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ORIGINAL ARTICLE

Health-related quality of life in pre-adolescent liver transplant recipients with biliary atresia: A cross-sectional study

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KEYWORDS
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Summary
Objective: Pediatric recipients of liver transplantation (LT) often report lower Health-Related Quality of Life (HRQOL) than healthy controls when assessed on generic HRQOL measurement tools. The recent addition of the Pediatric Liver Transplant Quality of Life (PeLTQL), a novel disease-specific HRQOL instrument for pediatric LT recipients, into the clinical armamentarium of tools now routinely available to clinical care teams, provides the unique opportunity to identify disease-related challenges in children who have undergone this life-saving intervention. This study assesses HRQOL in pre-adolescent aged patients with a primary diagnosis of biliary atresia (BA) who underwent LT as an infant, using both generic and disease-specific HRQOL instruments validated for children. We also examined modifiable factors associated with HRQOL after pediatric LT.

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Methods: HRQOL was the primary outcome of this study assessed using the disease-specific PeLTQL and the generic Pediatric Quality of Life Inventory 4.0 (PedsQL). Exposure variables of interest included medication status (e.g., monotherapy, dual therapy) and participation in sports.
Results: A total of 70 (56% female, mean age 9.89 ± 1.25 years) pediatric LT recipients (mean interval since LT was 9.0 ± 1.26 years) comprised the study cohort. LT recipients reported significantly lower PedsQL Scores relative to the general population. Immunosuppression monotherapy was associated with higher patient-reported PeLTQL Scores, and sports participation was associated with higher parent-reported PedsQL Scores.
Conclusions: Pre-adolescents who underwent LT as an infant with BA, self-report low HRQOL on both disease-specific and generic HRQOL tools. Further research targeting sports participation and simplifying immunosuppression may further optimize quality of life years restored by life-saving LT.
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Introduction

Biliary atresia (BA) is the most common pediatric liver disease leading to liver transplantation (LT) in children, with the majority of subjects undergoing LT before 2 years of age [1,2]. With 5-and 10-year patient survival rates above 80% after LT in children with BA, research has become appropriately focused on identifying the issues affecting quality as well as quantity of life-years restored by timely pediatric LT [3–6]. Multiple studies using generic health-related quality of life (HRQOL) instruments report lower HRQOL in heterogeneous groups of pediatric LT recipients compared to the age-matched norms, underscoring the importance of attention to patient-reported outcomes [7]. While generic HRQOL instruments, such as the Pediatric Quality of Life Inventory 4.0 (PedsQL), allow for the assessment and comparison of common dimensions amongst different populations with variable disease states, disease-specific tools have the advantage of capturing HRQOL aspects that are uniquely relevant to patients with that disease [8]. The need to further characterize the HRQOL of pediatric LT recipients across different cultures, using disease-specific tools, was recently flagged by an expert panel group as a key research priority [9]. The PeLTQL (Pediatric Liver Transplant Quality of Life) questionnaire, directly addressed this gap, enabling healthcare providers to better hear the patient's voice about the impact of LT on his/her broader determinants of health and wellness after this life-saving intervention [10].

To-date, research has largely identified individual clinical, demographic or socioeconomic predictors of HRQOL in the pediatric LT population, many of which are non-modifiable [11–13]. Recently, the SPLIT Research Group proposed looking at outcomes after pediatric LT as a composite ''ideal'' profile defined as a stable first allograft on immunosuppression monotherapy, normal growth, and absence of the most common post-LT complications [14]. Attention is often placed on the impact of individual post-transplant complications or clinical factors, rather than a composite outcome, on HRQOL. Also, studies assessing factors associated with HRQOL include heterogeneous samples of LT recipients with wide representation of underlying diseases, spectrum of age ranges at LT and at HRQOL assessment, making it difficult to generalize findings across pediatric LT centers and geographic borders. As each of these factors may impact HRQOL in pediatric LT recipients [7], we aimed to target HRQOL assessment in a homogeneous subgroup of pre-adolescent aged children all with BA who underwent LT early in life, before the age of 2 years.

Although identifying demographic and socioeconomic factors that are associated with HRQOL is important for targeted population interventions, identifying modifiable predictors can enable targeted interventions. Among adolescent LT recipients, medication non-adherence has been associated with poorer HRQOL outcomes [15,16]. Focusing in on the associations between medication burden and immunosuppression regimen and HRQOL during pre-adolescence will enable strategic opportunities to target non-adherent behaviors during adolescence. Another modifiable factor, potentially associated with HRQOL, is sports participation. One prior study described greater HRQOL in a cohort of healthy pre-adolescents engaged in sports, with benefits also reported in adult LT recipients engaged in physical activity [17,18]. Therefore, there is a need for studying the association between sports participation, and HRQOL in pre-adolescent LT recipients.

