

UCSF

UC San Francisco Previously Published Works

Title

Analysis of Liver Offers to Pediatric Candidates on the Transplant Wait List

Permalink

<https://escholarship.org/uc/item/0sg445wt>

Journal

Gastroenterology, 153(4)

ISSN

0016-5085

Authors

Hsu, Evelyn K
Shaffer, Michele L
Gao, Lucy
[et al.](#)

Publication Date

2017-10-01

DOI

10.1053/j.gastro.2017.06.053

Peer reviewed



Published in final edited form as:

Gastroenterology. 2017 October ; 153(4): 988–995. doi:10.1053/j.gastro.2017.06.053.

Analysis of Liver Offers to Pediatric Candidates on the Transplant Wait List

Evelyn K. Hsu¹, Michele L. Shaffer^{1,2}, Lucy Gao³, Christopher Sonnenday⁴, Michael L. Volk⁵, John Bucuvalas⁶, and Jennifer C. Lai⁷

¹University of Washington School of Medicine, Seattle, Washington;

²Seattle Children's Core for Biomedical Statistics, Seattle, Washington;

³Department of Biostatistics, University of Washington, Seattle, Washington;

⁴Department of Surgery, University of Michigan, Ann Arbor, Michigan;

⁵Loma Linda University Health, Loma Linda, California;

⁶Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio;

⁷Division of Gastroenterology and Hepatology, University of California San Francisco, San Francisco, California

Abstract

BACKGROUND & AIMS: Approximately 10% of children on the liver transplant wait-list in the United States die every year. We examined deceased donor liver offer acceptance patterns and their contribution to pediatric wait-list mortality.

METHODS: We performed a retrospective cohort study of children on the US liver transplant wait-list from 2007 through 2014 using national transplant registry databases. We determined the frequency, patterns of acceptance, and donor and recipient characteristics associated with deceased donor liver organ offers for children who died or were delisted compared with those who underwent transplantation. Children who died or were delisted were classified by the number of donor liver offers (0 vs 1 or more), limiting analyses to offers of livers that were ultimately transplanted into pediatric recipients. The primary outcome was death or delisting on the wait-list.

RESULTS: Among 3852 pediatric liver transplant candidates, children who died or were delisted received a median 1 pediatric liver offer (inter-quartile range, 0–2) and waited a median 33 days before removal from the wait-list. Of 11,328 donor livers offered to children, 2533 (12%) were transplanted into children; 1179 of these (47%) were immediately accepted and 1354 (53%) were initially refused and eventually accepted for another child. Of 27,831 adults, 1667 (6.0%; median, 55 years) received livers from donors younger than 18 years (median, 15 years), most (97%) allocated locally or regionally. Of children who died or were delisted, 173 (55%) received an offer

Reprint requests: Address requests for reprints to: Evelyn Hsu, MD, Seattle Children's Hospital, Division of Gastroenterology and Hepatology, 4800 Sandpoint Way NE, Mailstop OB.9.642, Seattle WA 98105. evelyn.hsu@seattlechildrens.org; fax: (206) 987-2721.

Conflicts of interest

The authors disclose no conflicts.

of 1 or more liver that was subsequently transplanted into another pediatric recipient, and 143 (45%) died or were delisted with no offers.

CONCLUSIONS: Among pediatric liver transplant candidates in the US, children who died or were delisted received a median 1 pediatric liver offer and waited a median of 33 days. Of livers transplanted into children, 47% were immediately accepted and 53% were initially refused and eventually accepted for another child. Of children who died or were delisted, 55% received an offer of 1 or more liver that was subsequently transplanted into another pediatric recipient, and 45% died or were delisted with no offers. Pediatric prioritization in the allocation and development of improved risk stratification systems is required to reduce wait-list mortality among children.

Keywords

Pediatric; Liver Transplant; Allocation; Organ Offers

Approximately 1 in 10 children on the US liver transplant wait-list dies every year.¹ Under the present liver allocation system, children are assigned a score that reflects 3-month mortality risk as determined by the Pediatric End Stage Liver Disease (PELD) score for children less than 12 years, or by the Model for End-Stage Liver Disease (MELD) score for adolescents 12–17 years. Children can be assigned priority “Status 1A” with a diagnosis of acute liver failure, primary non-function of the liver within 7 days of transplant, or hepatic artery thrombosis within 14 days of transplant. Children are assigned priority “Status 1B” with hepatoblastoma, organic acidemia, urea cycle defect, or decompensated chronic liver disease. A deceased donor is first offered to candidates who are Status 1A, then Status 1B, and then to all others on the wait-list, in order of decreasing PELD or MELD scores. Depending on the age of the donor, the allocation algorithm shifts between local, regional, and national priority (Figure 1).

