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Can non-directed living liver donation help improve access to grafts and correct socioeconomic disparities in pediatric liver transplantation?

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Abstract

Background: Each year, children die awaiting LT as the demand for grafts exceeds the available supply. Candidates with public health insurance are significantly less likely to undergo both deceased donor LT and D-LLD LT. ND-LLD is another option to gain access to a graft. The aim of this study was to evaluate if recipient insurance type is associated with likelihood of D-LLD versus ND-LLD LT.

Methods: The SRTR/OPTN database was reviewed for pediatric LDLT performed between January 1, 2014 (Medicaid expansion era) and December 31, 2019 at centers that performed ≥1 ND-LLD LDLT during the study period. A multivariable logistic regression was performed to assess relationship between type of living donor (directed vs. non-directed) and recipient insurance.

Results: Of 299 pediatric LDLT, 46 (15%) were from ND-LLD performed at 18 transplant centers. Fifty-nine percent of ND-LLD recipients had public insurance in comparison to 40% of

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AUTHOR CONTRIBUTION

DY, AGF, MAA, and WEJ made substantial contributions to the conception and design of the study. DY performed the analysis of the data and drafted the manuscript. RAC, HBM, SSS, TLN, MEW, EAP, MAA, and WEJ contributed to the interpretation of the data and revising the manuscript critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose as described by *Pediatric Transplantation*.

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D-LLD recipients (p = .02). Public insurance was associated with greater odds of ND-LLD in comparison to D-LLD upon multivariable logistic regression (OR 2.37, 95% CI 1.23–4.58, p = .01).

Conclusions: ND-LLD allows additional children to receive LTs and may help address some of the socioeconomic disparity in pediatric LDLT, but currently account for only a minority of LDLT and are only performed at a few institutions. Initiatives to improve access to both D-LLD and ND-LLD transplants are needed.

Keywords

liver transplantation; living donor

INTRODUCTION

A significant gap exists between supply and demand of liver grafts for children awaiting LT. Each year, 4%–12% of children on the LT waiting list are removed because they die or become too sick for transplant.[1,2] In addition, many children experience significant physical and cognitive morbidity while waiting for extended periods of time on the waiting list.[3–5] LDLT helps bridge this gap, providing increased access to LT for children. In 2019, 79 pediatric LDLTs were performed in the USA, representing 14% of all pediatric LTs in the nation.[6] Beyond expanding the donor pool, recent studies have demonstrated that LDLT achieves equal, if not superior, outcomes to DDLT in pediatric recipients.[7–9] In addition, LDLT offers other advantages over DDLT, such as the ability to transplant recipients in better overall health, greater control over surgical timing for families, enhanced pre-operative donor imaging, and better graft to recipient size matching.

Socioeconomic disparities in pediatric LT are apparent and have most commonly been demonstrated with the use of type of health insurance (private vs. public) as proxy for socioeconomic status. Pediatric liver candidates without private insurance are less likely to receive exception requests for their MELD or PELD scores.[10] Children with public insurance are also half as likely to undergo LDLT in comparison to dying on the list or DDLT.[11] Reflecting this reduced access to both deceased and living donor transplant options, pediatric liver candidates with public insurance have significantly greater risk of mortality on the waiting list.[11,12]

Since 2000, pediatric LDLT from anonymous ND-LLD has been increasingly performed across North America.[13] Although there is no formal policy regulating the allocation of ND-LLDs, the majority of programs performing LDLT from ND-LLD have reported allocating these unique donors based on blood type compatibility and medical urgency, with preference given to pediatric candidates.[14–16] The impact of ND-LLDs on access to LDLT among pediatric candidates with public insurance has not been explored. The aim of this study was to compare types of living donors (ND-LLD vs. D-LLD), by recipient insurance type among pediatric LDLT recipients. We hypothesized that pediatric LT recipients with public insurance would be more likely to undergo ND-LLD than D-LLD LDLT in comparison to recipients with private insurance.

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METHODS

The SRTR/OPTN database was reviewed for all pediatric (age <18 years) LDLT performed between January 1, 2014 (Medicaid expansion era) and December 31, 2019. Multi-organ transplants and re-transplants were excluded from the analysis. Recipients were categorized by type of insurance (public vs. private) and living donor (D-LLD vs. ND-LLD). Only transplants performed at centers that performed at least one ND-LLD in the study period were included to allow us to compare the likelihood of obtaining a directed versus non-directed living donor where ND-LLD was a possible alternative living donor option. Recipients with self-pay or foreign government as their primary payor were excluded from the analysis. This study was approved for institutional review board exemption.

