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Factors Predicting Health Related Quality of Life in Pediatric Liver Transplant Recipients in the Functional Outcomes Group

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Abstract

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Data from 997 pediatric liver transplant (LT) recipients were used to model demographic and medical variables as predictors of lower levels of health related quality of life (HRQOL). Data were collected through Studies of Pediatric Liver Transplantation (SPLIT) Functional Outcomes Group (FOG) project. Patients were between 2-18 years of age and survived LT by at least 12 months. Parents and children (age ≥ 8 years) completed PedsQL ™ 4.0 Generic Core and Cognitive Functioning Scales at one time point. Demographic and medical variables were obtained from SPLIT. HRQOL scores were categorized "poor" based on lower 25% of scores for each measure. Logistic regression models were generated. Single-parent households (OR 1.94, CI 1.13 – 3.33, p=0.017), anti-seizure medications (OR 3.99, CI 1.26 – 12.70, p=0.019) and number of days hospitalized (OR 1.03, CI 1.01 – 1.06, p=0.0067) were associated with lower self-reported HRQOL. Parent data identified increasing age at transplant, age 5-12 years at survey, hospitalization > 21 days at LT, re-operations, diabetes and growth failure at LT as additional predictors of generic HRQOL. Male gender, single-parent households, higher bilirubin levels at LT and use of anti-seizure medication predicted lower cognitive function scores. HRQOL following pediatric LT is related to medical and demographic variables.

Keywords

outcomes; children; organ transplantation; liver disease; quality of life

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The most important goal of pediatric liver transplantation (LT) is to extend the lives of children with end stage liver disease. Reducing medical disability and maintaining a health state that supports normal growth and development are important secondary objectives. Health related quality of life (HRQOL) is a construct that measures the subjective experience of a patient's health state, from their own perspective or from that of a proxy such as a parent. HRQOL has been measured in several cohorts of pediatric LT survivors (1-8) and results suggest that pediatric LT recipients struggle with significant ongoing health issues even in long-term follow-up. Results of a large multi-center cross-sectional study conducted by our research group revealed that pediatric LT recipients had significantly lower HRQOL than an age, gender and race/ethnicity matched healthy population with effect sizes for self-report that ranged from −0.25 for Emotional Functioning to −0.68 for School Functioning (1). The size of this sample and the extensive medical information readily available for this group through the Studies of Pediatric Liver Transplantation (SPLIT) registry allowed us to explore the potential impact of numerous factors on HRQOL from both the parental and patient perspective.

Multiple factors have been examined as predictors of HRQOL in adult LT recipients and in small groups of pediatric LT recipients. Assessment of HRQOL in both pediatric and adult recipients has demonstrated marked improvements in functional outcomes from the pre to post transplant period with steady increases over the first 12 months (6, 9). Preliminary analysis prior to our larger study also suggested that HRQOL would improve with increasing interval from transplant (5). However, studies in adult recipients have demonstrated that these improvements may not be sustained, especially in the areas of mental health and role function (10). The impact of primary diagnosis has also been well studied in adults. Patients with a primary diagnosis of viral hepatitis and alcohol related liver disease have the lowest HRQOL prior to LT and experience the largest incremental increases in the early post-LT period. However, many of these patients have recurrence of disease, thus their long-term HRQOL may be lower than adults transplanted for cholestatic liver diseases (9). The role of post-transplant complications has been explored in adults and graft related complications such as acute rejection appear to diminish HRQOL in the physical domains (11). Demographic variables have also been implicated as determinants of HRQOL post-transplant in both adults and children. In adults, employment is associated

with higher HRQOL (12). In children, higher maternal education, higher parental income and adherence are associated with higher HRQOL (5, 13). Based on these observations and our clinical experiences, we tested the hypotheses that generic HRQOL reported by parent-proxy report and child self-report would be (1) higher in patients with longer intervals from transplant, (2) lower in patients with recent post-transplant complications including rejection and (3) related to socioeconomic variables.