When an offer occurs, the transplant physician makes a decision to accept or decline the offer. If the offer is declined, the liver is then offered to the next candidate in the algorithm, and so-on, down the wait-list until the organ is ultimately transplanted or discarded. This decision to accept or decline an offer is made in real-time, incorporating donor and recipient factors. Cognitive bias and external forces such as allocation policy changes, regulatory oversight, and inter-center competition influence these decisions.² A study evaluating liver offer acceptance patterns found that adult liver transplant candidates received a median of 5 liver offers while on the wait-list; among those who ultimately died, 84% had received and declined at least 1 liver offer for transplantation.³ The effect of liver offer acceptance decisions on pediatric liver transplant candidates is not known. Small children, in particular, face unique challenges in receiving whole organ grafts of appropriate size, and not all deceased donors are deemed of appropriate quality to allow for reduced size or split liver transplantation. Based on these observations, we sought to determine if acceptance patterns for deceased donor liver offers to children were associated with increased risk for wait-list mortality.

Materials and Methods

We evaluated all US liver transplant candidates <18 years of age with an initial listing from May 1, 2007–December 31, 2012. Candidates were followed until (1) removal from the wait-list or (2) the end of the study period (June 30, 2014). This study period corresponds with the availability of the United Network for Organ Sharing Potential Transplant Recipient database, which provides information on all organ offers for wait-list candidates in the US. Data were obtained from the United Network for Organ Sharing/Organ Procurement Transplantation Network as of June 30, 2014. Data regarding wait-list candidates and their donors were obtained from the Standard Transplant Analysis and Research files as of the same date. The Institutional Review board at Seattle Children’s Hospital approved this study.

Characteristics Evaluated

Pediatric wait-list candidates.—Baseline demographic data of pediatric wait-list candidates included age, gender, race, and disease severity, and listing category (Status 1A, 1B, or MELD/PELD). Etiologies of liver disease were categorized as: chronic liver disease, acute liver failure, tumor, vascular, metabolic, graft failure, and other. In the event of listing at multiple centers, information from the earliest listing was retained, avoiding duplicate records of the same patient. We excluded patients listed for multi-visceral transplant because these children may have an accelerated wait-list trajectory and clinicians may have differing motivations for accepting or declining a liver offer compared with children listed for isolated liver transplant.

Six hundred eight candidates were censored from the analysis: 466 for (1) reaching age 18 years, (2) receiving a living donor liver transplant, or (3) remaining listed at the end of the study period. An additional 142 candidates were censored for having an “other category” removal code (refused transplant, transferred to another center, removed in error, other reason not specified).

Donor liver offers.—We analyzed all deceased donor liver offers that were transplanted into pediatric recipients. Donors were characterized by age, gender, Centers for Disease Control and Prevention high risk status, cause of death, mechanism of death, donation after cardiac death, and partial/split liver status. Refusal codes of liver offers were categorized into 8 groups: (1) “Donor age/quality,” (2) “Size mismatch,” (3) “Recipient Factors,” (4) “Multi-organ transplant,” (5) “Surgeon factors,” (6) “Immunologic Mismatch,” (7) “Aborted Transplant,” and (8) “Other.” To further examine size mismatch as the predominant reason for organ decline, we created “ideal in-range” variable defined as donor-to-recipient body surface area ratio >0.75 or <1.25 . Body surface area has been previously shown to more accurately predict liver size than body weight or body height alone.^{4–6}

Center and geographic characteristics.—We defined centers that had performed 25 or fewer pediatric transplants over a 5-year period as very low volume. The remaining centers were grouped based on (1) volume of pediatric transplants by tertiles (lowest = 26–45, middle = 46–83, and highest = 84) and (2) volume of technical variant pediatric transplants, which included split liver transplant, reduced liver transplant, or living donor liver transplant by tertile (lowest = 0–5, middle = 6–26, and highest tertile = 27) performed

per center over the 5-year period, based on data available in the Organ Procurement and Transplant Network registry.

Statistical Analysis

Pediatric candidates were classified by their wait-list outcome: deceased donor liver transplantation, removed for death/delisting for being too sick for liver transplantation, or removed for being too well for liver transplant. We compared those who died/were delisted with those who were transplanted. Children who died or were delisted were further categorized by the number of deceased donor liver offers before removal (0 vs 1). The analysis was repeated excluding the children with acute liver failure; this diagnosis represents a potentially more unstable subset of children who typically have higher mortality rates and shorter wait-times independent of donor offer behavior and allocation systems. Descriptive statistics were prepared for all factors, including percentages for categorical variables and median and interquartile range for quantitative variables. χ^2 or Fisher's exact tests were used to compare categorical variables among groups. Kruskal-Wallis and Wilcoxon rank sum tests were used to compare medians of quantitative variables. Analyses were performed using R version 3.0.3.⁷ *P* values <.05 were considered statistically significant.

Results

Characteristics of wait-list candidates.

Three thousand eight hundred fifty-two candidates met inclusion criteria; 316 (8%) died or were delisted, 2597 (67%) underwent liver transplantation, 331 (9%) were removed for clinical improvement, and 608 (16%) were censored. Compared with those who received deceased donor liver transplants, patients removed for death/delisting were younger (median, <1 year vs 2 years), more likely to have acute liver failure (26% vs 14%), and public insurance (65% vs 53%) (*P* < .001 for each) (Table 1). Compared with those who were privately insured, patients with public insurance were more likely to receive 1 offers (85% vs 81%; *P* = .002). The median number of liver offers was higher for those who ultimately underwent transplant compared with those who died/were delisted (2 vs 1; *P* < .001) (Table 1).