Categorical variables are presented as quantity (percentage) and compared using the chi-squared test. Continuous variables are presented as mean (SD) and compared using two-sample Student's *t*-test. Logistic regression was used to assess for an association between type of living donor and recipient insurance. Other recipient characteristics found to be significantly different between ND-LLD and D-LLD recipients on univariable comparisons were included in the multivariable logistic regression to determine adjusted ORs. Recipient and graft survival are demonstrated using Kaplan–Meier survival curves and compared with the log-rank test. Missing data were censored in pairwise fashion. A *p*-value of <.05 was set as the threshold of statistical significance for all tests of significance. All statistical analysis was performed using STATA® 16.0 (StataCorp). This study was exempt from review by the Colorado Institutional Review Board.

RESULTS

In total, 1232 pediatric LTs were performed that met inclusion criteria during the study period, including 299 pediatric LDLT. Forty-six (15%) of the LDLT were from ND-LLD performed at 18 centers. Of the 46 ND-LLD, 27 (59%) had public insurance in comparison to 102 (40%) of D-LLD recipients ($p = .02$; Table 1). A greater proportion of D-LLD recipients were status 1A or 1B, while a greater proportion of ND-LLD recipients had a MELD/PELD score of 20–30. ND-LLD and D-LLD recipients were similar in regard to age and weight at transplant, sex, race/ethnicity, ABO blood group, diagnosis, and hospitalization status.

Upon univariable logistic regression, public insurance was significantly associated with greater odds of undergoing a LDLT from an ND-LLD than a D-LLD (OR 2.10, 95% CI 1.11–3.98, $p = .02$). After adjusting for MELD/PELD score, public insurance remained significantly and independently associated with increased odds of ND-LLD LDLT (adjusted OR 2.37, 95% CI 1.23–4.58, $p = .01$; Table 2). Additionally, recipients with a MELD/PELD score of 20–30 also had significantly greater odds of receiving a LDLT from an ND-LLD than a D-LLD in comparison to recipients with a score <20 (adjusted OR 2.78, 95% CI 1.13–6.83, $p = .03$).

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There was no significant difference in recipient or graft survival by type of donor ($p = .5$ and .3, respectively; Figure 1). Similarly, no significant difference in recipient or graft survival was detected by type of insurance ($p = .2$ for both; Figure 2).

DISCUSSION

In this retrospective analysis of pediatric LDLT performed in the USA since Medicaid expansion, we demonstrated that recipients with public insurance were twice as likely to receive a living donor graft from a non-directed donor rather than a directed donor. This finding is of dual importance, as it not only highlights the socioeconomic disparity in access to D-LLD LDLT but also illustrates the potential for ND-LLDs to help offset this disparity.

Mortality on the pediatric LT waiting list persists and is highest for children younger than 1 year of age.[1,17] Split and living donor grafts expand the pool of size-matched organs for pediatric candidates but remain infrequently utilized in the USA despite achieving excellent outcomes.[5,7–9,18] LDLT especially has been associated with superior survival outcomes in comparison to DDLT in recent years. Directed donation is the most commonly utilized living donation option. However, not every child has a directed donor. Potential living donors may not ultimately be able to donate due to ABO incompatibility or medical, anatomic, or psychological contraindications identified during the donor evaluation process.[1,15] Additionally, potential donors may ultimately decide not to donate secondary to concerns about the financial implications about donation or lack of a sufficient support system to help them through the process. While the recipient's insurance covers the living donor operation and hospitalization, additional expenses from missed work, travel and lodging, and child care arrangements are frequently out of pocket.[19–27] Finally, the families of certain pediatric candidates may have difficulty or hesitancy communicating their child's need for a living donor through social media and other outlets.[28,29] These barriers may be more significant for socioeconomically disadvantaged and racial and ethnic minorities, as evident by significantly lower rates of LDLT among these groups.[11]

ND-LLD is uniquely situated to address disparities in LDLT as their evaluation and donation process is independent of the recipient, as is their financial situation and social support system. ND-LLDs are most often allocated to candidates with the highest medical urgency that are without an eligible directed living donor.[16] Therefore, while ND-LLDs are not actively allocated to adjust for disparities in LDLT, our analysis demonstrates they "passively" do so because disadvantaged groups, such as those with public insurance, are less likely to have a directed living donor and therefore have a higher likelihood of receiving an ND-LLD.[11] While recipients with public insurance were more likely to receive an ND-LLD than a D-LLD, the same pattern was not seen with racial and ethnic minorities, who have also been shown to have lower rates of directed LDLT.[11] This may be due to the "sickest first" MELD/PELD allocation of ND-LLDs in which minorities are known to be disadvantaged due to lower rates of exception point appeals.[10] It is critical to develop a standardized method for allocating ND-LLD grafts and be transparent with all families about how non-directed grafts will be allocated.

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Until more deceased grafts are split, living donation will be the only way to increase the graft pool available for pediatric candidates. Currently, only about 14% of pediatric LTs come from living donors and fewer than 20 centers have performed an LDLT from an ND-LLD. Initiatives to support utilization of living donation are needed.[28] First, educational opportunities such as training seminars, coursework, cadaver models, and/or simulation experiences should be designed to help more surgeons gain experience and comfort with living donation. Similar educational tools have been utilized in kidney transplant to increase expertise with living donation.[30,31] Second, societal efforts to limit the financial burden of living donation (such as paid time off from work) are imperative and could increase both D-LLD and ND-LLD.[24] Third, research utilizing stakeholder engagement is desperately needed to help understand the best processes for educating all families about the opportunity for living donation for their child.[28] Each family with a pediatric LT candidate in the USA should be made aware of the possibility of both directed and non-directed living liver donation and centers that offer it. Additional research on the impact of social determinants of health on living donation rates and transplant outcomes is required to identify further initiatives and interventions to address persistent disparities.[32–37]

This study is limited by its retrospective nature and the relatively small number of centers across the USA that perform both D-LLD and ND-LLD. Furthermore, type of healthcare insurance was assumed to be an indicator of socioeconomic status, which is an imperfect, but commonly used, surrogate and is a limitation of the variables collected in the SRTR/OPTN database.[10–12,38–40] Future studies assessing more granular data on social determinants of health are required to further describe disparities in LDLT and the role of ND-LLD in mitigating these disparities.

Socioeconomic disparities in pediatric LDLT from directed living donors persist. The novel phenomenon of non-directed living liver donation may help provide grafts to those candidates from lower socioeconomic status who do not have access to a directed living donor but currently only account for a minority of pediatric LDLTs performed in the USA. Initiatives to improve access to both D-LLD and ND-LLD transplants are needed to increase overall graft supply for pediatric candidates and to address disparities in pediatric LT.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from SRTR/OPTN. Restrictions apply to the availability of these data. Data are available from the authors with the permission of SRTR/OPTN.

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Abbreviations:

CI	confidence interval
DDLT	deceased donor liver transplant
D-LLD	directed living liver donor
ICU	intensive care unit
LDLT	living donor liver transplantation
LT	liver transplant
MELD	model for end-stage liver disease
ND-LLD	non-directed living liver donor
OPTN	Organ Procurement and Transplantation Network
OR	odds ratio
PELD	pediatric end-stage liver disease
SD	standard deviation
SRTR	Scientific Registry of Transplant Recipients

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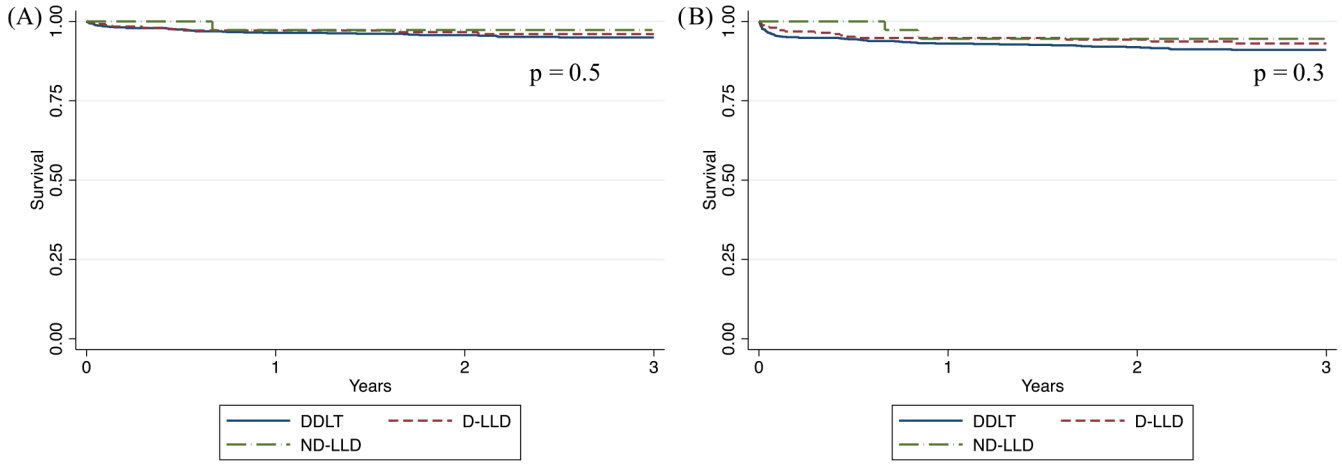