Methods

Study Design

The data collection methods for this ancillary study of the SPLIT registry have been previously described (1). In brief, the study cohort included a cross-section of pediatric liver transplant recipients between 2 and up to18 years of age, who had survived LT by at least 12 months. Patients and parents/guardians were also required to be fluent in English or Spanish. The study was approved by the Institutional Review Boards at the participating SPLIT centers and written informed consent was obtained prior to participation. Data was collected at 23 centers in the United States and Canada from June 2005 to December 2009. Eligible patient and parent or guardian dyads were recruited during a routine follow-up visit at their transplant center. Three of the 22 centers supplemented recruitment by mail. Overall, fewer than 50 patients included in the sample completed the survey by mail. The parent/guardian and patient (if age 8 or older) completed one of four age-specific versions of the PedsQL ™ 4.0 Generic Core Scales. The completion of the PedsQL ™ surveys by the parent/guardian and patient occurred only once. The PedsQL ™ Cognitive Functioning (CF) Scale was added to the study design in August 2006 to gather more specific data regarding perceived cognitive function in this group.(14, 15) Demographic and medical variables were obtained from SPLIT registry data collected at registration, at transplant and at the annual follow-up visit coinciding with the time of survey administration.

Statistical Analysis and Model Development

The primary outcomes measure was the PedsQL ™ 4.0 Total Scale Score from child self-report for children age 8-18 years and the PedsQL ™ 4.0 Total Scale Score from parent proxy-report for children age 2-18 years. Secondary outcomes included parent proxy-report results for the PedsQL ™ Cognitive Functioning Scale. The self-report version of the PedsQL™ Cognitive Functioning Scale was not included in these analyses since the sample size for patient self-report (n=214) was considered too small for multivariate analyses.

Varni *et al* have investigated the cutoff points for ‘at-risk status’ for impaired quality of life. (16) In a large pediatric population, they determined that one standard deviation below the mean of the total sample was a clinically meaningful measure of impaired quality of life since it represented scores comparable to patients with a severe chronic health condition. Therefore, we dichotomized a score as “poor” if the score fell within the lower 25% of scores for each measure, and all other scores were considered “good”. The logistic regression models were generated using predictor variables detailed in Supplemental Table 1 which included both pre-transplant, early post-transplant and current factors that were significant in univariate analysis at a level of $p \leq 0.10$. Statistical analyses including the logistic regression modeling were conducted with SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Liver Transplant Sample

Demographic and clinical characteristics of the patient sample are included in Table 1. The sub-set of 441 patients for whom PedsQL ™Cognitive Functioning (CF) Scale data were collected was not significantly different from the overall cohort (Table 1). For all 997 participants, the average age of the 546 boys (54.8%) and 451 girls (45.2%) was 8.44±4.43 years. For the 444 patients completing the child self-report, the average ages of the 246 boys (55.4%) and 198 girls (44.6%) were 12.56±3.00 years. The median interval from transplant to survey was 3.73 years (range 1.00-12.69). Hospital admission since the last annual follow-up was reported for 40% of the group, with 18% reporting more than 7 in-patient hospital days. Diagnosis of a vascular complication or biliary tract complication since the last follow-up was reported for 3% and 5%, respectively. Diabetes was reported for 2% and none of the patients were on dialysis. Eight-eight percent were receiving tacrolimus, 20% were receiving steroids and 2% were on medications to control seizures. Twelve percent had experienced a rejection episode in the previous year.

Mean parent proxy-report and self-report PedsQL™ scores for this sample are also included in Table 1. Mean PedsQL™4.0 Generic Core parent proxy-report Total scores did not vary by interval from transplant (1-3 versus ≥ 3 years, P=0.19), but did vary by donor type (living donor better than deceased donor, p=0.05) and Pediatric End Stage Liver Disease Score (PELD ≥ 15 better than PELD < 15, p=0.0014). Mean PedsQL™4.0 Generic Core self-report scores did not differ by interval from transplant, donor type or PELD score. Intraclass Correlations (ICC) between child self-report and parent proxy-report across the PedsQL™ 4.0 Generic Core Scales for the liver transplant sample (n=873) have previously been reported to be in the moderate agreement range and across each of the PedsQL™ Scales parents reported a lower mean score compared to their children (1).

PedsQL™ 4.0 Generic Core Scales Child Self-report

The PedsQL ™ 4.0 Total Scale Score from the child self-report version was dichotomized at the 25th percentile as described above. Univariate analysis to predict low scores identified 2 demographic (race p=0.082, marital status p=0.039) and 7 medical variables (days hospitalized in the first month after LT p=0.06, cGFR ≤ 80 at follow-up p=0.05, CNI use at follow-up p=0.084, seizure medication use at follow-up p=0.0025, serum albumin at follow-up p=0.063, total bilirubin at follow-up p=0.055 and days hospitalized since last annual follow-up p=0.0153) as candidate variables for inclusion in the model of lower HRQOL scores. Age category at survey (p=0.150) did not meet the specified cut, but was included in the model since this variable was highly significant in the univariate analysis of parent proxy-reported scores (p<0.0001). Of the 444 patients with self-report data, 321 had complete data for all of these variables and were included in the generation of the logistic regression model, Table 2. Of note, only 6 of the patients reported seizure medication use since their last annual follow-up.