Characteristics of deceased donor liver offers.

Eleven thousand three hundred twenty-eight discrete deceased donor livers were offered to pediatric recipients, including 190 donor livers that were offered as 2 segments to children. There were 8795 (78%) donor offers turned down at least once for a pediatric recipient before being offered to adults. The remaining 2533 donors were transplanted into 2597 pediatric recipients. There were 64 cases where a unique donor offer was split with both segments transplanted into children.

Of the 2533 livers transplanted into pediatric patients, 2019 (80%) were from donors <18 years of age and 514 (20%) were from donors 18 years. Of these same 2533 liver donors, 1179 (47%) of donors were immediately accepted for the first pediatric recipient they were offered to: 517 (44%) were local, 587 (50%) were regional, 74 (6%) were national, and 1

was foreign. Two hundred ninety-six of the 1179 (25%) of those immediately accepted by the first pediatric candidate were first offered to an adult. For those 296, 178 (60%) were local, 112 (38%) were regional, and 6 (2%) were national.

There were 1354 (53%) donor livers refused for a child and eventually accepted and transplanted into another child; 393 (29%) of these were local, 492 (36%) were regional, 467 (34%) were national, and 2 were foreign. Organ offers initially refused and subsequently accepted for children were more likely to be from younger donors (median, 3 years vs 14 years; $P < .001$).

There were no significant differences in organs designated Centers for Disease Control high risk, or for those that were donated after cardiac death; these did not represent a large proportion of pediatric liver donors (Table 2).

There were 5307 discrete refusals for children of 1213 livers from deceased pediatric donors that were eventually transplanted into children. The median number of times pediatric liver donors were refused for a pediatric wait-list candidate was 3. (interquartile range [IQR]: 1,5) Within the database, each refusal was designated 1 or more refusal codes: 57% cited donor quality, 30% size mismatch, 7% recipient factors, 4% multi-organ transplant needed, 4% other, and 0.45% surgeon factors.

Of the 5307 discrete refusals, body surface area ratio of donor to recipient and refusal code were available for 5276 (99%). For all discrete refusals, 2686 of 5276 (51%) were within size range and 2590 of 5276 (49%) were out of range. Of those offers that were refused for primary reason "size mismatch," 797/1590 (50%) were in range and the remainder 793/1590 (50%) were out of range. Of the 2533 livers that were transplanted into children, the median body surface area donor to recipient ratio was 1.2 (IQR 1.0, 2.4).

Liver allocation to adults after refusals for pediatric patients.

A total of 27831 adults underwent liver transplantation during this time period; 1667 (5.6%) were transplanted with livers from donors <18 years of age. Of the 1667 adults transplanted with livers from children, allocation was predominantly local or regional (1263 [76%] local, 360 [22%] regional). Median age of a graft <18 years of age allocated to an adult was 15 years (IQR 13, 17). The median age of an adult recipient of these grafts was 55 years (IQR 47, 60).

For the 1667 pediatric-age donors, there were 6203 refusals of discrete offers made to children. The median number of times each pediatric-age donor was refused for a pediatric candidate was 1 (IQR: 0, 4). Of the total 6203 refusals, 4246 (68%) were local and 877 (14%) regional. Of the 514 adult-age donors transplanted into children, 415 (81%) were immediately accepted, and 99 (19%) were refused for a child before eventually being transplanted into another child.

Characteristics of liver offers to candidates who died/were delisted.

Of the 316 children who died or were delisted, the median number of pediatric liver offers was 1 (IQR 0, 2); 173 (55%) received 1 pediatric liver offers before their death/delisting.

Those who had received 1 offer before death/delisting were more likely to be <1 year (61% vs 43%) than those who received no offers ($P = .002$). Children 6–11 years were more likely to die/be delisted with no offers (15% vs 9%), as were children 12–17 years (24% vs 11%) ($P = .002$).

There were variations in etiology of disease. Children with chronic liver disease were more likely to die/be delisted with 1 offer (69% vs 48%; $P < .001$). Those who died/were delisted with no offers had a shorter wait-time (12 days vs 67 days; $P < .001$) (Table 3).

When children with acute liver failure were excluded from analysis, wait-time remained different between those who died/were delisted with 1 offer and those with no offers (89 vs 22 days; $P < .001$), as did median age (0 vs 0.5 years; $P = .021$).

Sensitivity analysis (acute liver failure and chronic liver disease).

Children with acute liver failure have a markedly different clinical course from those with chronic liver disease. To account for these differences, we conducted a sensitivity analysis comparing offer and refusals for these 2 groups. Children with acute liver failure removed for death or delisting received a median 0 offers (IQR 0,1), while those with chronic liver disease received a median 1 offer (IQR 0, 3.25) (Table 4). In the acute liver failure group, there were median 0 refusals [IQR 0,1] of organs eventually transplanted into a child, while in the chronic liver disease group, the median number of refusals was 1 (IQR 0,3).

