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Racial Differences in Hospital Readmission Days and Readmission Rate in Pediatric Liver Transplant: A Single-Center Experience

By

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Master of Public Health

Epidemiology

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An abstract of

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We conducted a retrospective analysis among pediatric (ages 0 to 22) liver transplant recipients from 1998 to 2008, and followed for health outcomes through April 2011 at the Children's Hospital of Atlanta (CHOA). Our main exposure of interest was race (white, black, others). We examined the relationship between race and hospital readmission days (HRD) and readmission rate within one year post-transplant. However, we did not detect racial differences in HRD and readmission rate among a pediatric liver transplant recipient population in the Southeastern United States (US).

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Chapter I: Abstract, Background/Literature Review

Abstract

Few studies have examined the impact of racial disparities on outcomes in pediatric liver transplantation. While some relationships have been described in other solid organ transplantation, this topic has not been studied in depth in pediatric liver transplantation. As the Southeastern U.S. has a high percentage of individuals who are black and/or have low socioeconomic status (SES), this question is particularly relevant to clinical outcomes in the Southeast.

We conducted a retrospective analysis among pediatric (ages 0 to 22) liver transplant recipients from 1998 to 2008, and followed for health outcomes through April 2011 at the Children's Hospital of Atlanta (CHOA). Our main exposure of interest was race (white, black, others). We examined the relationship between race and hospital readmission days (HRD) and readmission rate within one year post-transplant. However, we did not detect racial differences in HRD and readmission rate among a pediatric liver transplant recipient population in the Southeastern United States (US).

Background and Literature Review

Liver transplantation (LT) has been very successful in treating children with end-stage liver disease (ESLD) and offers the opportunity for a long, healthy life. In the pediatric population (ages ≤18 years old), liver transplantation is indicated for a variety of reasons. The main indications for liver transplantation in the pediatric population are as

follows: (1) Extra-hepatic cholestasis: biliary atresia; (2) Intra-hepatic cholestasis: sclerosing cholangitis; Alagille's syndrome; non-syndromic paucity of intrahepatic bile ducts; and progressive familial intrahepatic cholestasis; (3) Metabolic diseases: Wilson's disease; α1-antitrypsin deficiency; Crigler-Najjar syndrome; inborn error of bile acid metabolism; tyrosinemia; disorders of the urea cycle; organic acidemia; acid lipase defect; oxaluria type I; and disorders of carbohydrate metabolism; (4) Acute liver failure; and (5) Other reasons: primary liver tumor and cystic fibrosis[10].

Racial disparities in health outcomes of liver transplantation are an important topic given the increasing diversity in the US. The effect of racial disparities on liver transplant outcomes is not well understood. Several studies have examined the impact of race among adult populations, yielding differing results [3, 4]. Among pediatric liver transplant recipients, however, very few studies have examined the impact of racial disparities on transplant outcomes. A study of national pediatric and adult data showed no significant difference in patient survival (at 1, 3, 5, and 10 years) between racial/ethnic groups when examining national Scientific Registry of Transplant Recipients (SRTR) data from 1994 to 2006, although regional differences were not explored [5]. Another study showed African American race was an independent predictor of chronic graft rejection and decreased patient survival[6]. In other solid organ transplantation, research has suggested an effect of race and/or SES on patient outcomes in pediatric populations [7]. Research among adult liver transplant recipients suggests there may be racial disparities in transplant outcomes. In particular there is a disproportionate decrease in patient and graft survival among

African Americans in comparison with Caucasians and Hispanics [9].However, little is known about the impact of racial disparities among pediatric liver transplant recipients.

Few studies have examined racial disparities in hospitalization (length of stay in hospital) and hospital readmission rate following pediatric liver transplantation. Some previous kidney transplant studies in the 1990s showed that length of stay (LOS) is a well-known predictor of the total cost of the surgical experience [15]. This is especially true of transplantation surgery, which has many potential complications that can compound the LOS [15]. The literature on LOS began in 1983 with the implementation of the prospective payment system (PPS) by the Health Care Finance Administration (HCFA)[16]. The concern over LOS was not initially prompted by clinical indicators, rather by the financial implications of the PPS. The articles, papers and reports on LOS seem to center around high-cost, common admissions for coronary artery bypass grafts, acute myocardial infarctions and obstetrics [17, 18].