PedsQL™ 4.0 Generic Core Scales Parent Proxy-report

The PedsQL ™ 4.0 Total Scale Score from the parent proxy-report version was also dichotomized as described and univariate analysis was used to identify factors associated with low scores. Five demographic (age at LT p=0.0006, race p=0.0014, marital status p<0.0001, primary insurance p=0.0003 and age category at survey, lowest age 2-4 years, p=<0.0001) and 19 medical variables met the cut-off for inclusion in the model. Of the 997 patients with parent proxy-report data, 704 had complete data for all of these variables, see Table 3. Seizure medication use at long-term follow-up was again a significant predictor

(OR 4.86, CI 2.03-11.66), but only 13 of the 704 patients in the model reported this exposure.

PedsQL ™ Cognitive Functioning Scale Parent Proxy-report

Univariate analysis of predictors of the lower 25th percentile for scores on the cognitive scale revealed 4 demographic (age group 5-13 years at LT p=0.062, male gender p=0.0093, one parent household p=0.0048 and age category at survey lowest 2-4 years of age, p=0.0011) and 9 medical factors (re-transplantation p=0.031, intubated at LT p=0.099, dialysis in the ICU at LT p=0.0713, INR at LT > 3.0 p=0.0304, albumin at LT > 2.0 mg/dL p=0.0863, total bilirubin at LT as a continuous variable p=0.0174, seizure medication use at follow-up p=0.0010, GGTP > 80 IU/L p=0.0649, and Total bilirubin at follow-up as a continuous variable p=0.0763). Of the 441 patients with parent proxy-report data, 326 had complete data for all of these variables and were thus included in generation of the logistic regression model, Table 4. Seizure medication use at follow-up was reported in only 4 patients.

Discussion

We present the first multi-center analysis of risk factors that predict HRQOL in pediatric liver transplant recipients. In this large and diverse sample set, we identified that both demographic and medical factors predicted HRQOL and found factors varied depending upon whether they were reported from the parent or child perspective. Among the risk factors included in our a priori hypotheses, only socioeconomic factors had a significant impact. We did not find a significant association between interval from transplant and HRQOL, although the median interval from LT was more than three years and many children had survived LT by more than 10 years. Also, conflicting with our original hypotheses, graft dysfunction and history of recent rejection episodes were not associated with lower outcomes. We did identify other medical factors which were associated with lower scores including recent hospitalization, seizure medications, recent re-operations and diabetes.

Few studies have modeled risk factors for lower HRQOL in large, pediatric, multi-site samples. Two recent examples utilizing the PedsQL™ 4.0 Generic Core Scales also revealed that medical and socioeconomic factors both influence outcomes. In children with Acute Lymphoblastic Leukemia (ALL), HRQOL was lower in patients with high risk disease and higher in children with married parents and greater family income levels.(17) For children with Type 1 Diabetes, being on Medicaid, receiving insulin by injection rather than pump administration, poor glycemic control and medical co-morbidities were all associated with lower HRQOL. (18) Developing a better understanding of not only the relative impact of demographic versus medical factors on patient reported outcomes, but also the interaction between these different categories of risk will be important in designing strategies to minimize the burden of disease in children with chronic health conditions.

The choices we made in our approach to this analysis warrant discussion. First, we chose to dichotomize outcomes at the 25th percentile because incremental changes in scores may not have the same clinical relevance throughout the continuum. Also, the upper limit of scores for the bottom quartile for both parent and child report were at least one standard deviation lower than the healthy population mean and more than 6 times the estimated minimal clinically important difference (MCID) for the instruments. This provided assurance that our focus was on patients with functional decrements that were truly relevant(19). In choosing to use logistic regression, we were unable to determine the degree of variability predicted by a given variable. Yet, the associated odds ratios suggest that HRQOL in this population is

determined by complex dynamics, with no single factor playing a large role for the majority of patients.

There were some notable differences between the child and parent-proxy report models. Our previous work has suggested that correlation between parent proxy-scores and child self-report scores for pediatric LT recipients are in the moderate range and may be stronger than for other pediatric patient groups(1). One might expect medical factors such as recent re-operations, living with diabetes and short stature would have a larger impact on perceived HRQOL from the patient's perspective, but these factors were actually more significant in the parent model. Undoubtedly, while attempting to report HRQOL for their child, parents are actually reporting some of their own values and perspectives on a given medical condition. It is also likely children may place a higher value than their parents on some events such as recent hospitalization, which could lessen the association with less common but seemingly more critical events such as re-operations on their HRQOL. There were some factors that displayed consistent associations from both the parent and child perspective. The recent need for treatment with anti-seizure medication was uncommon, but was associated with an odds ratio of approximately 4.0 in both the parent and child model. Likewise, having experienced LT while living in a single parent household increased the risk of lower outcomes at least two-fold from both perspectives.

What is the advantage of being able to predict HRQOL outcomes in surviving patients? Providing parents and older patients with expectations for both physical and psychosocial function following LT can help them anticipate future needs and limitations. Ideally, we could use data from such analyses to individualize these expectations, but this may be difficult since we did not identify individual factors that strongly predicted outcomes. However, we were able to identify some high risk medical conditions such as linear growth failure and diabetes that could be treated more aggressively pre and post-LT and some sub-groups of patients that might benefit from more intensive psychosocial support. These interventions might include support programs for single parents and focused educational programs for pre-adolescent recipients regardless of interval from transplant. Targeted support for high risk patients might help improve functional outcomes while reserving expensive resources for the patient most in need. Although family structure is not a modifiable risk factor for poor outcomes per se, the potential disadvantage experienced by recipients who live in a single parent household at the time of transplant deserves special comment. This risk factor was evident in both the parent and self-report logistic models. In the SPLIT registry, marital status is only queried at the time of LT, and we cannot assume that marital status remained the same in long-term follow-up. It is likely the association might have been even stronger if current marital status was included as a variable. As such, a single parent home may indicate the "tip of the iceberg" of potential risk for a family. It may represent past and ongoing familial and social factors that increase vulnerability of the child and parent to poor outcomes. Further studies will be required to better understand the dynamics of this risk, but these data would support strategies that concentrate our limited nursing and social work support services on this special population.

Successful approaches to supporting social versus medical risk factors are likely very different. Some of the medical risk factors such as re-operations and length of initial hospitalization may not be avoidable, and efforts should be made to limit these exposures in all recipients for reasons that reach beyond HRQOL. Conversely, changes in medical therapies such as elimination of steroids for recipients with both diabetes and linear growth failure might be expected to improve HRQOL for this sub-group. The added risk of inflammatory injury to the graft would be offset by this advantage.

This analysis has several limitations. The most important was we could not assess factors not included in the SPLIT data collection registry, especially those that might be difficult to measure including psychological traits such as resiliency and/or forms of social support or stress. Also, HRQOL is likely dynamic in nature and was measured only at a snapshot in this study. Future studies should include assessment of what impacts changes in HRQOL, especially after a period of stability.

In summary, we used modeling to identify which factors were associated with having HRQOL measurements that were within the lowest quartile following pediatric liver transplantation. This allowed us to identify targets for future intervention trials to improve outcomes for patients at risk for lower than average HRQOL. We focused on factors that were experienced by a significant percentage of the population and not those that were unique to a small sub-set of patients. The results of this analysis suggest that HRQOL following pediatric LT is related to several variables with demographic factors including marital status having an important impact. From the patient's perspective, recent hospitalization has a significant impact that is related to duration of hospitalization. Graft function and rejection episodes did not have a strong impact, independent of hospitalization. These findings support the need for future studies to further explore the relationship between HRQOL and family structure and clinical interventions to support single parents caring for LT recipients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

(CF)	Cognitive Functioning
(FOG)	Functional Outcomes Group
(HRQOL)	Health Related Quality of Life
(ICC)	Intraclass Correlations
(LT)	Liver Transplant
(MCID)	Minimal Clinically Important Difference
(SPLIT)	Studies of Pediatric Liver Transplantation

References

1. ALONSO EM, LIMBERS C, NEIGHBORS K, et al. Cross-sectional analysis of health-related quality of life in pediatric liver transplant recipients. J of Pediatr. 2010; 156:270–276. [PubMed: 19846110]