Split liver transplantation in adults and children.

Adult donors were identified as ideal candidates for splits if they met the following criteria: (1) donors >18 and <40 years of age, (2) on no more than a single vasopressor, (3) transaminases no greater than 3 times normal, (4) body mass index ≤ 28 . There were 797 adult donor offers that qualified as good candidates for splits; 169 were first allocated to adults, and 628 were first allocated to children. Twenty-seven of the 797 organs (3.4%) were used for split liver transplantation. When the organ was first allocated to a pediatric recipient, 26/628 (4.1%) were split, all between a child and an adult. When first allocated to an adult, 1/169 (0.6%) were split, and this 1 split was between 2 adults.

Center characteristics.

Very low volume centers (≤ 25 in 5-year period), while accounting for 11% of all patients listed, comprised 17% of those patients who died/were delisted without offers. Those in the middle and highest tertile for pediatric transplant volume and technical variant transplant volumes were more likely to have patients who died/were delisted on the wait-list with offers. Centers with more experience were more likely to accept donors that had been turned down by another pediatric recipient when compared with those centers with less experience.

Wait-list and transplantation for children <5 years of age.

Figure 2 represents the percentage of technical variant transplants in children <1 year of age by center pediatric transplant volume in a 5-year period. There was a wide range of percentage of technical variant transplants as pediatric transplant volume increased, with

several low volume pediatric transplant centers performing no technical variant transplants for children under 1 year of age.

Discussion

Using national registry data from nearly 4000 pediatric transplant wait-list candidates and more than 11,000 donor liver offers made to children in the US, we found that children who die or are delisted on the liver wait-list receive a median of 1 offer and spend 30 days on the wait-list before their death/delisting. Although patients with public insurance were more likely to receive 1 offers, they were also more likely to die or be delisted. Nearly half of children who died/were delisted received no liver offers at all before their death/delisting. Higher-volume centers were more likely to accept an organ that had been previously turned down for a prior pediatric candidate.

Thirty percent of organ refusals were primarily coded as size mismatch, as expected, given the younger age and size of pediatric recipients compared with adults. Unexpectedly, 50% of organ offers that were declined for size were considered to be in the ideal range for size match by body surface area. Because of a liver allocation algorithm that prioritizes non-status 1A local and regional adults on the liver wait-list over children listed nationally, 1667 adults were transplanted with pediatric organs that were turned down by a median of 1 pediatric candidate; 97% of these adults were transplanted with pediatric-age donors before they could be offered to potential pediatric candidates on the national wait-list.

It is noteworthy how different these pediatric liver offer data are compared with studies performed in adults. Adults, when compared with children who die/are delisted, receive more donor liver offers and have longer survival on the wait-list before removal, with the majority (85%) receiving at least 1 liver offer before death/delisting.³ This is in the context of pediatric liver transplants accounting for a relatively small fraction of liver transplants overall (Table 5). In contrast, nearly half of children who died or were delisted received no offers at all. The current allocation algorithm appears to systematically disadvantage older children and adolescents. Nonetheless, pediatric providers caring for children on the liver wait-list should accept any suitable offers on their behalf because it is unlikely they will be allocated more organs before their decline. The difference in both outcomes and offers for wait-listed children with public insurance is troubling and suggests there are unmeasured confounders among these children that are associated with increased wait-list mortality. There has not been a model developed to determine which organs are suitable for pediatric liver transplant. A decision support tool, as has been modeled in adult liver transplantation,⁸ could potentially assist in standardizing approaches to pediatric donor liver offers and reducing overall wait-list mortality. The turndown codes for offer refusals do not appear to be representative – a portion of the refusals could have been for technical reasons that would have rendered transplantation prohibitive. Future real-time qualitative surveys of transplant physicians would provide more insight into offer refusals.

There is a striking difference in rate of split liver transplantation depending on primary allocation, with an increased rate of splitting of appropriate organs when the first offer was to a child, compared with a nearly nonexistent rate of splitting when the first offer was to an

adult. This suggests underutilization of splitting of appropriate donor organs. We offer several reasons for this. Decision-making surrounding the decision to split a donor liver is complex and related to technical expertise and risk assessment. Split grafts are perceived by centers that primarily transplant whole livers as carrying greater morbidity and mortality after transplant. Furthermore, in the current US allocation system, there is no incentive to split livers allocated to adults.

Current allocation for liver (and all solid organ) transplant in the US is determined by the United Network for Organ Sharing, which administers the Organ Procurement and Transplant Network database, capturing all patients listed for transplantation in the US; it remains the most utilized resource in transplantation to evaluate pre-transplant and post-transplant outcomes and survival. This analysis is limited by the use of a large database with patient-specific information collected for research. In our dataset, missing data were negligible, and our cohort is large and nationally representative.