FIGURE 1.

(A) Recipient and (B) graft survival by type of donor

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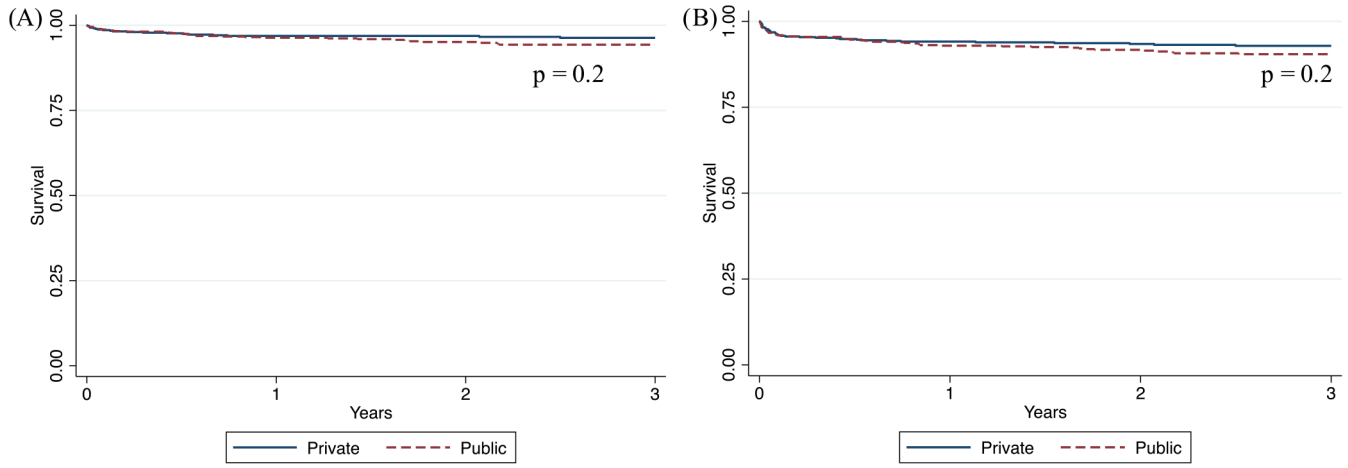

FIGURE 2.
(A) Recipient and (B) graft Survival by Type of Insurance

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TABLE 1

Characteristics of pediatric LDLT recipients by living donor type

***N* (%)**	**Directed living donor recipients (*n* = 253)**	**Non-directed living donor recipients (*n* = 46)**	***p*-value**
Public insurance	102 (40%)	27 (59%)	.02
Age, years	3.05 (4.81)	3.26 (4.27)	.8
Weight, kg	16.16 (15.99)	14.70 (8.74)	.5
Female	117 (46%)	21 (46%)	.9
Non-White race or Hispanic ethnicity	97 (38%)	21 (46%)	.4
O blood group	131 (52%)	24 (52%)	1.0
Biliary atresia primary diagnosis	136 (54%)	24 (52%)	.8
MELD/PELD with exception			.04
<20	84 (33%)	14 (30%)	
20–30	30 (12%)	12 (26%)	
>30	99 (39%)	17 (37%)	
Status 1A or 1B	40 (16%)	3 (7%)	
Condition			.4
Home	166 (66%)	35 (76%)	
Hospitalized, non-ICU	62 (25%)	8 (17%)	
Hospitalized, ICU	25 (10%)	3 (7%)	

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TABLE 2

Multivariable logistic regression of living donor type

Variable	Reference	Adjusted OR [95% CI]	*p*-value
Public insurance	Private insurance	2.37 [1.23–4.58]	.01
MELD/PELD with exception			
20–30	<20	2.78 [1.13–6.83]	.03
>30		1.14 [0.52–2.47]	.7
Status 1A or 1B		0.44 [0.12–1.62]	.2