More recently, a study of adult kidney transplant recipients showed a strong correlation between LOS and post-transplant hospitalization cost. The study concluded that increasing efforts should be directed at controlling costs and resource utilization associated with kidney transplantation [11]. Prior studies have reported that for kidney transplantation, the costs of hospitalization and its duration sometimes equal or surpass transplantation surgery itself [12, 13]. Health care reform has emphasized a decrease in healthcare resource utilization without sacrificing the quality of patient care. One paper published in April 2011 investigated kidney transplant Medicare payments and LOS. Regression models for payments and LOS included: 1) baseline recipient, donor and

transplant factors from the Organ Procurement and Transplant Network (OPTN), 2) OPTN variables and individual comorbidities and 3) OPTN variables and counts of Charlson or Elixhauser comorbidities. They concluded that their methodology could be used to explore whether Medicare reimbursement for transplantation of higher-risk recipients and using non- standard organs is financially adequate as well as in the analysis of related questions in other healthcare systems [14].

In a single center study of 83 pediatric liver transplant recipients in 2001, total cost was directly correlated to post-transplant length of stay [8]. Approximately 100 million dollars are spent each year for liver transplantation and the ensuing hospitalization for the 500–600 pediatric liver transplant recipients in the United States. In a previous study of pediatric liver transplant recipients at a single center, white children had lower costs and shorter length of stay [8]. Another single center included 47 children who underwent orthotopic liver transplantation (OLT) from September 1996 to April 1999 in the study intervention group and the control group included 36 children who underwent OLT from March 1994 to August 1996. They hypothesized that an intervention designed to decrease the length of hospitalization would reduce costs without jeopardizing clinical outcome. The study showed that for the intervention group, the mean length of stay, total costs, and surgical costs were 29%, 36%, and 34% lower, respectively [19]. However the basis for the relationship between LOS and race was not included in this study.

Previous studies reported that hospitalizations are costly, accounting for approximately 31 percent of total health care expenditures [20]. In Medicare, inpatient care

accounts for 37 percent of spending and readmissions contribute significantly to that cost [21]. To our knowledge, there were no previous studies focused on the relationship between race and hospital readmission days (HRD) (days hospitalized within the first year post-transplant) as well as readmission rate among pediatric liver transplant patients. Therefore, the purpose of our study was to examine whether racial disparities exist in outcomes of HRD and hospital readmission rate (the time from discharge at transplant until first readmission, censoring at the date of death) among pediatric liver transplant recipients at CHOA.

Chapter II: Methods and Results

Methods

Research Question

The purpose of this study was to determine whether there were racial differences in hospital readmission days (HRD) and readmission rate among a pediatric liver transplant recipient population in the Southeastern U.S

Study Population and Data Sources

We included all 328 children who underwent liver transplantation between 1998 and 2008, and who were followed for health outcomes through April 2011 at the Children's Hospital of Atlanta (CHOA). The main source of data used in this analysis was from patient medical charts from CHOA. Other data sources include Georgia Transplant Foundation (GTF) data on SES and United Network for Organ Sharing

(UNOS) data on donor characteristics, intraoperative characteristics, and post-transplant outcomes. Patient medical charts from CHOA gathered basic demographic information (age, race, gender), as well as the hospital charges, HRD and readmission information.

Patients were excluded from the multivariable linear regression and Cox proportional hazards models analysis of this study if they had missing data on outcome variables (n=136), HRD (n=192) and readmission information (n=192). In addition, patients who have had multiple transplants were analyzed for the first transplant only.

The study was approved by the CHOA IRB Review Board in August 2011.

Study Variables

The primary outcome variable was HRD within one year of post-transplant (continuous). Variables collected for this calculation included total hospital days after the discharge date of first transplant within one year. These were summed to calculate the total readmission hospital days within one year for each patient. The second outcome variable for this study was time to hospital readmission defined as the time from discharge at transplant until first readmission (total number of days; censoring at the date of death).