Despite limitations, our findings have important implications for children on the liver wait-list. This analysis is the first of its kind undertaken in pediatric liver transplantation and identifies allocation policy changes that have the potential to significantly reduce pediatric liver transplant wait-list mortality and morbidity with minimal impact on adult wait-list outcomes. There is notable variation regarding which donor organs are appropriate for split-liver transplantation, and in the determination of appropriate size matching between donor organs and recipients. Pediatric liver transplantation remains a resource-intensive and technically complex procedure, and transplant centers vary in their volume of technical variant liver transplants performed. Centers without robust technical variant liver transplant programs are less likely to access reduced size transplantation, with a lower likelihood that any given donor could potentially be utilized to transplant 2 recipients. In the international experience, the approach to this lack of technical expertise is to adopt a centralized system and restrict the care of certain children to large centers with the necessary expertise, which has resulted in increased organ utilization and improved outcomes. In the United Kingdom, allocation is center-based, allowing a single center to split a liver for 2 of their recipients, allowing for more autonomy and flexibility in the selection of recipients. In the US, allocation rules dictate that in the majority of cases livers are split for recipients at different centers, adding complexity that further limits incentive for splitting. Furthermore, efforts to regulate and centralize care for pediatric patients in the US have met with significant resistance, with opponents citing hardship on families and impaired access to care.

There are no validated standards in the field of pediatric liver transplantation in terms of determining appropriate size-matching between donors and recipients. Indeed, half of the refusals for “size mismatch” were in the ideal size range. These decisions are complex, and made based largely on surgeon intuition and experience, but collaborative multi-center efforts to create guidelines for organ offer decision-making could increase pediatric liver transplantation and limit variation in access to transplant across centers.

In the last 20 years, the number of children transplanted annually has been stable, in contrast to the linear increase in the number of adults added to the wait-list.¹ As children compete with other adults on the wait-list for pediatric and younger adult donor organs (donors <30

years of age) they often decline clinically or die while they wait. Wait time and its related comorbidities are not equivalent between adults and children. Children on the wait-list have diminished quality of life in childhood, loss of schooling, poor growth, pubertal delay, risk for social isolation, and potential depression, the effects of which may extend into adulthood.^{9,10}

Pediatric priority in allocation still needs to remain at the forefront of any discussion that addresses pediatric liver wait-list mortality. The Ethics and Pediatric Committees of the United Network for Organ Sharing published a white paper delineating several ethical arguments justifying pediatric priority in organ allocation.¹¹ In the international experience, particularly in the United Kingdom, Brazil, and Eurotransplant countries, when children are given priority for adult organs, there are increased transplantation rates, increased organ utilization through the use of splitting, and improved long-term outcomes for all children on the wait-list.^{12–15} The effects of a change in US allocation policy to allow for national sharing of pediatric donor organs after local allocation to status 1A adults should be modeled to predict the effects on organ utilization rate for liver splitting and technical variant grafts, as well as both pediatric and adult liver wait-list outcomes.

Acknowledgments

The authors thank Sue Rhee, MD, for the contribution of Figure 1 and Matthew Kronman, MD, MSCE, and Simon Horslen, MBChB, who provided editing assistance on the manuscript.

Funding

This research was supported by Seattle Children's Hospital Research Institute Translational Research Ignition Projects Program (TRIPP) funding.

Abbreviations used in this paper:

IQR	interquartile range
MELD	Model for End-Stage Liver Disease
PELD	Pediatric End Stage Liver Disease

References

1. Kim WR, Lake JR, Smith JM, et al. Liver. *Am J Transplant* 2016;16(Suppl 2):69–98. [PubMed: 26755264]
2. Halldorson JB, Paarsch HJ, Dodge JL, et al. Center competition and outcomes following liver transplantation. *Liver Transplantation* 2013;19:96–104. [PubMed: 23086897]
3. Lai JC, Feng S, Roberts JP. An examination of liver offers to candidates on the liver transplant wait-list. *Gastroenterology* 2012;143:1261–1265. [PubMed: 22841780]
4. Urata K, Kawasaki S, Matsunami H, et al. Calculation of child and adult standard liver volume for liver transplantation. *Hepatology* 1995;21:1317–1321. [PubMed: 7737637]
5. Vauthey J-N, Abdalla EK, Doherty DA, et al. Body surface area and body weight predict total liver volume in Western adults. *Liver Transplantation* 2002;8:233–240. [PubMed: 11910568]
6. Heinemann A, Wischhusen F, Püschel K, et al. Standard liver volume in the Caucasian population. *Liver Transpl Surg* 1999;5:366–368. [PubMed: 10477836]
7. R Core Team. R: A language and environment for statistical computing (2014). Available at: <http://www.R-project.org>. R Foundation for Statistical Computing, Vienna, Austria.