2. ALONSO EM, NEIGHBORS K, BARTON FB, et al. Health-related quality of life and family function following pediatric liver transplantation.[see comment]. Liver Transplantation. 2008; 14:460–468. [PubMed: 18383090]
3. ALONSO EM, NEIGHBORS K, MATTSON C, et al. Functional outcomes of pediatric liver transplantation. J Pediatr Gastroenterol Nutr. 2003; 37:155–160. [PubMed: 12883302]
4. APAJASALO M, RAUTONEN J, SINTONEN H, HOLMBERG C. Health-related quality of life after organ transplantation in childhood. Pediatr Transplant. 1997; 1:130–137. [PubMed: 10084773]
5. BUCUVALAS JC, BRITTO M, KRUG S, et al. Health-related quality of life in pediatric liver transplant recipients: A single-center study. Liver Transpl. 2003; 9:62–71. [PubMed: 12514775]
6. COLE CR, BUCUVALAS JC, HORNUNG RW, et al. Impact of liver transplantation on HRQOL in children less than 5 years old. Pediatric Transplantation. 2004; 8:222–227. [PubMed: 15176957]
7. FREDERICKS EM, MAGEE JC, OPIPARI-ARRIGAN L, SHIECK V, WELL A, LOPEZ MJ. Adherence and health-related quality of life in adolescent liver transplant recipients. Pediatric Transplantation. 2008; 12:289–299. [PubMed: 18282211]
8. SUNDARAM SS, LANDGRAF JM, NEIGHBORS K, COHN RA, ALONSO EM. Adolescent health-related quality of life following liver and kidney transplantation. American Journal of Transplantation. 2007; 7:982–989. [PubMed: 17391138]
9. BOWNIK H, SAAB S. Health-related quality of life after liver transplantation for adult recipients. Liver Transplantation. 2009; 15(Suppl 2):S42–49. [PubMed: 19876941]
10. RATCLIFFE J, LONGWORTH L, YOUNG T, et al. Assessing health-related quality of life pre- and post-liver transplantation: a prospective multicenter study. Liver Transplantation. 2002; 8:263–270. [PubMed: 11910572]
11. CASTALDO ET, FEURER ID, RUSSELL RT, PINSON CW. Correlation of health-related quality of life after liver transplant with the Model for End-Stage Liver Disease score. Archives of Surgery. 2009; 144:167–172. [PubMed: 19221329]
12. ABERG F, RISSANEN AM, SINTONEN H, ROINE RP, HOCKERSTEDT K, ISONIEMI H. Health-related quality of life and employment status of liver transplant patients. Liver Transplantation. 2009; 15:64–72. [PubMed: 19109833]
13. DEVINE KA, REED-KNIGHT B, LOISELLE KA, SIMONS LE, MEE LL, BLOUNT RL. Predictors of long-term health-related quality of life in adolescent solid organ transplant recipients. Journal of Pediatric Psychology. 2011; 36:891–901. [PubMed: 21343144]
14. MCCARTHY ML, MACKENZIE EJ, DURBIN DR, et al. The Pediatric Quality of Life Inventory: An evaluation of its reliability and validity for children with traumatic brain injury. Archives of Physical Medicine and Rehabilitation. 2005; 86:1901–1909. [PubMed: 16213229]
15. VARNI JW, BURWINKLE TM, SZER IS. The PedsQL Multidimensional Fatigue Scale in pediatric rheumatology: reliability and validity. Journal of Rheumatology. 2004; 31:2494–2500. [PubMed: 15570657]
16. SEID M, VARNI JW, SEGALL D, KURTIN PS. Health-related quality of life as a predictor of pediatric healthcare costs: a two-year prospective cohort analysis. Health Qual Life Outcomes. 2004; 2:48. [PubMed: 15361252]
17. SUNG L, YANOFSKY R, KLAASSEN RJ, et al. Quality of life during active treatment for pediatric acute lymphoblastic leukemia. Int J Cancer. 2011; 128:1213–1220. [PubMed: 20473921]
18. NAUGHTON MJ, RUGGIERO AM, LAWRENCE JM, et al. Health-related quality of life of children and adolescents with type 1 or type 2 diabetes mellitus: SEARCH for Diabetes in Youth Study. Arch Pediatr Adolesc Med. 2008; 162:649–657. [PubMed: 18606936]
19. VARNI JW, BURWINKLE TM, SEID M, SKARR D. The PedsQL™ 4.0 as a pediatric population health measure: Feasibility, reliability, and validity. Ambulatory Pediatrics. 2003; 3:329–341. [PubMed: 14616041]

Table 1

Study Population Characteristics.