Race, age, gender, cold ischemic time, donor age, graft type, etiology of liver disease, patients' insurance and length of stay (LOS) as the total number of days a patient was in the hospital at the time of transplant were considered covariates in the analysis. Race was reported as white, black or other race. Age was categorized into subgroups as <1-year-old, 1 to 5 years old, 6 to 10 years old, 11 to 17 years old and 18 to 22 years old. Gender was categorized as male or female. Donor age was categorized into subgroups as <1 year old, 1 to 17 years old and >17 years old. Graft type was categorized as whole

liver, partial liver and split liver. Patients' insurance was categorized as public or private insurance.

Statistical Analysis

Chi-square tests and ANOVA tests were used to examine baseline demographic and clinical characteristics of the study population. Results were considered significant at the $p < 0.05$ levels.

Crude and multivariable-adjusted linear regression models were built for computing the RHD as the dependent variable and race and other factors as the independent variables. This model was used to examine adjusted R-squared, parameters and p-values with corresponding 95% confidence intervals. We used crude and multivariable-adjusted Cox proportional hazards model to examine the association between readmission rate and race. For time until readmission, patients were censored when they died (due to any cause). For the Cox proportional hazards model, we reported hazard ratios with corresponding 95% confidence intervals and p values. All the multivariable-adjusted models included bivariate analysis, race-adjusted models for clinical/demographic factors and the fully adjusted model.

All statistical analyses were performed with SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Description of the Study Population

Table 1 summarizes the demographic and clinical characteristics of the study population. Among the 328 patients included in the baseline analysis, the mean age was 5.8 years (± 6.2), 244 (74.4%) were older than one year old, 148(45.1%) were male, 149 (45.4) had private insurance, the mean LOS (days) was 36.9 (±36.4) days, the median time to hospital readmission was 15 days and IQR is 0 to 69 days , the mean Cold Ischemic Time was 8.3 (4.0) hours, 166 (51.2%) had whole liver transplant graft type, and 109 (32.%) had biliary atresia as their primary cause of liver disease (**Table 1**).

A total of 130 patients (39.6%) were white, 80 patients (24.4%) were black and 118 (36%) were other race. Patients with other race/ethnicity were significantly younger than black and white patients (3.5 ± 4.8 years vs. 6.3 ± 6.7 and 6.6 ± 6.3 years, p=0.0201), more black patients had public insurance than white (55.0% vs. 24.6%) and more black patients had biliary atresia as their primary cause of liver disease than white (50.0% vs. 18.5%) (**Table 1**).

Hospital Readmission Days

Figure 1 shows the number of patients who readmitted to the hospital at least once within one year after the LT from 1999 to 2011. There were a 19 patients readmitted after LT in 2010, however, there were only 4 patient readmitted in 2000.

Table 2 reported the parameter estimates and p-values and corresponding 95% CI for the fully adjusted linear regression model for HRD. Black patients had a hospital readmission stay of 1.22 days less than white patients, and other races had a longer readmission stay (4.66 days). However, these differences were not statistically significant.

Patients who have a split liver transplant have significantly longer HRD (35.63) compared to those patients who had a whole liver transplant graft (p=0.01). Patients whose disease etiology was biliary atresia will have significantly shorter HRD (15.14) comparing patients who had neither biliary atresia nor non-cholestatic liver disease/cirrhosi (p=0.01) (**Table 2**).

Table 3 reported the R-Square, parameter estimates for race and p-values with 95%CI. In the crude model, we did not find statistically significant differences in HRD between races. Results were consistent in bivariate and multivariable-adjusted models that adjusted for clinical/demographic factors (**Table 3**).

Figure 1 shows the time from discharge at transplant until first readmission (total number of days; censoring at the date of death). We categorized readmission time into subgroups as 0 (not readmitted), 1 to 50 days, 51-100 days and >100 days. We found that there were more white patients who were readmitted than black and other races (**Figure 2**).

Readmission Rate

In crude analysis, there was no significant difference in readmission rate between black and white patients (HR = 0.961, 95% CI = 0.657-1.405, p=0.836). In bivariate analysis, we did not find any differences between the two groups (all p-values were greater than 0.05). In the fully adjusted model, black patients were 1.17 times as likely to be readmitted to the hospital as white patients, but results were not statistically significant (HR = 1.172, 95% CI = 0.709-1.936, p=0.536). (**Table 4**).