8. Volk ML, Goodrich N, Lai JC, et al. Decision support for organ offers in liver transplantation. *Liver Transplantation* 2015;21:784–791. [PubMed: 25779757]
9. Mohammad S, Alonso EM. Approach to optimizing growth, rehabilitation, and neurodevelopmental outcomes in children after solid-organ transplantation. *Pediatr Clin North Am* 2010;57:539–557. [PubMed: 20371051]
10. Braveman P, Barclay C. Health disparities beginning in childhood: a life-course perspective. *Pediatrics* 2009; 124(Suppl 3):S163–S175. [PubMed: 19861467]
11. United Network for Organ Sharing Pediatric and Ethics Committees. Ethical principles of pediatric organ allocation. Available at: <http://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-of-pediatric-organ-allocation/>. 2014 Accessed June 4, 2015.
12. Neto JS, Carone E, Pugliese RPS, et al. Modified pediatric end-stage liver disease scoring system and pediatric liver transplantation in Brazil. *Liver Transplantation* 2010; 16:426–430. [PubMed: 20213836]
13. Herden U, Grabhorn E, Briem-Richter A, et al. Developments in pediatric liver transplantation since implementation of the new allocation rules in Eurotransplant. *Clin Transplant* 2014;28:1061–1068. [PubMed: 25040668]
14. Herden U, Wischhusen F, Heinemann A, et al. A formula to calculate the standard liver volume in children and its application in pediatric liver transplantation. *Transpl Int* 2013;26:1217–1224. [PubMed: 24118382]
15. Hsu EK, Mazariegos GV. Global lessons in graft type and pediatric liver allocation: A path toward improving outcomes and eliminating wait-list mortality. *Liver Transplantation* 2016;23:86–95.

EDITOR'S NOTES**BACKGROUND AND CONTEXT**

Roughly 1 in 10 children dies while waiting for a life-saving liver transplantation in the United States.

NEW FINDINGS

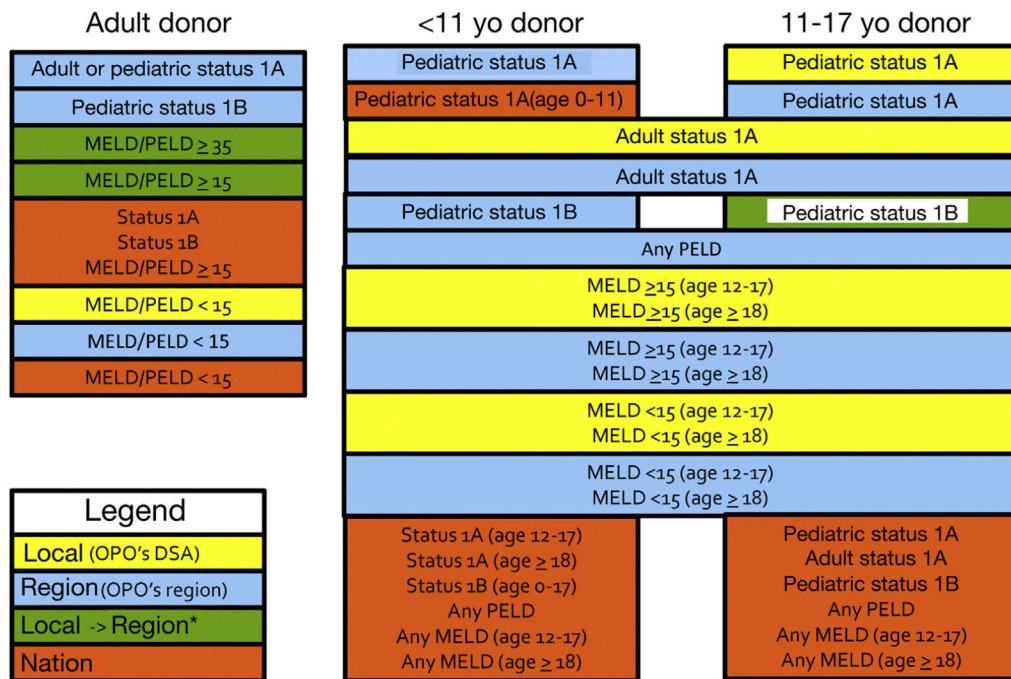
Fifty-five percent of children who died on the liver waitlist received 1 or more offers of organs ultimately transplanted into another child. Due to a liver allocation algorithm that prioritizes adults on regional status, more than 1500 pediatric livers were transplanted into adult recipients before children nationally.

LIMITATIONS

This analysis is limited by the use of a large database with patient-specific information collected for research.

IMPACT

There is heterogeneity in deceased donor offer acceptance behavior for children on the liver wait-list that may contribute to mortality. Pediatric priority in allocation continues to be critical to reduce wait-list mortality among children.



*Allocation will occur at the OPO's DSA followed by OPO's region.
For MELD/PELD scores, allocation will occur at each given score prior to proceeding to next lower score.

Figure 1. Liver allocation algorithm, United Network for Organ Sharing. Figure created by Sue Rhee, MD.

