)	0.9588
History of earlier LT, n (%)	337 (14)	9 (13)	0	0.0357	72 (25)	16 (15)	8 (16)	0.0446
Urgent LT, n (%)	303 (13)	19 (26)	1 (2)	0.0003	83 (29)	47 (43)	15 (31)	0.0251
Donor								
Median age, y	37	20	35	<0.0001	3	18	31	<0.0001
Median hospital stay, d	2	3	n/a	0.2418	3	2	n/a	0.3089
Vasopressor agents ≥ 2, n (%)	388 (17)	22 (31)	n/a	0.0032	75 (26)	35 (32)	n/a	0.785
Graft ischemia								
Median graft cold ischemia, min	402	348	45	<0.0001	468	330	60	<0.0001
Median graft warm ischemia, min	30	41	48	<0.0001	48	66	66	<0.0001

Adult-WL, adult deceased-donor whole-organ graft; LD-LL, living-donor left lateral graft; LD-R, living-donor right graft; LT, liver transplantation; Ped-WL, pediatric deceased-donor whole-organ graft; SL-ER, split extended right graft; SL-LL, split left lateral graft.

atric liver transplant recipients and to determine predictors for patient and graft survival for different graft types.

METHODS

Data collection

Using a prospectively collected transplant database, we performed a retrospective analysis of 2,988 liver transplantations in both adults (18 years or older) and children (18 years or younger) at the Dumont-UCLA Transplant Center, from August 1993 through May 2006. The UCLA Institutional Review Board approved the study. The median followup time was 5 years.

Patient characteristics

All patients with end-stage liver disease were evaluated for LT by a multidisciplinary team, as previously described.[13] Before the year 2002, patients were listed for liver transplant candidacy according to the United Network for Organ Sharing (UNOS) status categories; from 2002 to the present, the current Model for End-Stage Liver Disease (MELD) system has been used.[14] Patient and graft survival outcomes were analyzed by the type of graft received: whole-organ graft from deceased donors and partial hepatic grafts from either deceased or living donors. In addition, results were compared among adult and pediatric transplant recipients.

Operative procedures

Deceased-donor, whole-organ liver transplantation

The surgical procedure for whole-organ orthotopic liver transplantation was performed in a standard manner, with either preservation or replacement of the recipient's inferior vena cava.[15]

Deceased-donor, in situ split-liver transplantation

The in situ split technique was performed on livers from deceased donors that met criteria for splitting, as previously described.[16] Figure 1 demonstrates isolation of the left hepatic artery, left branch of the portal vein, and the extrahepatic portion of the left hepatic vein followed by transection of the parenchyma at about 0.5 cm to 1 cm to the right of the falciform ligament, yielding a left lateral graft (SL-LL; segments II and III) and an extended right graft (SL-ER; segments I, IV to VIII). The left hilar plate and bile ducts were divided sharply with scissors so as not to devascularize the duct. The middle hepatic vein, the entire length of the celiac axis, portal vein, bile duct, and vena cava were retained with the extended right graft.

The recipient operation in children was performed by native hepatectomy with retention of the inferior vena cava, and the left lateral graft was implanted using a piggyback technique in which the venous outflow was anastomosed to the confluence of the recipient hepatic veins. In adults, the extended right graft was prepared in the manner identical to preparation of a whole graft, with the addition of oversewing the left hepatic and portal vein orifices and the left hepatic duct stump. The extended right graft was implanted in the same manner as a whole graft.

Living-donor liver transplantation

The techniques of living-donor partial hepatectomy have been described.[17-19] In adult-to-child LDLT, the left lateral graft (LD-LL; segments II and III) is procured. In adult-

to-adult living-donor liver transplantation, the right lobe (LD-R; segments V to VIII) is procured in the donor with preservation of middle hepatic vein. The living-donor segmental grafts (left lateral and right lobe) were transplanted with recipient caval preservation (piggyback technique) and previously described vascular and biliary reconstruction.[17,18]

Immunosuppression

The primary maintenance immunosuppression regimen consisted of cyclosporine (CyA, Sandimmune or Neoral, Novartis Pharmaceuticals) until 1994 and tacrolimus (Prograf, Astellas Pharmaceutical Inc) thereafter. Most patients received triple immunotherapy with steroids and either azathioprine or mycophenolate mofetil (CellCept, Roche Pharmaceuticals).[13]

Statistical analysis

Patient and graft survival curves were computed using Kaplan-Meier methods and compared using log rank tests. Medians were compared using the Wilcoxon test and proportions using the chi-squared test. Both univariate and multivariate analyses were conducted using Cox's proportional hazard model. The backward stepwise procedure was used for variables selection with retention criteria at a p value of ≤ 0.25 level of significance. In the multivariate analysis, a p value of < 0.05 was considered significant. Statistical analysis was performed using SAS software, version 9.1 (SAS Institute).

RESULTS

Recipient characteristics

Among the 2,988 liver transplantations during the 13-year study period, 2,546 were performed in adults (85%) and 442 in children (15%). Graft types in adults included adult deceased-donor whole liver graft (adult-WL) in 2,433 (95%), SL-ER in 72 (3%), and living-donor right liver graft in 41 (2%). Graft types in children included pediatric deceased-donor whole liver graft (ped-WL) in 284 (64%), SL-LL in 109 (25%), and LD-LL in 49 (11%).

Patient characteristics are compared by graft type in Table 2. In adults, the median recipient ages among the three groups were similar. Although both whole and split grafts were used more often than living-donor grafts for recipients with previous liver transplants, split grafts were frequently used for recipients requiring urgent transplants. The most common liver disease in adult recipients was hepatitis C cirrhosis (32%) followed by alcohol-induced liver disease (15%) and acute liver failure (14%). Comparing indications for LT for all graft types, acute liver failure was more frequent in SLT compared with adult-WLT and LDLT (26% versus 13% versus 2.4%; $p = 0.0003$); primary sclerosing cholangitis was a frequent reason for LDLT. The frequency of hepatitis B, hepatitis C, alcohol-induced liver disease, and cryptogenic cirrhosis were similar for all graft types.

In children, recipients of split and living-donor grafts were smaller children younger than 1 year of age (Table 2). More recipients with previous transplants received whole-organ grafts. Split grafts as with adults, were used more often for urgent transplantation. The most common indications for LT in children were biliary atresia (42%) and acute liver failure (34%). A higher proportion of pediatric recipients with biliary atresia received a split graft compared with a living-donor segmental or deceased-donor whole-organ graft (54% versus 41% versus 34%, respectively, $p = 0.0023$). The distribution of other liver diseases, including neonatal hepatitis, cryptogenic cirrhosis, and malignancy, was similar among all graft types.

Donor characteristics and graft ischemia times

Table 2 compares the donor characteristics and graft ischemia duration for both adults and children. In adults, donors of split grafts were younger than whole-organ and living donors ($p < 0.0001$). There were more deceased donors for split than whole grafts that required two or more vasopressor agent support during organ procurement (31% versus 17%, $p = 0.0032$). The cold ischemia duration for living-donor segmental grafts, as would be expected, was shorter compared with that for deceased-donor grafts. The need for complex microvascular reconstructions in segmental grafts accounted for a longer warm ischemia time compared with whole-organ grafts.

In children, whole-organ donors were younger than deceased and living donors of segmental grafts. The duration of both cold and warm graft ischemia varied between deceased- and living-donor graft types, as in adults (Table 2).

Patient survival

The 10-year patient survival curves for adults and children are shown in Figure 2A. For both adults and children, survival was similar for all graft types. When data were analyzed separately for adult and pediatric recipients, there were distinct differences in outcomes based on graft types. Figure 3A shows that the longterm patient survival curve in adults for SL-ER was significantly lower compared with LD-R and adult-WL (57% versus 73% versus 71%; $p = 0.033$). In contrast to the adults, longterm outcomes for all graft types in children were similar, as shown in Figure 3B.

Multivariate analysis of patient survival in adult recipients is shown in Table 3. Statistically significant independent predictors of diminished survival in adult recipients included recipient age older than 60 years, retransplanta-

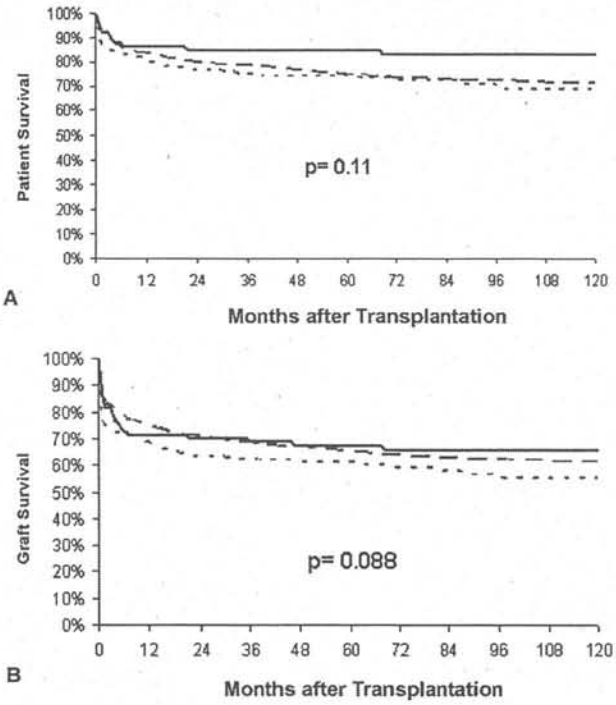

Figure 2. Overall survival of different graft types after liver transplantation. (A) Patient; (B) graft. Solid line, living donor; dashed line, whole liver; dotted line, split-graft liver transplantation.

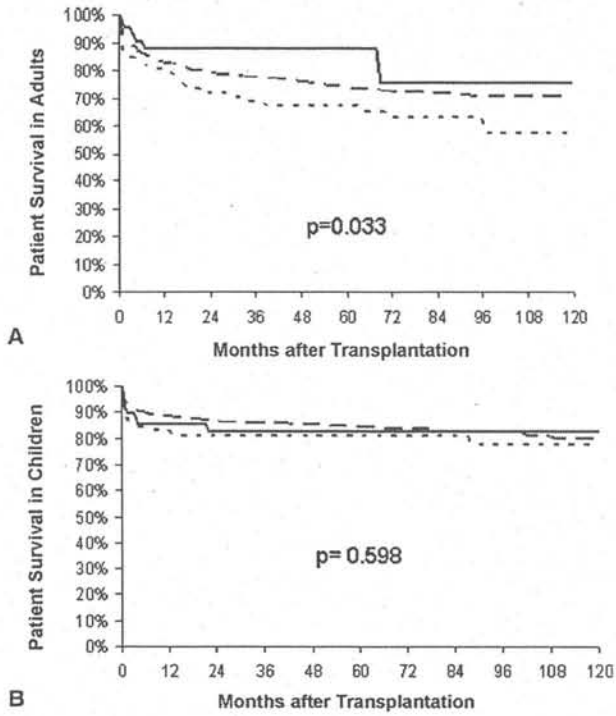

Figure 3. Patient survival after liver transplantation. (A) Adult. Solid line, living-donor right liver graft; dashed line, whole liver; dotted line, split extended right liver graft. (B) Children. Solid line, living-donor left lateral liver graft; dashed line, whole liver; dotted line, split-graft left-lateral liver transplantation.

tion, SL-ER graft, donor age older than 45 years, and cold ischemia time > 10 hours. In children, Table 4 shows that a history of previous LT and use of split grafts were associated with lower survival outcomes.

Table 3. Multivariate Analysis of Patient and Graft Survival in Adults

Variables	Hazard ratio	p Value
Patient survival		
Recipient age >60 y	1.6	0.0002
Previous LT	2.6	<0.0001
Graft type		
Whole	1	
SLT	2	0.0008
LDLT	0.8	0.6320
Donor age >45 y	1.5	0.0361
Cold ischemia time >10 h	1.4	0.0066
Graft survival		
Previous LT	1.8	<0.0001
Graft type		
Whole	1	
SLT	1.9	0.0010
LDLT	1.1	0.6572
Donor age >45 y	1.4	0.0223
Cold ischemia time >10 h	1.3	0.0077

LDLT, living-donor segmental graft liver transplantation; LT, liver transplantation; SLT, split-graft liver transplantation.

Graft survival

Figure 2B demonstrates that overall 10-year graft survival outcomes for SLT, LDLT, and WLT were comparable (55% versus 65% versus 62%, respectively; p = 0.088). Graft survival curves in adults and children are compared separately in Figure 4. There were no significant differences

Table 4. Multivariate Analysis of Patient and Graft Survival in Children

Variables	Hazard ratio	p Value
Patient survival		
Previous LT	4.9	<0.0001
Graft type		
Whole	1	
SLT	2.2	0.0011
LDLT	1.7	0.1923
Graft survival		
Previous LT	1.7	0.0031
Graft type		
Whole	1	
SLT	1.5	0.0198
LDLT	1.1	0.8433

LDLT, living-donor segmental graft liver transplantation; LT, liver transplantation; SLT, split-graft liver transplantation.

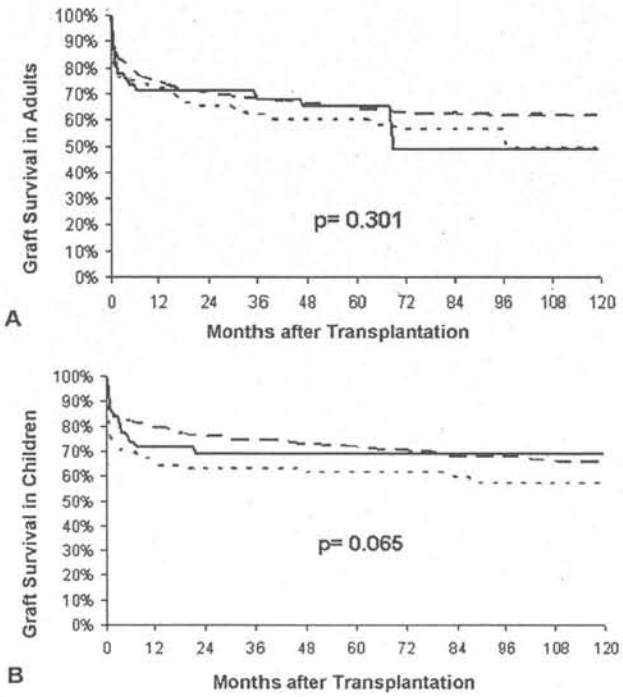

Figure 4. Graft failure-free survival after liver transplantation. (A) Adult. Solid line, whole liver; dashed line, split extended right liver graft; dotted line, living-donor right liver graft. (B) Children. Solid line, living-donor left lateral liver graft; dashed line, whole liver; dotted line, split-graft left-lateral liver transplantation.

in graft survival for all graft types in both adults (Fig. 4A) and children (Fig. 4B).

Multivariate analysis of graft survival in adults is shown in Table 3. The predictors of graft failure included history of previous LT, SL-ER grafts, donor age older than 45 years, and cold ischemia time > 10 hours. In children, history of previous LT and SL-LL graft were independent predictors of diminished survival (Table 4).

Causes of loss

For both adults and children, sepsis and multi-organ system failure was the most common cause of patient death. Regarding graft failure, recurrence of liver disease and chronic rejection were frequent causes of graft loss in adults. The noteworthy difference between the three groups was that recurrence of liver disease in transplanted segmental grafts from deceased and living donors was more common than in whole-organ grafts (50% versus 56% versus 16%, respectively; p = 0.0133). For children, chronic rejection and hepatic artery thrombosis were common reasons for graft loss. There were no significant differences in causes of graft failure among the three groups.

Complications

The major posttransplant complications for various graft types are compared in Table 5. In adults, there were no differences except for a higher rate of retransplantation in recipients of living-donor grafts. In children, there was a higher frequency of primary graft nonfunction in split grafts because of increased use in urgent and redo transplantations. Living-donor grafts had a higher rate of portal venous thrombosis than whole grafts.

DISCUSSION

This study compared longterm outcomes for whole and segmental grafts in adult and pediatric liver transplant recipients. Earlier studies report conflicting short- and midterm survival outcomes. Although single-center studies[6,7,11] demonstrated no difference in 1-, 3-, and 5-year outcomes after SLT and WLT, registry data report SLT as an independent predictor of poor patient outcomes for both adults and children.[20-23]

Our study showed equivalent overall longterm outcomes after whole, split, and living-donor graft LT. When results were analyzed separately by recipient age, there were distinct differences in outcomes and factors that affect survival. Although the 10-year graft survival after whole, split, and living-donor transplantation was comparable in adults, the patient survival was lower for split grafts compared with whole grafts when used in retransplants and critically ill recipients. Patients who require retransplanta-

Table 5. Complications

	Adult							Children						
	SL-ER (n = 72)		LD-R (n = 41)		Adult-WL (n = 2,433)		p	SL-LL (n = 109)		LD-LL (n = 49)		Ped-WL (n = 284)		p
Complication	n	%	n	%	n	%	Value	n	%	n	%	n	%	Value
Primary graft nonfunction	4	5.5	5	12.2	206	8.4	0.4811	9	8.3	2	4.1	5	1.8	0.0097
Biliary complications	3	4.2	6	14.6	178	7.3	0.1126	3	2.7	3	6.1	9	3.2	0.5632
Hepatic artery thrombosis	3	4.2	3	7.3	89	3.7	0.5112	6	5.5	2	4.1	19	6.7	0.7597
Portal vein thrombosis	0		0		24	1	0.763	4	3.7	4	8.2	2	0.7	0.0037
Retransplantation	5	6.9	9	22	271	11.1	0.0476	24	22	8	16.3	44	15.5	0.3035

Adult-WL, adult deceased-donor whole-organ graft; LD-LL, living-donor left lateral graft; LD-R, living-donor right graft; Ped-WL, pediatric deceased-donor whole-organ graft; SL-ER, split extended right graft; SL-LL, split left lateral graft.

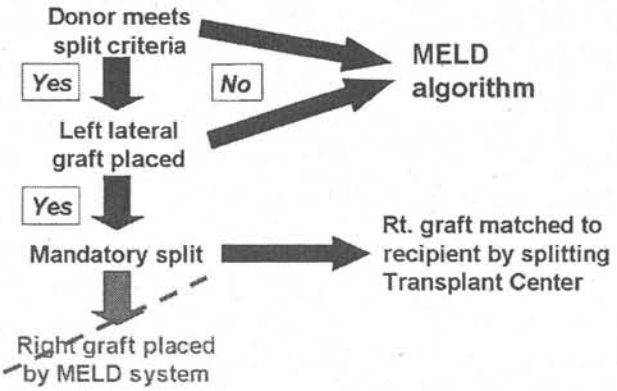

Figure 5. Proposed organ allocation system for optimal use of split liver grafts. MELD, Model for End-Stage Liver Disease.

tion of the liver have higher acuity of illness, including multi-organ system failure, and undergo complex redo transplantation procedures that may be associated with hemodynamic instability during the perioperative period. These operative circumstances, in addition to both donor graft and recipients predictors, affect patient outcomes after transplantation and should be considered in the allocation of split grafts to recipients.

We found it interesting as for graft failure, that recurrence of liver disease was more common in segmental grafts from both deceased and living donors compared with whole grafts. A possible explanation may be that ischemia and reperfusion injury inherent in segmental grafts synergistically activates and perpetuates stellate cells leading to accelerated fibrosis in cases of hepatitis C infection[24] or immunologic mechanisms in malignancy and autoimmune liver diseases.[25-27] Another theory that may explain a more severe recurrence of hepatitis C after segmental liver transplantation is attributed to intense proliferation and regeneration of the hepatocytes in segmental grafts that augment viral translation and replication.[28,29] The relationship between hepatocellular injury, hepatic proliferation, and viral replication remains unproved, and several studies have shown similar frequency of disease recurrence and outcomes between whole grafts and segmental grafts.[30,31]

For children, segmental grafts from deceased and living donors have increased available organs for smaller and younger recipients and have significantly decreased the pediatric waitlist mortality. Several studies have reported conflicting results after LT with segmental liver grafts in children using registry data. Although analysis of the United Network of Organ Sharing (UNOS) database by Becker and colleagues[32] demonstrated comparable short-term outcomes between SLT and WLT, several studies using the same pooled data from the United Network of Organ Sharing[33] and transplant registry data from the Studies of Pediatric Liver Transplantation (SPLIT)[22] reported inferior outcomes after SLT compared with WLT. We found no significant differences in longterm patient and graft survival outcomes between whole and segmental liver grafts in pediatric recipients.

In summary, our study demonstrates equivalent overall longterm outcomes for whole and segmental grafts in adult and pediatric liver transplant recipients. The major challenge toward optimal use of these grafts lies in the organ allocation policy. Under the current MELD system, each split graft is allocated to patients according to their MELD scores. Because the patient with the highest MELD score receives the organ, this system allocates the split graft to the sickest transplant candidates and limits graft-to-recipient matching, which is crucial for best results. Allocation of the split extended right grafts to adults with lesser acuity of illness may improve patient survival outcomes. We propose an alternate system to allow optimal use of split grafts (Fig. 5). If the donor fails to meet split criteria or the left lateral graft is not allocated to a recipient, the whole organ is assigned by the MELD algorithm. But when the donor meets split criteria and the left lateral graft is allocated, the liver is split, and rather than allocating the right graft through the MELD system, the right graft instead is matched to an ideal recipient by the splitting transplant center. An organ allocation system with such flexibility would encourage adult-to-child candidate pairing from the same transplantation center and allow preoperative surgical and logistic planning to minimize graft ischemia duration. This proposal aims to optimize graft-to-recipient matching that not only would substantially reduce the loss of lives on the transplant waiting list but also improve outcomes after liver transplantation.

Author contributions

Study conception and design: Hong, Yersiz, Farmer, Ghobrial, Hiatt, Busuttil
Acquisition of data: Hong, Duffy, Nonthasoot, Collins
Analysis and interpretation of data: Hong, Duffy
Drafting of manuscript: Hong, Yersiz, Farmer, Duffy, Ghobrial, Nonthasoot, Collins, Hiatt, Busuttil
Critical revision: Hong, Hiatt, Busuttil

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Discussion

DR LYNT B JOHNSON (Washington, DC): I would like to thank Dr Hong and Dr Busuttil for the privilege of discussing their paper and congratulate the authors on yet another large single center experience in liver transplantation.

Methods to successfully increase availability of donor organs are necessary given the continued shortage of organ donors. This shortage is particularly acute for patients with end-stage liver disease since there are not alternative methods for liver function replacement as there is for patients with end-stage renal disease.

The authors show that in their large single center experience the longterm overall patient and graft survival were similar between patients with split liver transplants, whole liver transplants, and live donor liver transplantation with a median follow-up of five years. But the adult ten-year patient survival was worse with split liver extended right grafts. And this leads to several questions for the authors.

The majority of split liver extended right grafts in adults were used for patients requiring urgent transplantation. Ordinarily, these patients would have access to adult whole liver grafts if they were status I or II liver failure. Does the center have an internal policy of splitting ideal donor grafts obtained in adult extended right graft along with a

参考資料4

UNOS 小児ドナーの分配システム

Allocation of pediatric donors

recipient age	donor age 0–10			donoe age 11–17		
	1A			1A		
	local	regional	national	local	regional	national
0－11	①		②	①	②	⑯
12－17			⑮			
18－	③	④	⑯	③	④	⑰
	1B			1B		
	local	regional	national	local	regional	national
0－11	⑤		⑰	⑤	⑥	⑱
12－17						
	PELD/MELD≥15			PELD/MELD≥15		
	local	regional	national	local	regional	national
0－11	⑥		⑱	⑦		⑲
12－17	⑦	⑨	⑲	⑧	⑩	⑳
18－	⑧	⑩	⑳	⑨	⑪	㉑
	PELD/MELD＜15			PELD/MELD＜15		
	local	regional	national	local	regional	national
0－11	⑥		⑱	⑦		⑲
12－17	⑪	⑬	⑲	⑫	⑭	⑳
18－	⑫	⑭	⑳	⑬	⑮	㉑

1A:fluminant hepatic failure, PNF, HAT, acute decompensated Wilson

1B:chronic liver disease in children

参考資料5

年齢別小児身長体重の幅と標準肝容積の幅

年齢	身長(3%/−2SD)	体重(3%/−2SD)	BSA(−)	SLV(最少)	身長(97%/+2SD)	体重(97%/+2SD)	BSA(+)	SLV(最大)
12ヶ月	0.709	7.79	0.378	269	0.785	10.77	0.466	331
6歳	1.052	15.49	0.673	478	1.251	28.03	0.982	696
10歳	1.264	20.12	0.859	609	1.538	50.98	1.471	1041
15歳	1.467	35.14	1.213	859	1.804	82.2	2.023	1431
17歳	1.474	36.98	1.244	881	1.824	83.74	2.055	1454

参考資料6

肝臓移植希望者の転帰

登録時年代	希望	%	死体肝移植済	%	死亡	%	取消	%	生体肝移植済	%	海外渡航	%	総計
0歳	3	20	2	13	4	27	1	7	4	27	1	7	15
1歳	0	0	0	0	3	38	0	0	5	63	0	0	8
2歳	4	16	5	20	3	12	2	8	10	40	1	4	25
11～20歳	11	20	8	15	14	25	3	5	16	29	3	5	55
21～30歳	28	34	11	13	22	27	8	10	11	13	2	2	82
31～40歳	41	24	22	13	53	31	16	9	33	19	6	4	171
41～50歳	75	27	17	6	108	38	26	9	46	16	10	4	282
51～60歳	92	26	18	5	147	41	41	12	51	14	6	2	355
61歳～70歳	30	21	4	3	80	56	15	11	12	8	1	1	142
71歳以上	0		0		0		0		0		0		0
総計	284		87		434		112		188		30		1135

2010/12/14現在

参考資料７

改正法施行後の脳死下での臓器提供事例について(平成22年12月18日現在)

	脳死判定事例(提供事例)	提供日	原疾患	提供施設	書面による意思表示	心臓	肺	肝臓	膵臓	腎臓	小腸	眼球
1	第88例目(第87例目)	平成22年8月10日	20代 男性 交通外傷	関東甲信越	なし	国立循環器病研究センター	岡山大(両肺)	東大 —	藤田保健衛生大(腎同時)	群馬大	—	東京歯科大学市川総合病院 東京歯科大学市川総合病院
2	第89例目(第88例目)	平成22年8月19日	男性	近畿	なし	東大	阪大(両肺)	京大 —	名古屋第二赤十字(腎同時)	神戸大	—	— —
3	第90例目(第89例目)	平成22年8月22日	50代 女性 脳血管障害	東海	なし	東北大	東北大(両肺)	阪大 —	名古屋第二赤十字(腎同時)	藤田保健衛生大	—	名古屋大 藤田保健衛生大
4	第91例目(第90例目)	平成22年8月27日	40代 女性 くも膜下出血	松山赤十字病院	あり	—	—	北海道大 —	東京女子医大(腎同時)	愛媛県立中央病院	—	愛媛大 愛媛大
5	第92例目(第91例目)	平成22年8月29日	40代 男性 蘇生後脳症	関東甲信越	なし	—	京大 京大	国立成育医療研究センター 京大	九州大(腎同時)	千葉大	東北大	東京歯科大学市川総合病院 東京歯科大学市川総合病院
6	第93例目(第92例目)	平成22年9月2日	40代 女性 くも膜下出血	北部九州	なし	国立循環器病研究センター	東北大(両肺)	名古屋大 —	—	東京女子医大 長崎医療センター	東北大	— —
7	第94例目(第93例目)	平成22年9月4日	成人 男性 頭部外傷	東北	なし	東京女子医大	岡山大 京大	名古屋大 —	藤田保健衛生大	福島県立医大 福島県立医大	九州大	— —
8	第95例目(第94例目)	平成22年9月7日	成人 男性 蘇生後脳症	関東甲信越	なし	国立循環器病研究センター	—	北海道大 —	東京女子医大(腎同時)	長野赤十字	—	長野赤十字 長野赤十字
9	第96例目(第95例目)	平成22年9月12日	40代 男性 心疾患	市立札幌病院	なし	—	岡山大(両肺)	東大 —	藤田保健衛生大(腎同時)	市立札幌	—	— —
10	第97例目(第96例目)	平成22年9月18日	30代 男性	近畿	なし	国立循環器病研究センター	—	京大 岡山大	阪大(腎同時)	近江八幡市立総合医療セン	—	— —
11	第98例目(第97例目)	平成22年9月25日	70代 男性 脳幹梗塞	北部九州	なし	—	—	— —	—	熊本赤十字 熊本赤十字	—	— —
12	第99例目(第98例目)	平成22年9月27日	50代 男性 脳血管障害	北海道	なし	埼玉医科大学国際医療セン	東北大 福岡大	京大 —	—	北海道大 市立札幌	—	— —
13	第100例目(第99例目)	平成22年9月30日	50代 女性 くも膜下出血	市立札幌病院	なし	阪大	東北大	京大 —	東北大(腎同時)	札幌北楡	—	— —
14	第101例目(第100例目)	平成22年9月30日	30代 男性 蘇生後脳症	東北大学病院	なし	国立循環器病研究センター	—	京大 —	阪大(腎同時)	仙台社会保険	—	東北大 東北大
15	第102例目(第101例目)	平成22年10月3日	70代 女性 脳出血	関東	なし	—	—	岡山大 —	—	東邦大医療センター 東京女子医大	—	— —
16	第103例目(第102例目)	平成22年10月13日	18歳以上 男性 脳血管障害	西日本	なし	—	—	阪大 —	東京女子医大(腎同時)	日赤和歌山医療セン	—	— —
17	第104例目(第103例目)	平成22年11月3日	30代 女性 くも膜下出血	九州大学病院	なし	阪大	岡山大(両肺)	広島大 —	藤田保健衛生大(腎同時)	福岡赤十字	—	— —
18	第105例目(第104例目)	平成22年11月21日	50代 男性 脳血管疾患	高山赤十字病院	なし	東大	福岡大(左肺) —	東大 —	—	静岡県立総合病院 岐阜大	—	岐阜大 眼科杉田病院
19	第106例目(第105例目)	平成22年11月26日	60代 男性 低酸素脳症	福山市民病院	なし	阪大	岡山大(両肺)	— —	—	県立広島 岡山医療センター	—	広島大 木村眼科内科病院
20	第107例目(第106例目)	平成22年11月26日	60代 女性 脳血管障害	札幌医科大学附属病院	なし	—	長崎大 東北大	国立成育医療研究センター —	東北大(腎同時)	市立札幌	—	— —
21	第108例目(第107例目)	平成22年12月2日	40代 男性 脳血管障害	関東	なし	東大	京大(左肺) —	順天堂大医学部附属順天堂医院 —	国立病院機構千葉東(腎同時)	東京女子医大	—	— —
22	第109例目(第108例目)	平成22年12月4日	30代 女性 脳血管障害	九州大学病院	なし	阪大	阪大 福岡大	— —	藤田保健衛生大(腎同時)	九州大	—	— —
23	第110例目(第109例目)	平成22年12月10日	60代 女性 くも膜下出血	大阪市立総合医療センター	なし	—	— —	岡山大 —	国立病院機構千葉東(腎同時)	大阪市立大	—	— —
24	第111例目(第110例目)	平成22年12月13日	60代 女性 脳血管障害	国立病院機構長崎医療センター	なし	東大	— —	広島大 —	九州大(腎同時)	長崎大	—	— —
25	第112例目(第111例目)	平成22年12月17日	18歳以上 男性 脳血管障害	北海道	なし	—	— —	信州大 —	— —	—	—	施設名確認中 施設名確認中
26	第113例目(第112例目)	平成22年12月18日	30代 男性 くも膜下出血	岐阜県総合医療センター	なし	東大	— —	名古屋大 —	京都府立医科大 岐阜大	豊橋市民病院	—	— —
27	第114例目(第113例目)	平成22年12月18日	30代 男性 脳血管障害	関東	なし	阪大	— —	京大 —	香川大(腎同時)	北里大	—	— —

肝臓移植希望者（レシピエント）選択基準（案）

（略）

２．優先順位

（略）

（３）臓器提供者（ドナー）が 18 歳未満の場合には、選択時に１８歳未満の移植希望者（レシピエント）に限り、１点を加点する。

３．具体的選択方法

適合条件に合致する移植希望者（レシピエント）が複数存在する場合には、優先順位は、以下の順に勘案して決定する。

（１）優先すべき親族を優先する。

（２）２．の（１）、（２）、（３）の合計点数が高い順とする。ただし、これらの条件が同一の移植希望者（レシピエント）が複数存在した場合は、待機期間の長い者を優先する。

（略）

Longterm Outcomes for Whole and Segmental Liver Grafts in Adult and Pediatric Liver Transplant Recipients: A 10-Year Comparative Analysis of 2,988 Cases

Johnny C Hong, et al (UCLA).

(J Am Coll Surg 2009;208:682–691)

BACKGROUND: Data on longterm outcomes after liver transplantation with partial grafts are limited. We compared 10-year outcomes for liver transplant patients who received whole grafts (WLT), split grafts from deceased donors (SLT), and partial grafts from living donors (LDLT).

STUDY DESIGN: We conducted a single-center analysis of 2,988 liver transplantations performed between August 1993 andMay 2006 with median followup of 5 years. Graft types included 2,717 whole-liver, 181 split-liver, and 90 living-donor partial livers. Split-liver grafts included 109 left lateral and 72 extended right partial livers. Living-donor grafts included 49 left lateral and 41 right partial livers.

RESULTS: The 10-year patient survivals forWLT, SLT, and LDLT were 72%, 69%, and 83%, respectively (p = 0.11), and those for graft survival were 62%, 55%, and 65%, respectively (p =0.088). There were differences in outcomes between adults and children when compared separately by graft types. In adults, 10-year patient survival was significantly lower for split extended right liver graft compared with adult whole liver and living-donor right liver graft (57% versus 72% versus 75%, respectively, p = 0.03). Graft survival for adults was similar for all graft types. Retransplantation,, recipient age older than 60 years, donor age older than 45 years, split extended right liver graft, and cold ischemia time >10 hours were predictors of diminished patient survival outcomes. In children, the 10-year patient and graft survivals were similar for all graft types.

CONCLUSIONS: Longterm graft survival rates in both adults and children for segmental grafts from deceased and living donors are comparable with those in whole organ liver transplantation. In adults, patient survival was lower for split compared with whole grafts when used in retransplantations and in critically ill recipients. Split graft-to-recipient matching is crucial for optimal organ allocation and best use of a scarce and precious resource.