Table 5 reported the parameter estimates, hazard ratio, p-values and corresponding 95% CI for the fully adjusted model for readmission rate. We found that patients who are older than one year old except age group 6 to 10 are more likely be readmitted (HR= 1.552, 1,798, 1.403, 1.153), however, this is not statistically significant. We did not find any other differences between black and white patients for all the other independent variables in our study (**Table 5**).

Chapter III: Discussion and Possible Future Directions

Discussion

Readmission to the hospital after discharge is an important metric for evaluating the cost-effectiveness and quality of patient health services. Although readmission does not universally indicate suboptimal quality of care at the time of initial hospitalization, readmission is costly and sometimes preventable [22, 23].

LT is an expensive procedure with an estimated US annual cost of over 3 billion dollars and a per patient cost of over half a million dollars for the first year after LT. Post discharge requirement of inpatient rehabilitation and skilled nursing facilities by some LT recipients further increase expenditure and resource utilization [24].

To date, although some clinical factors have been examined as predictors of readmission after LT, the race disparities and other SES factors for readmission to the hospital after liver transplant have not been well described in the literature especially in

pediatric liver transplants. Therefore, we sought to determine whether there are racial differences in HRD and readmission rate among a pediatric liver transplant recipient population. Previous studies have shown that recipient age, donor factors such as donor age, cold ischemia time, and the type of donor graft were not associated with readmission in adult liver transplant [25].

In our study, we found that patients who had split liver transplant graft have significantly longer HRD (35.63) compared to patients who had whole liver transplant graft. Patients who had biliary atresia had significantly shorter HRD (15.14) compared to those with other disease etiology. However, we did not find any significant racial differences in healthcare resource utilization using multivariable linear regression and Cox proportional hazards models.

This study has several strengths and weaknesses. Its strengths include its linkage of medical records from 1998 to 2011 to multiple data sources. Another strength is its single center design, which minimizes variables that could impact readmission and would be difficult to ascertain in a multi-center study with variations in LT teams. Additionally, the potential confounder of patients' insurance information was included.

The weaknesses inherent in this study's single center design are small sample size and some missing data of outcome variables. Another flaw is that we were unable to obtain MELD scores from patient medical records, therefore we could not include it in the analysis; if MELD is associated with both race and with healthcare resource utilization, our results may not account for this potential confounding factor. In addition, the nature of this study was that of a retrospective cohort study, which inherently has its own limitations.

Despite the weaknesses of our study, this study provides an important initial examination of the influence of race on healthcare resource utilization among pediatric liver transplant recipients. To our knowledge, this is the first study to examine the association between race and HRD and readmission rate in pediatric liver transplantation. Future studies should include larger regional and national studies to examine whether results are consistent. Also, the association between cost and LOS and HRD should be examined in future analyses.

Possible Future Directions

Future directions may include larger regional and CHOA study in order to get large sample size. Also, hospital cost can be an outcome variable in the study to examine the relationship between RHD and hospital cost.

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Table 1. Demographic and Clinical Characteristics of Study Population by Race