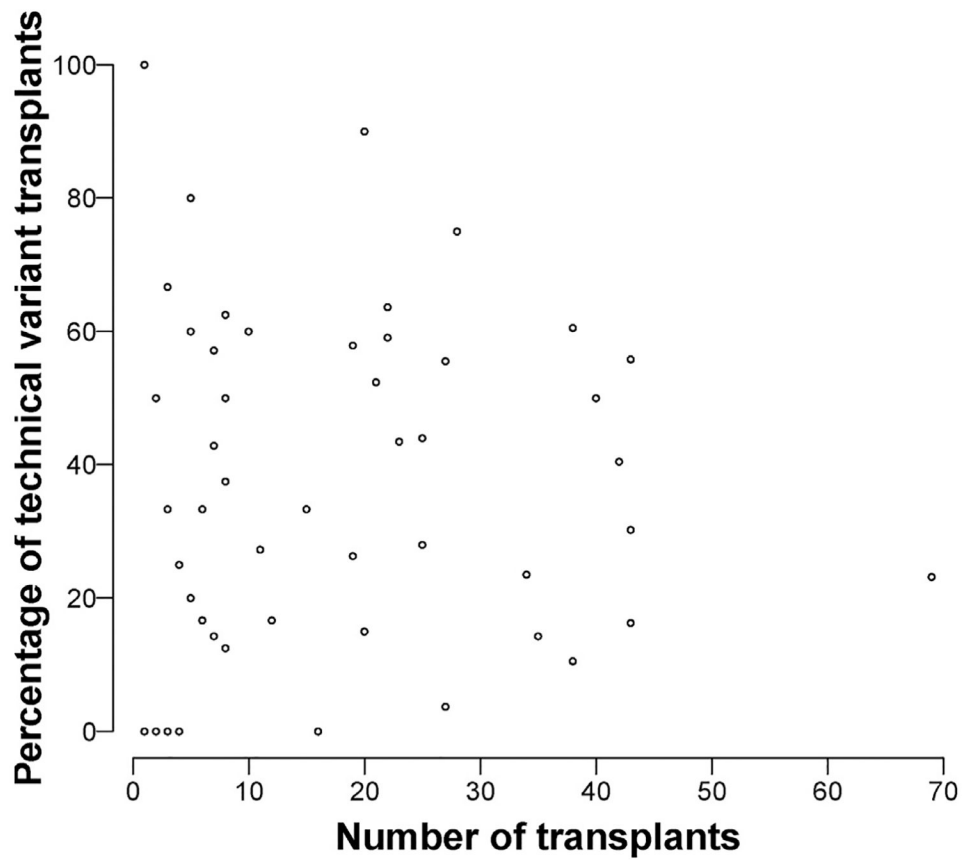


Figure 2. Percentage of technical variant transplants by pediatric center volume for children under 1 year of age.

Table 1.

Characteristics of Wait-list Candidates

Characteristic	All (n=3852)	Transplanted Patients (n=2597)	Removed for Death/Delisting (n=316)	Transplanted vs Death/Delisting P Value
Age, median [IQR], years	2 [0, 9]	2 [0, 9]	0 [0, 8]	P < .001
Age category, No. (%)				
< 1 year	1459 (38)	957 (37)	168 (53)	P < .001
1–5 years	1062 (28)	767 (30)	58 (18)	
6–11 years	569 (15)	398 (15)	37 (12)	
12–17 years	762 (20)	475 (18)	53 (17)	
Female, No. (%)	1952 (51)	1284 (49)	181 (57)	P = .010
Race/ethnicity, No. (%)				
White	1959 (51)	1339 (52)	133 (42)	P < .001
Black	614 (16)	444 (17)	46 (15)	
Hispanic	941 (24)	585 (23)	106 (34)	
Asian	202 (5)	137 (5)	12(4)	
Other	136 (4)	92 (4)	19(6)	
Etiology of liver disease, No. (%)				
Chronic Liver Disease	2366 (61)	1604 (62)	189 (60)	P < .001
Acute Hepatic Necrosis	675 (18)	367 (14)	83 (26)	
Graft Failure	38 (1)	28 (1)	5 (2)	
Tumor	319 (8)	250 (10)	16(5)	
Vascular	27(1)	20 (1)	0 (0)	
Metabolic	337 (9)	277 (11)	9 (3)	
Other	90 (2)	41 (2)	14(4)	
Insurance, No. (%)				
Public	2003 (52)	1384 (53)	206 (65)	P < .001
Disease severity category, No. (%) ^a				
Status 1A	483 (13)	276 (11)	73 (23)	P < .001
Status 1B	77(2)	50 (2)	19(6)	
MELD/PELD Score	3237 (85)	2242 (87)	222 (71)	
Wait-time, median [IQR], days	63 [16, 201]	52 [14, 140]	33 [7, 105]	

Characteristic	All (n=3852)	Transplanted Patients (n=2597)	Removed for Death/Delisting (n=316)	Transplanted vs Death/Delisting P Value
No. of Pediatric Offers, median [IQR] ^b	1 [1,3]	2 [1,4]	1 [0, 2]	P < .001

^a55 missing for all; 29 missing for transplanted; 2 missing for death/delisting.

^b16 missing for transplanted; 3 missing for death/delisting.

Table 2.

