Geographical Rural Status and Health Outcomes in Pediatric Liver Transplantation: An Analysis of 6 Years of National United Network of Organ Sharing Data

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Objective To determine whether children in rural areas have worse health than children in urban areas after liver transplantation (LT).

Study design We used urban influence codes published by the US Department of Agriculture to categorize 3307 pediatric patients undergoing LT in the United Network of Organ Sharing database between 2004 and 2009 as urban or rural. Allograft rejection, patient death, and graft failure were used as primary outcome measures of post-LT health. Pediatric end-stage liver disease/model of end-stage liver disease scores >20 was used to measure worse pre-LT health.

Results In a multivariate analysis, we found greater rates of allograft rejection within 6 months of LT (OR 1.27; 95% CI 1.05-1.53) and a lower occurrence of posttransplantation lymphoproliferative disorder (OR 0.64; 95% CI 0.41-0.99) in patients in rural areas. The difference in allograft rejection was eliminated at 1 year of LT (OR 1.18; 95% CI 0.98-1.42). Rural location did not impact other outcome measures.

Conclusion We conclude that rural location makes a negative impact on patient health within the first 6 months of LT by increasing the risk for allograft rejection, although patients in rural areas may have lower rates of developing posttransplantation lymphoproliferative disorder. Long-term adverse health effects were not seen. *(J Pediatr 2013;162:313-8)*.

Excellent patient survival rates are the current standard in pediatric liver transplantation (LT), with 1- and 5-year survival after LT approaching 90% and 95%, respectively.[1,2] Advances in immune suppression (eg, calcineurin inhibitors) and close outpatient care at pediatric LT centers before and after LT contribute to the general trends in improved health outcomes in LT.[3,4] Markers for success in transplanting living-related or cadaveric livers in children have been evaluated by qualitative measurements, including quality of life, growth parameters, and school achievement.[5-9] Despite the overall good outcomes in pediatric LT, it is not clear how poor geographical access to highly specialized LT centers affects patients' risk for graft rejection or posttransplantation lymphoproliferative disorder (PTLD), 2 serious consequences of failing to balance immune suppression levels after LT.

Appropriate access to specialized health care—as is the case in LT—is increasingly recognized as a predictor for health in patients with complex chronic diseases.[10-12] A growing body of literature exists showing that rural status is a risk factor for worse health in various other nontransplantation diseases,[13-24] but only few efforts have attempted to describe the potential health care and health disparities between urban and rural LT patients in the US.[25-27] In particular, for pediatric LT patients in rural areas, frequent outpatient monitoring may be difficult because of long travel distance to the LT center, lack of reliable transportation, and infrequent or poor primary care near their home residence.

Our hypothesis is that pediatric LT patients living in remote geographical areas in the US are at increased risk for worse health outcomes after LT because routine access to specialized health care at major pediatric LT centers may be more difficult. The primary aim of our study is to determine whether pediatric LT patients living in rural areas of the US are at increased risk for worse health, as defined by patient and allograft survival, allograft rejection, and PTLD.

Methods

We performed a database analysis of the United Network of Organ Sharing (UNOS) data of all pediatric LT in the US between January 2004 and

LT	Liver transplantation
MELD	Model of end-stage liver disease
PELD	Pediatric end-stage liver disease
PTLD	Posttransplantation lymphoproliferative disorder
UI	Urban influence
UNOS	United Network of Organ Sharing
USDA	US Department of Agriculture

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December 2009. Data extraction was prepared by UNOS. Patients between 0 and 21 years of age at the time of LT with one home address in the continental US were included in the study. LT patients who were multiorgan recipients were included, but their known differences in health outcomes were identified and controlled in the data analyses. Our database included a total of 3307 patients.

Primary Outcome Measures and Model Covariates

Primary outcome measures used to evaluate health pre- and post-LT were: (1) patient survival; (2) allograft survival; (3) acute allograft rejection before hospital discharge after LT; (4) allograft rejection within 6 months after LT; (5) allograft rejection within 1 year of LT; (6) model of end-stage liver disease (MELD) and pediatric end-stage liver disease (PELD) scores; and (7) the occurrence of PTLD after LT. Clinically relevant predictor variables were used in controlling the multivariate logistic regression models: (1) age at the time of LT; (2) sex; (3) race; (4) days on the waiting list before LT; (5) multiorgan recipient status; and (6) rural or urban status.