Figure 3. Patient survival after liver transplantation. (A) Adult. Solid line, living-donor right liver graft; dashed line, whole liver; dotted line, split extended right liver graft. (B) Children. Solid line, living-donor left lateral liver graft; dashed line, whole liver; dotted line, split-graft left-lateral liver transplantation.

Figure 3A shows that the longterm patient survival curve in adults for SL-ER was significantly lower compared with LD-R and adult-WL (57% versus 73% versus 71%; p = 0.033). In contrast to the adults, longterm outcomes for all graft types in children were similar, as shown in Figure 3B.

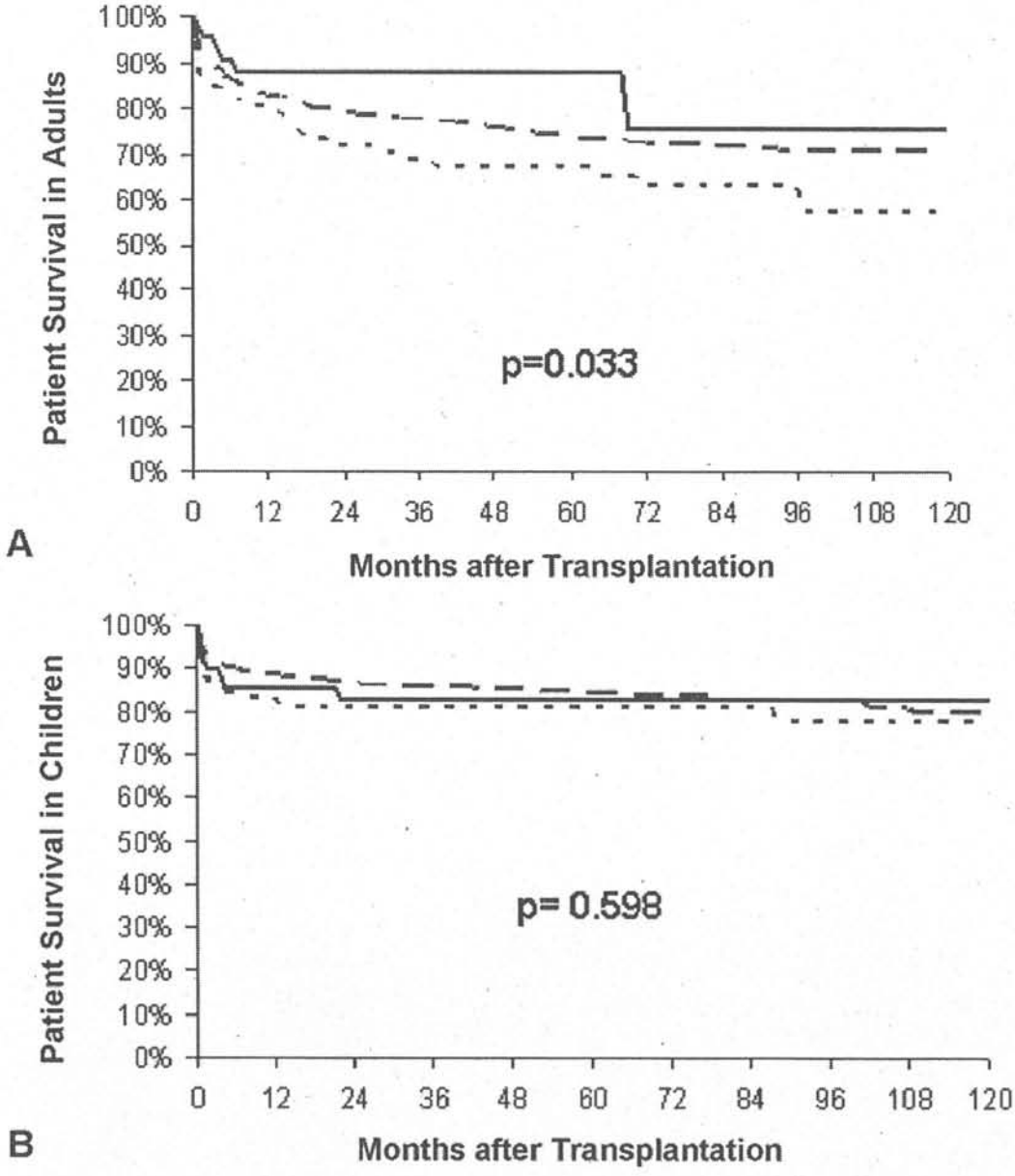

Table 4. Multivariate Analysis of Patient and Graft Survival in Children

In children, Table 4 shows that a history of previous LT and use of split grafts were associated with lower survival outcomes.

Variables	Hazard ratio	p Value
Patient survival		
Previous LT	4.9	<0.0001
Graft type		
Whole	1	
SLT	2.2	0.0011
LDLT	1.7	0.1923
Graft survival		
Previous LT	1.7	0.0031
Graft type		
Whole	1	
SLT	1.5	0.0198
LDLT	1.1	0.8433

LDLT, living-donor segmental graft liver transplantation; LT, liver transplantation; SLT, split-graft liver transplantation.