Characteristics of Deceased Donor Liver Offers

Characteristic	Donor Immediately Accepted on First Offer (n=1179)	Donor Turned Down by Pediatric Recipient but Eventually Transplanted into Another Pediatric Recipient (n=1354)	Immediately Accepted vs Eventually Accepted P Value
Age, median [IQR], years	14 [3, 22]	3 [1, 12]	$P < .001$
Age category, No. (%)			
<11 years	486 (42)	988 (73)	$P < .001$
11–17 years	278 (24)	267 (20)	
18–19 years	61 (5)	20 (1)	
20–29 years	174 (15)	52 (4)	
30–39 years	93 (8)	9 (1)	
40–49 years	55 (5)	12 (1)	
> 50 years	32 (3)	6 (<1)	
Female, No. (%)	480 (41)	560 (41)	$P = .772$
CDC high risk, No. (%) ^a	49 (4)	54 (4)	$P = .818$
Cause of death, No. (%)			
Trauma	659 (56)	670 (49)	$P < .001$
Stroke	149 (13)	105 (8)	
Anoxia	314 (27)	514 (38)	
Other	57 (5)	65 (5)	
Mechanism of death, No. (%) ^b			
Blunt injury	436 (37)	529 (39)	
Intracranial hemorrhage	200 (17)	155 (11)	
Gunshot wound	171 (15)	83 (6)	
Asphyxiation	91 (8)	128 (9)	
Cardiovascular	81 (7)	137 (10)	
None of the above	64 (5)	112 (8)	
Drowning	50 (4)	101 (7)	
Drug intoxication	34 (3)	15 (1)	
Death from natural causes	26 (2)	39 (3)	
Seizure	14 (1)	30 (2)	

Characteristic	Donor Immediately Accepted on First Offer (n=1179)	Donor Turned Down by Pediatric Recipient but Eventually Transplanted into Another Pediatric Recipient (n=1354)	Ultimately Accepted vs Eventually Accepted P Value
SIDS	10 (1)	21 (2)	
Stab	1 (<1)	3 (<1)	
Not reported	0	1 (<1)	
Donation after cardiac death, No. (%) ^c	9 (1)	11 (1)	
Partial/split liver, No. (%)	458 (39)	266 (20)	P < .001

^a 2 missing for immediately accepted; 4 missing for eventually accepted.

^b 1 missing for immediately accepted.

^c 1 missing for eventually accepted.

Table 3.

Characteristics of Candidates who Died or were Delisted by Number of Offers

Candidate Characteristic	Dead/Delisted with 1 or More Offers (n=173)	Dead/Delisted with No Offers (n=143)	P Value
Age, median [IQR], years	0 [0, 2]	1 [0,11]	$P < .001$
Age category, No. (%)			
< 1 year	106 (61)	62 (43)	$P = .002$
1–5 years	32 (18)	26 (18)	
6–11 years	16(9)	21 (15)	
12–17 years	19(11)	34 (24)	
Etiology of liver disease, No. (%)			$P < .001$
Chronic liver disease	120 (69)	69 (48)	
Acute hepatic necrosis	32 (18)	51 (36)	
Graft failure	3 (2)	2(1)	
Tumor	4 (2)	12(8)	
Vascular	0 (0)	0 (0)	
Metabolic	5 (3)	4 (3)	
Other	9 (5)	5 (3)	
Disease severity listing category, No. (%) ^a			$P < .001$
STATUS 1A	26 (15)	47 (33)	
STATUS 1B	10(6)	9 (6)	
MELD/PELD score	137 (79)	85 (60)	
Wait-time, median [IQR], days ^b	67.0 [24.0, 146.5]	12.0 [2.0, 41.0]	$P < .001$

^a2 missing for no offers.^b2 missing for 1 or more offers; 1 missing for no offers.

Table 4. Sensitivity Analysis in Donor Offers and Refusals by Diagnosis: Acute Liver Failure and Chronic Liver Disease

	Acute Liver Failure (n=675)		
	All	Transplanted Patients (n=365)	Removed for Death/Delisting (n=82)
No. of Pediatric Offers, median [IQR]	1 [0, 2]	1 [1, 2]	0 [0, 1]
No. of Refusals of Pediatric Offers, median [IQR]	0 [0, 1]	0 [0, 1]	0 [0, 1]
	Chronic Liver Disease (n=2366)		
	All	Transplanted Patients (n=1592)	Removed for Death/Delisting (n=188)
No. of Pediatric Offers, median [IQR]	2 [1, 4]	2 [1, 4]	1 [0, 3.25]
No. of Refusals of Pediatric Offers, median [IQR]	1 [0, 3]	1 [0, 3]	1 [0, 3.25]

NOTE. "Pediatric offer" designates any offer of an organ eventually transplanted into a pediatric patient.

Table 5.

A Comparison of Adult and Pediatric Donor Offers, Wait-Time Before Death/Delisting, and Deceased Donor Liver Transplants

Characteristic	Adult	Pediatric
Donor liver offers for all candidates before removal, median [IQR]	5 [2–12]	1 [1–3]
Wait-time (days) before death/delisting, median [IQR]	92 [9–383]	33 [7–105]
Deceased donor liver transplants (SRTR, 2014), No.	6199	537

NOTE. Data combined from: Lai JC, et al, An Examination of Liver Offers to Candidates on the Liver Transplant Wait-List, *Gastroenterology* 2012;143:1261–1265, and Kim WR, et al. Liver. *American Journal of Transplantation*, 2016;16:69–98.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript