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.

REFERENCES

1. Cohen B, D'Amaro J. Some contemporary ethical considerations related to organ transplantation. Transpl Int 1995; 8: 238.
2. Bollinger RR. A UNOS perspective on donor liver allocation. United Network for Organ Sharing. Liver Transpl Surg 1995; 1: 47.
3. Yoshida EM. Selecting candidates for liver transplantation:a medical ethics perspective on the micro allocation of a scarce and rationed resource. Can J Gastroenterol 1998; 12: 209.
4. Neuberger J, Adams D, MacMaster P, Maidment A, Speed M. Assessing priorities for allocation of donor liver grafts: survey of public and clinicians. BMJ 1998; 317: 172.
5. Lucey MR, Brown KA, Everson GT, et al. Minimal criteria for placement of adults on the liver transplant waiting list: a report of a national conference organized by the American Society of Transplant Physicians and the American Association for the Study of Liver Diseases. Liver Transplant Surg 1997; 3: 628.
6. Showstack J, Katz PP, Lake JR, et al. Resource utilization in liver transplantation: effects of patient characteristics and clinical practice. NIDDK Liver Transplantation Database Group. JAMA 1999; 281: 1381.
7. An update on liver transplantation in the United States: recipient characteristics and outcome. In: Belle SH, Beringer KC, Detre KM, eds. UNOS Liver Registry, Pittsburgh. Clinical Transplants 1995. Chapter 2, p. 18–32.
8. Colombani PM, Cigarroa FG, Schwarz K, Wise B, Maley WE, Klein AS. Liver transplantation in infants younger than 1 year of age. Ann Surg 1996; 223: 658.
9. Van der Werf WJ, D'Alessandro AM, Knechtle SJ, et al. Infant pediatric liver transplantation results equal those for older pediatric patients. J Pediatr Surg 1998; 33: 20.
10. Bonatti H, Muiesan P, Connelly S, et al. Hepatic transplantation in children under 3 months of age: a single centre's experience. J Pediatr Surg 1997; 32: 486.
11. Woodle ES, Millis JM, So SKS, et al. Liver transplantation in the first three months of life. Transplantation 1998; 66: 606.
12. Broelsch CE, Emond JC, Thistlethwaite JR, et al. Liver transplantation, including the concept of reduced-size liver transplants in children. Ann.Surg 1988; 208: 410.
13. Goyet Jd, Hausleithner V, Reding R, Lerut J, Janssen M, OTTE J-B. Impact of innovative techniques on the waiting list and results in pediatric liver transplantation. Transplantation 1993; 56: 1130.
14. Emond JC, Heffron TG, Thistlethwaite JR. Innovative approaches to donor scarcity: A critical comparison between split liver and living related liver transplantation. Hepatology 1991; 14: 92.
15. Pritsker AAB, Martin DL, Renst J, et al. Organ Transplantation Policy Evaluation: In Proceedings of the Winter Simulation Conference, 1995; 1314.
16. Slooff MJ. Reduced size liver transplantation, split liver transplantation, and living related liver transplantation in relation to the donor organ shortage. Transplant Int 1995; 8: 65.
17. Sindhi R, Rosendale J, Mundy D, et al. Impact of segmental grafts on pediatric liver transplantion-a review of the United Network for Organ Sharing Scientific Registry data (1990–1996), J Pediatr Surg 1999; 34: 107.
18. Broelsch CE, Burdelski M, Rogiers X, et al. Living donor for liver transplantation. Hepatology 1994; 20: 49S.
19. Busuttil RW, Goss JA. Split liver transplantation. Ann Surg 1999; 229: 313.
20. Goss JA, Yersiz H, Shackleton CR, et al. In situ splitting of the cadaveric liver for transplantation. Transplantation 1997; 64: 871.
21. Cacciarelli TV, Esquivel CO, Moore DH, et al. Factors affecting survival after orthotopic liver transplantation in infants. Transplantation 1997; 64: 242.
22. Moukarzel AA, Najm I, Vargas J, McDiarmid SV, Busuttil RW, Ament ME. Effect of nutritional status on outcome of orthotopic liver transplantation in pediatric patients. Transplant Proc 1990; 22: 1560.
23. Stewart S, Uauy R, Waller DA, Kennard B, Benser M, Andrews W. Mental and motor development, social competence, and growth one year after successful liver transplantation. J Pediatr 1989; 114: 574.
24. Moukarzel AA, Najm I, Vargas JV, McDiarmid SV, Busuttil RW, Ament ME. Effect of nutritional status on outcome of orthotopic liver transplantation in pediatric patients. Transplant Proc 1990; 22: 1560.
25. Shepherd RW, Chin SE, Cleghorn GJ, et al. Malnutrition in children with chronic liver disease accepted for liver transplantation: clinical profile and effect on outcome. J Paediatr.Child Health 1991; 27: 295.
26. McDiarmid SV, Gornbein JA, DeSilva P, et al. Factors affecting growth after pediatric liver transplantation. Transplantation 1999; 67: 404.
27. Hess UJ, Pattyn P, Kerremans I, et al. The course of shipped livers used as full size, reduced or split grafts. Acta Chir Belg 1997; 2: 76.
28. Rogiers X, Malago M, Gawad KA, et al. One year of experience with extended application and modified techniques of split liver transplantation. Transplantation 1996; 61: 1059.
29. Mirza DF, Achilles O, Pirenne J, Buckels JA, McMaster P, Mayer AD. Encouraging results of split-liver transplantation. Br J Surg 1998; 85: 494.

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