	PedsQL™ Cognitive Functioning Scale Parent Proxy-Report (n=441)	**PedsQL™4.0 Generic Core TotalScore Parent Proxy-Report (**n=997)	**PedsQL™4.0 Generic Core TotalScore Child Self-Report (**n=444)
Age at LT (years) (median, range)	2.98 (0.04-16.85)	2.17 (0.04 – 16.85)	7.66 (0.04 – 16.85)
Gender			
Female	196 (44.4%)	451 (45.2%)	198 (44.6%)
Male	245 (55.6%)	546 (54.8%)	246 (55.4%)
Race/Ethnicity			
White	277 (62.8%)	596 (59.7%)	270 (60.8%)
Black	65 (14.7%)	150 (15.0%)	76 (17.1%)
Hispanic	63 (14.2%)	154 (15.4%)	56 (12.6%)
Other	34 (7.7%)	93 (9.3%)	42 (9.4%)
Missing	2 (0.4%)	0.3 (0.4%)	0 (0%)
Primary Diagnosis			
Biliary Atresia	164 (37.1%)	437 (43.8%)	151 (34.0%)
Other Cholestatic	53 (12.0%)	123 (12.3%)	54 (12.1%)
Acute Liver Failure	69 (15.6%)	129 (12.9%)	80 (18.0%)
Metabolic	87 (19.7%)	156 (15.6%)	77 (17.3%)
Other	68 (15.4%)	152 (15.2%)	82 (18.5%)
Age at Survey(years) (mean±SD)	9.03±4.42	8.44±4.43	12.56±3.00
Interval from LT(years) (median, range)	3.55 (1.00 –12.69)	3.73 (1.00 – 12.69)	4.82 (1.00 – 12.69)
PedsQL™4.0 Generic Core TotalScore (mean±SD)	72.09±24.03	76.06±17.21	77.10±14.31

Table 2

Logistic Regression Model of Poor PedsQL ™ 4.0 Total Scale Score from Child Self-Report (n=321).

Variable	Comparison Group	Reference group	Final Model Odds Ratio (95% CI)	p-value
Marital status	One parent household	2 parent household	1.94 (1.13 – 3.33)	0.0170
Seizure medication since last long term follow-up visit	Yes	No	3.99 (1.26 – 12.70)	0.0191
Days hospitalized since last long term follow-up visit	continuous		1.03 (1.01 – 1.06)	0.0067

Table 3

Logistic Regression Model of Poor PedsQL ™ 4.0 Total Scale Score from Parent Proxy-Report (n=704).

Variable	Comparison Group	Reference group	Final Model Odds Ratio (95% CI)	p-value
Age at LT (years)	continuous		1.09 (1.01 – 1.18)	0.0349
Marital status	One parent households	2 parent household	2.88 (1.92 – 4.30)	<0.0001
Calcineurin inhibitor use at LT	Cyclosporine Other/None/missing	Tacrolimus	1.02 (0.58 – 1.80) 2.27 (1.18 – 4.35)	0.9409 0.0137
Days hospitalized during 1st post-LT month	>21 days	<=21 days	1.52 (1.03 – 2.24)	0.0372
Age at FOG visit (years)	2-4 5-7 8-12	13-18	1.91 (0.67 – 5.45) 3.21 (1.22 – 8.46) 2.57 (1.19 – 5.54)	0.2285 0.0182 0.0161
Re-operations related to LT since last long term follow-up visit	Yes	No	6.54 (2.10 – 20.38)	0.0012
Diabetes/glucose intolerance since last long term follow-up visit	Yes	No	4.42 (1.52 – 12.89)	0.0065
Height z score at long term follow-up visit	continuous		0.78 (0.68 – 0.90)	0.0008
Seizure medication since last long term follow-up visit	Yes	No	4.86 (2.03 – 11.66)	0.0004

Table 4

Logistic Regression Model of Poor PedsQL ™ Cognitive Function Scale Score from Parent Proxy-Report (n=326).

Variable	Comparison Group	Reference group	Final Model Odds Ratio (95% CI)	p-value
Sex	Female	Male	0.45 (0.27– 0.76)	0.0031
Marital status	One parent households	2 parent household	2.05 (1.14 – 3.70)	0.0167
Total bilirubin at LT	continuous		0.97 (0.94 – 0.996)	0.0252
Seizure medication since last long term follow-up visit	Yes	No	10.40 (2.00 – 54.10)	0.0054
Gamma-glutamyltransferase (U/L) at long term follow-up visit	80-200 201-400 >400	<80	0.18 (0.05 – 0.64) 1.26 (0.36 – 4.45) 2.68 (0.39 – 18.39)	0.0085 0.7187 0.3150