MELD/PELD scores were dichotomously categorized as >20 or <20 to capture the severity of liver failure and urgency for donor livers. Allograft rejection was determined by a reported clinical diagnosis from each transplantation center reporting UNOS; biopsy-confirmation information of allograft rejection was not available. Predictor variables age and days on the waiting list before LT were continuous variables. Race information was captured in the UNOS dataset as 7 distinct groups and was coded in our analysis as a categorical variable: white, black, Hispanic, Asian, Pacific Islander, Native American, and multiracial/other. Other predictor variables were coded as binary variables.

Defining Rural and Urban Status and Urban Influence Codes

Rural or urban status was determined using urban influence (UI) codes, published and updated every 10 years by the US Department of Agriculture (USDA).[28] The most recent UI codes from 2003 were used in this analysis. According to the USDA, US counties are dichotomously categorized using UI codes as either "metropolitan" or "non-metropolitan" on the basis of population density. UI codes numerically are stratified 1 through 12 based on population density in each of the 3141 counties in the US, but only codes 1 and 2 (counties with >132 persons per square mile) are categorized as metropolitan. In this analysis, we chose to keep USDA's binary classification of urban (UI codes 1 and 2) or rural (UI codes 3 or greater) because the UI codes originally were published on the basis of: (1) previous research by the federal government on metropolitan versus nonmetropolitan counties based on "access to larger economies"; and (2) the economic effects of all US counties based on population density. (Refer to http://www.ers.usda.gov/briefing/rurality/urbaninf/ for more information on UI codes.)

Statistical Analyses

All analyses were performed with the use of unadjusted and adjusted logistic regression models in Stata (StataCorp, College Station, Texas). Differences between groups were compared using *t*-tests for continuous variables and χ^2-tests for categorical variables. The univariate and multivariate logistic regression models were used to evaluate the association between outcome variables and predictor variables in the model. $P < .05$ was considered statistically significant.

Results

A total of 3307 pediatric LT patients were represented in our study; 3212 included complete home addresses to extrapolate patients' urban or rural status (1836 urban vs 1376 rural). Table I summarizes the patient demographics in our database. Urban and rural groups had equal distributions of males and females. There was no difference in the average age for either group, with a mean age of 6.5 and 6.3 for urban and rural patients, respectively. Urban areas compared with rural areas had a greater proportion of black (20.1% vs 13.4%, $P < .001$), Hispanic (23.8% vs 16.3%, $P < .001$), and Asian (6.8% vs 2.3%, $P < .001$) subjects. Rural areas compared with urban areas had a greater proportion of white (64.0% vs 46.7%, $P < .001$) and Native American (1.2% vs 0.3%, $P < .005$) subjects. Patients from urban and rural areas had no difference in mean days on the waiting list before LT (144 + 318 days vs 125 + 274 days), MELD/PELD scores (>20) at the time of LT (39.4% vs 40.4%), and likelihood of needing a multiorgan transplantation (13.0% vs 13.8%).

MELD/PELD Scores

There was no difference in the acuity of the patients at the time of LT in either urban or rural groups.

Table I. Patient demographics

Variable	Urban patients n = 1836	Rural patients n = 1376	*P* value
Sex distribution	51% male	50% male	NS
Mean age at LT, y	6.5 (SD +7.1)	6.3 (SD +7.1)	NS
Ethnicity			
White	857 (46.7%)	881 (64.0%)	<.001
Black	370 (20.1%)	185 (13.4%)	<.001
Hispanic	438 (23.8%)	224 (16.3%)	<.001
Asian	124 (6.8%)	31 (2.3%)	<.001
Native American	5 (0.3%)	16 (1.2%)	<.005
Hawaiian/Pacific Islander	8 (0.4 %)	9 (0.6%)	NS
Other	34 (1.9%)	30 (2.2%)	NS
Mean days on waiting list	144 (SD +318)	125 (SD +274)	NS
Multiorgan recipients	240 (13.0%)	190 (13.8%)	NS
MELD/PELD > 20 at LT	724 (39.4%)	555 (40.4%)	NS
Graft rejection before hospital discharge	237 (12.8%)	198 (14.4%)	NS
Graft rejection within 6 months of LT	307 (22.9%)	285 (27.0%)	<.05
Graft rejection within 1 year of LT	370 (28.6%)	313 (31.6%)	NS
Patient death after LT	234 (12.7%)	195 (14.1%)	NS
Graft failure	382 (20.7%)	294 (21.3%)	NS
PTLD occurrence	67 (3.8%)	32 (2.4%)	<.05

NS, not statistically significant.