	Race				
	Study Population N=328 N (%) or Mean ± SD	**White N (%) N=130 (39.6)**	**Black N (%) N=80 (24.4)**	**Others N (%) N=118 (36)**	**P-value**
Mean Age (years) ± SD	5.8 ± 6.2	6.6± 6.3	6.3 ± 6.7	3.5 ± 4.8	0.0201
Age (years), N (%)					0.0496
<1	81 (24.7)	25 (19.2)	20 (25.0)	22 (43.1)	
1 to 5	116 (35.4)	47 (36.2)	26 (32.5)	15 (29.4)	
6 to 10	42 (12.8)	17 (13.1)	9 (11.3)	8 (15.7)	
11 to 17	70 (21.3)	33 (25.4)	17 (21.3)	6 (11.8)	
18 to 22	16 (4.9)	8 (6.2)	7 (8.8)	0	
Male Sex, N (%)	148 (45.1)	70 (53.8)	32 (40.0)	24 (47.1)	0.0496
Health Insurance Categories, N (%)					<0.0001
Public (other)	110 (33.5)	32 (24.6)	44 (55.0)	30 (58.8)	
Private	149 (45.4)	95 (73.1)	30 (37.5)	21 (41.2)	
Net Yearly Income ($)<30,000, N (%)	77 (23.5)	23 (17.7)	37 (46.3)	14 (27.5)	0.0021
Mean LOS (days) ± SD	36.9 ± 36.4	30.1± 23.7	41.6± 38.7	46.1 ± 54	0.0768
Readmission Hospital Days Median (IQR)	15.0 (0, 69)	25.5 (3.5, 71.0)	14.0 (0, 41)	12.0 (0, 94)	0.4830
Readmission Rate in one year ± SD	50.4 ± 75.8	53.6 ± 71.8	46.1 ± 78.8	56.3 ± 85.5	0.4859
Mean Total Payment/ Hospital Charges ± SD	1.8 ± 2.3	0.7 ± 0.7	0.5 ± 0.2	0.6 ± 0.3	0.0663
Transplant Graft Type, N (%)					0.7370
Whole Liver	166 (51.2)	66 (50.8)	52 (65.0)	22 (43.1)	
Split Liver	10 (2.9)	2 (1.5)	4 (5.0)	2 (3.9)	
Partial Liver	72 (22.0)	27 (20.8)	18 (22.5)	10 (19.6)	
Mean Cold Ischemic Time ± SD	8.3 ± 4.0	8.8 ± 4.5	7.9 ± 2.3	7.8± 5.5	0.3334
Donor Age (years), N (%)					0.0836
<1	11 (3.4)	5 (3.8)	2 (2.5)	2 (3.9)	
1-17	142 (43.3)	49 (37.7)	53 (66.3)	15 (29.4)	

>17	100 (30.5)	43 (33.1)	19 (23.8)	18 (35.5)	
Disease Etiology, N (%)					0.0077
Acute hepatic necrosis	3 (0.9)	2 (1.5)	0 (0)	0 (0)	
Biliary atresia	109 (32.2)	24 (18.5)	40 (50)	15 (29.4)	
Cholestatic liver disease/cirrhosis	3 (0.9)	1 (0.8)	0 (0)	2 (3.9)	
Metabolic disease	20 (5.9)	9 (6.9)	4 (5.0)	0 (0)	
Neoplasms (benign and malignant)	14 (4.1)	8 (6.2)	2 (2.5)	2 (3.9)	
Non-cholestatic liver disease/cirrhosis	41 (12.1)	18 (13.8)	9 (11.3)	3 (5.9)	
Others	84 (24.8)	36 (27.7)	20 (25.0)	13 (25.5)	

Figure 1: Number of patients who were readmitted within one-year post-transplant

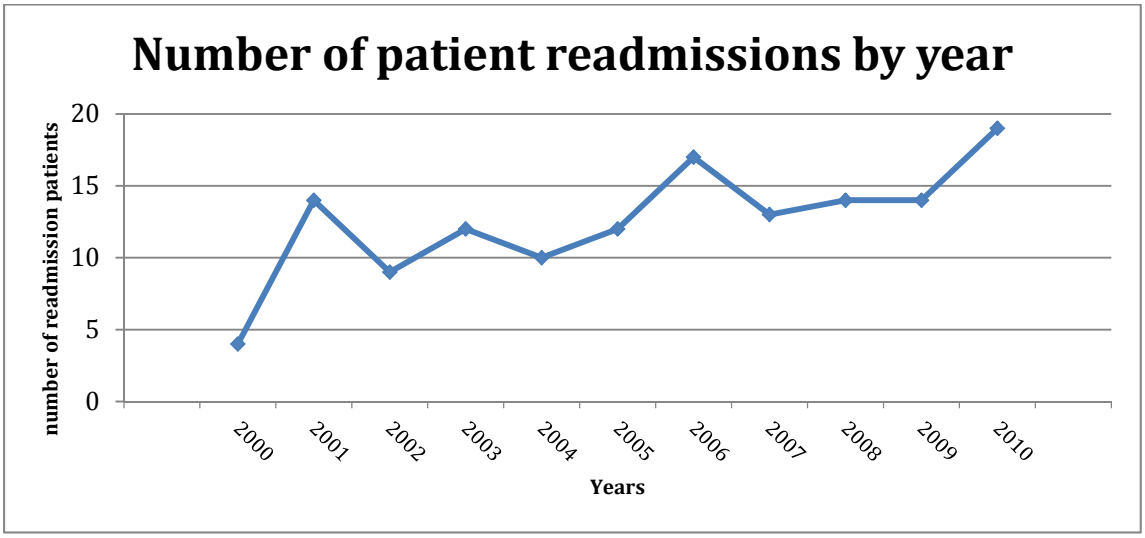

TABLE 2. Fully Adjusted Linear Regression Models for Hospital Days Within One-Year Post-Transplant: Children's Healthcare of Atlanta Study Population

Variables	Parameter Estimates	p-value	95% CI
Age (years)			
<1	*Reference*		
1 to 5	-10.18704	0.1431	(-23.85923, 3.48515)
6 to 10	-11.96236	0.1669	(-28.97686, 5.05214)
11 to 17	-14.99194	0.0901	(-32.35208, 2.36820)
18 to 22	13.59622	0.2332	(-8.842403, 6.03483)
Male	0.24557	0.9600	(-9.39902, 9.89015)
Race			
White	*Reference*		
Black	-1.22591	0.8401	(-13.20490, 10.75307)
Other	4.66055	0.5025	(-9.03334, 18.35444)
Health Insurance			
Public (others)	*Reference*		
Private	2.50247	0.6430	(-8.13858, 13.14352)
LOS (days)	0.00153	0.9833	(-0.14212, 0.14517)
Transplant Graft Type			
Whole Liver	*Reference*		
Partial liver	9.18448	0.1708	(-3.99717, 22.36614)
Split Liver	35.62918	0.0105	(8.43729, 62.82108)
Donor Age (years)			
<1	*Reference*		
1-17	11.35150	0.3553	(-12.82827, 35.53128)
>17	13.37480	0.3167	(-12.92076, 39.67036)
Disease Etiology			
Biliary atresia	-15.13607	0.0079	(-26.25351, -4.01864)
Non-cholestatic liver disease/cirrhosi	-8.40773	0.2849	(-23.88228, 7.06683)
Others	*Reference*	0.0079	(4.01864, 26.25351)

TABLE 3. Multivariate Linear Regression Models for Hospital Days Within One-Year Post-Transplant

Variables	R-Square (White as reference)	Parameter Estimate	p-value (95% CI)
Crude Model			
Race alone	0.0063	-4.1241	0.5404 (-14.1120, 5.8638)
Bivariate Analysis			
Race + Age	0.0536	-5.4823	0.2814 (-15.4926, 4.5279)
Race + Sex	0.0061	-3.4042	0.5144 (-13.6840, 6.8756)
Race + Etiology	0.0339	-1.3493	0.8025 (-11.9801, 9.2814)
Race + Donor Age	0.0354	-2.6604	0.6036 (-12.7502, 7.4293)
Race + Graft Type	0.0503	-5.3077	0.3146 (-15.9634, 5.0781)
Race + Insurance	0.0073	-3.6528	0.4966 (-14.2295, 6.9239)
Race + LOS	0.0098	-4.6793	0.3613 (-14.7649,5.4062)
Race Adjusted Model for Clinical/Demographic Factors			
Race +Age +Sex +Etiology +Donor Age + Graft Type	0.1546	-1.8598	0.7460 (-13.1749, 9.4553)
Fully Adjusted Model			
Race +Age +Sex +Etiology +Donor Age + Graft Type + Insurance + LOS	0.1497	-1.2123	0.8419 (-13.1910, 10.7665)

Figure 2: Patients' Readmission Time (days) from Discharge at Transplant Until First Readmission Post-transplant

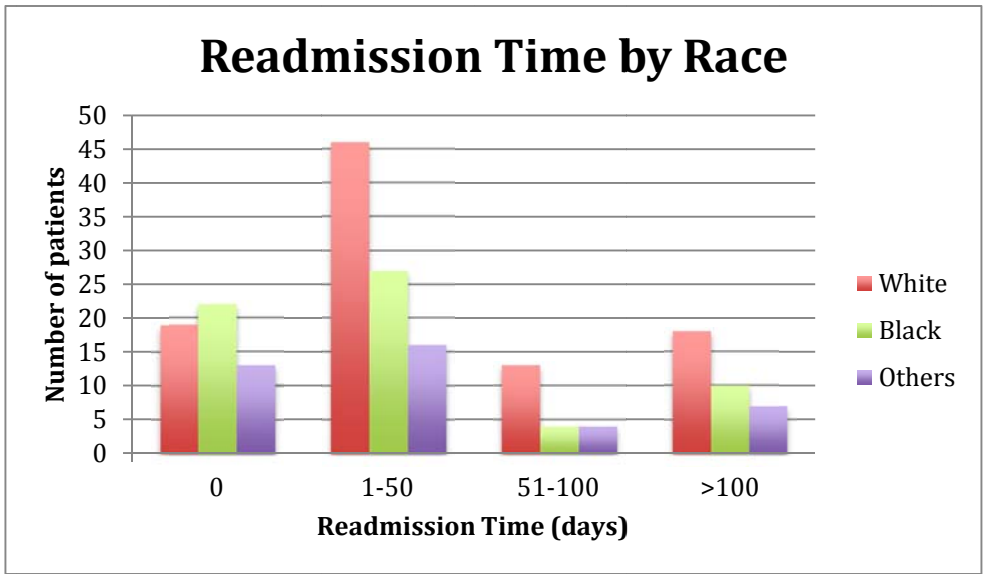

TABLE 4. Multivariable Cox Proportional Hazards Models for Transplant Readmission Rate Within One-Year Post-Transplant

Variables	HR (White as reference)	95% CI	p-value
Crude Model			
Race alone	0.961	(0.657, 1.405)	0.8355
Bivariate Analysis			
Race + Age	0.921	(0.625, 1.358)	0.6791
Race + Sex	0.927	(0.628, 1.368)	0.7027
Race + Etiology	1.099	(0.730, 1.654)	0.6519
Race + Donor Age	0.937	(0.629, 1.396)	0.7505
Race + Graft Type	0.930	(0.626, 1.382)	0.7202
Race + Insurance	1.138	(0.742, 1.746)	0.5533
Race + LOS	0.936	(0.639, 1.370)	0.7322
Race Adjusted Model for Clinical/Demographic Factors			
Race +Age +Sex +Etiology +Donor Age + Graft Type	1.046	(0.653, 1.677)	0.8518
Fully Adjusted Model			
Race +Age +Sex +Etiology +Donor Age + Graft Type + Insurance + LOS	1.172	(0.709, 1.936)	0.5357

TABLE 5. Fully Adjusted Cox Proportional Hazards Models for Transplant Readmission Rate

Variables	Parameter Estimate	HR (95% CI)	p-value
Age (years)			
<1	*Reference*		
1 to 5	0.43966	1.552 (0.903, 2.667)	0.1114
6 to 10	-0.04909	0.952 (0.487, 1.860)	0.8858
11 to 17	0.58640	1.798 (0.939, 3.441)	0.0767
18 to 22	0.33849	1.403 (0.619, 3.178)	0.4172
Male	0.14210	1.153 (0.785, 1.693)	0.4691
Race			
White	*Reference*		
Black	0.15869	1.172 (0.709, 1.936)	0.5357
Other	0.13395	1.143 (0.640, 2.042)	0.6507
Health Insurance			
Public (others)	*Reference*		
Private	0.35928	1.432 (0.932, 2.202)	0.1015
LOS	-0.00278	0.997 (0.991, 1.003)	0.3617
Transplant Graft Type			
Whole Liver	*Reference*		
Partial liver	-0.52868	0.589 (0.342, 1.016)	0.0572
Split Liver	-0.67863	0.507 (0.178, 1.448)	0.2047
Donor Age (years)			
<1	*Reference*		
1-17	-0.58384	0.558 (0.186, 1.675)	0.2982
>17	-0.47983	0.619 (0.187, 2.049)	0.4322
Disease Etiology			
Biliary atresia	*Reference*		
Non-cholestatic liver disease/cirrhosis	0.06901	1.071 (0.533, 2.155)	0.8465
Others	0.18805	1.207 (0.758, 1.922)	0.4283