Herein, the specific aims of this study are to:

- describe HRQOL in an international sample of pre-adolescent LT recipients with a unifying underlying disease of BA, using both validated generic and LT-specific HRQOL instruments;
- explore the association between HRQOL and an ''ideal'' LT survivor composite outcome and [19];
- identify modifiable factors that influence HRQOL.

Methods

Study population

Between January 2014 and September 2016, all children attending LT clinics at either The Hospital for Sick Children in Canada or one of six centers of the European Pediatric Liver Transplantation Network (EPLTN) registered within the European Network of Pediatric Research at the European Medicines Agency (Enpr-EMA) [20], were invited to participate in this international cross-sectional study. Patient

inclusion criteria included participant age between 8 and 12 years, primary diagnosis of BA, and isolated LT performed before the age of 2 years. Subjects with chronic graft dysfunction listed for re-transplantation or those with severe neurological impairment estimated to preclude ability to accurately provide self-reported HRQOL assessment were excluded. The Quality Management Department at The Hospital for Sick Children, or the Ethics Review Board at each EPTLN institution approved all aspects of the study.

Procedures

HRQOL was measured using age-appropriate validated generic (PedsQL™ 4.0 Generic Core Scales) and disease-specific (Pediatric Liver Transplant Quality of Life) instruments. Post-LT BA children (self-report) and one of their parents or guardian (proxy-report) completed both instruments when attending a follow-up clinic visit. Children also completed a survey questionnaire gathering data on socio-demographics, health care needs and sports participation. Patients' treating physician also collected demographic and medical data from each institution's medical records.

Ideal survivor definition

An ''ideal'' survivor of pediatric LT was defined as an isolated LT recipient fulfilling the 13 criteria of the Studies of Pediatric Liver Transplantation (SPLIT) research definition of ''ideal survivor'' outcome [19]. The SPLIT ''ideal'' survivor composite concept was categorized into the 3 subdomains of allograft stability (no re-transplantation, no previous or present chronic rejection; normal values for serum total bilirubin, albumin, GGT and ALT) on immunosuppression monotherapy (no need for additional medications), with absence of immunosuppression-induced comorbid conditions (lack of post-transplant lymphoproliferative disorder or diabetes, normal height z-Score > -2 SD, and calculated GFR > 90 mL/min/1.73 m^2).

Measures

Primary outcome

Generic HRQOL: PedsQL™ 4.0 Generic Core Scales (PedsQL)

Generic HRQOL was measured using the PedsQL instrument. Reliability and validity of the PedsQL have been demonstrated in its English version and the measure can be applicable in clinical, research and, community settings [21].The child self-report and the parent-proxy PedsQL questionnaires for children 8 to 12 years are available in the following available validated language versions: English; Spanish; Italian; French; German and Polish. The PedsQL is a 5-level Likert 23-item survey with reversed scored answers that are linearly transformed to a 0 to 100 Scale, with higher scores reflecting higher HRQOL. The published validation study identified a value one standard deviation below the population mean for the PedsQL Total Score (69.7 for child self-report and 65.4 for parent-proxy) as a threshold score for an at-risk status for impaired HRQOL relative to the population sample [22]. The PedsQL assesses HRQOL across physical, emotional, social, and school functioning domains and it yields 3 summary scores: Total Scale Score, Physical Health Summary and Psychosocial Health Summary.

Disease Specific HRQOL: Pediatric Liver Transplant Quality of Life tool (PeLTQL)(10)

The child self-report and the parent-proxy report versions of the PeLTQL questionnaire for children 8 to 17 years old were used. As described in the PeLTQL development and validation study, robust psychometric properties (validity, reliability, and sensibility) in the English-speaking population have been reported in the PeLTQL questionnaire [10].

The PeLTQL is a 26-item questionnaire offered with a 5-point rating scale (0 = ''never'' to 4 = ''very often'') with reversed scored answers that are linearly transformed to a 0 to 100 Scale, with higher scores reflecting higher HRQOL. The PeLTQL assesses disease-specific HRQOL across 3 domains: future health, coping and adjustment and social-emotional, yielding a Total Scale Score and a Score for each domain [23]. Following rigorous translation and cross-cultural adaptation published methodology, Spanish, Italian, French, German and Polish versions from the originally created English PeLTQL versions were derived and validated [10,24]. This process included forward and back translations along with a pretest field-testing and cognitive debriefing of the questionnaire in dyads of pediatric LT recipients and their parents by trained individuals at each of the study sites. Retention of psychometric properties of the cross-culturally adapted questionnaires was assumed.

Exposure variables

The association between ''ideal'' survivor of pediatric LT, total number of medications, immunosuppression regimen (monotherapy vs. polytherapy) and sports participation and HRQOL was explored. Sports participation was assessed via two targeted questions, including ''In the last 12 months, have you regularly participated in team sport (e.g., soccer or basketball)?'' and ''In the last 12 months, have you regularly participated in individual sport (e.g., tennis, karate or gymnastics)? ''Regularly'' was defined as at least once per week for 3 months or more (e.g., a sports season) [18].

Covariates

Disparities in countries of residence well-being were identified as potential covariates, based on a study on HRQOL of children with Duchenne muscular dystrophy from six European countries [25]. We adjusted for the covariate country's child well-being rank status as collected in the UNICEF's report on child well-being in rich countries [26]. The UNICEF's report ranks 29 developed countries according to the overall well-being of their resident children. Each country's overall rank is based its average rank for the following five dimensions: ''Material well-being'', ''Health and safety'', ''Education'', ''Behaviors and risks'' and ''Housing and Environment''. The variable country of residence well-being was collapsed into three categories to distinguish children living in countries ranked within the upper third (Germany and Switzerland), mid third (France, Canada and

Table 1 Characteristics of the investigated sample of pre-adolescent LT recipients with BA ($n = 70$).

	n (%)	Median (Interquartile range)
Gender		
Female	39 (55.7)	
Ethnicity		
White	57 (81.4)	
Asian	5 (7.1)	
Hispanic	4 (5.7)	
Black	2 (2.8)	
Other	2 (2.8)	
Age at LT (months)		8.9 (7—11.9)
Weight at LT (Kg)		7.7 (6.4—8.3)
Total bilirubin at LT (mg/dL)		11.7 (6—19.4)
Interval from listing to LT (days)		61 (30.7—92)
Location at LT		
Intensive Care Unit	2 (2.8)	
Hospital not Intensive care	39 (55.7)	
Home	25 (35.7)	
Age at time of study (years)		9.7 (8.9—10.9)
Interval from LT (years)		8.9 (7.9—10.2)
Interval from last hospitalization (days)		905 (241—2215)
Labs at time of study		
ALT (IU/L)		25.5 (10—35.7)
GGT (IU/L)		19 (14—26.7)
Total bilirubin (mg/dL)		0.5 (0.4—0.8)
Albumin (g/dL)		4.3 (4.1—4.49)
Platelet count (plat/mm^3		212 (163—277)
Height/age z-score at time of study		−0.22 (−0.9—0.4)
BMI (Kg/m^2) at time of study		16.6 (15.4—21.1)

LT: liver transplantation; BA: biliary atresia; BMI: body mass index.

Spain) and lower third (Italy and Poland) of 29 developed countries [26].

Statistical analysis

Mean and median PedsQL and PeLTQL total scores and domain scores were calculated. Aggregate data including mean and standard deviation for the healthy population were cited from the literature [22]. Effect sizes were calculated by subtracting the LT BA mean from the healthy mean and then dividing by the standard deviation for the healthy population. Effect sizes are designated as small (0.20—0.49), medium (0.50—0.79), or large (0.80 or >) in magnitude [27]. Agreement between PedsQL and PeLTQL child and parent-proxy-report total scores and their domains were examined by Intra-class Correlation Coefficients (ICCs) with the 95% confidence intervals [28]. ICCs are designated as poor to fair (< = 0.40), moderate (0.41—0.60), good (0.61—0.80), or excellent (0.81—1.00) in agreement [29].

Univariate regression analysis was employed to identify variables in our cohort that were associated with HRQOL outcomes (PedsQL and PeLTQL Total Scores). Factors identified in univariate analysis at the $P < 0.05$ level as potential predictors of HRQOL entered a multiple model adjusting for country's child well-being rank status. Separate analyses were conducted for the child self-report and parent-proxy-report scores, given the possibility that different predictors could emerge. All statistical analyses and plots were performed in SAS 9.2 for Windows (SAS Inc., Cary, NC).

Results

Demographics

A total of 70 (median age 9.7 years, interquartile range 8.9—10.9) children who underwent pediatric LT prior to 2 years of age in Poland ($n = 20$), Spain ($n = 18$), Canada ($n = 12$), Italy ($n = 10$), Germany ($n = 5$), France ($n = 3$) and Switzerland ($n = 2$) and their parent/guardian comprised the study cohort. The median interval from LT to study enrolment was 8.9 years (interquartile range 7.9—10.2 years). Median age at LT was 8.9 months (interquartile range 7—11.9 months), receiving grafts from 40 (57%) living donors ($n = 24$ from their mother; $n = 10$ from their father and $n = 6$ from other) and 30 (43%) deceased donors ($n = 17$ split; $n = 8$ reduced and $n = 5$ whole organ). Characteristics of the total sample are detailed in Table 1.

Post-LT complications

Diagnosis of a vascular complication ($n = 14$ portal vein thrombosis; $n = 2$ hepatic artery thrombosis and $n = 2$ other) after LT was reported for 18 (26%) children in the study

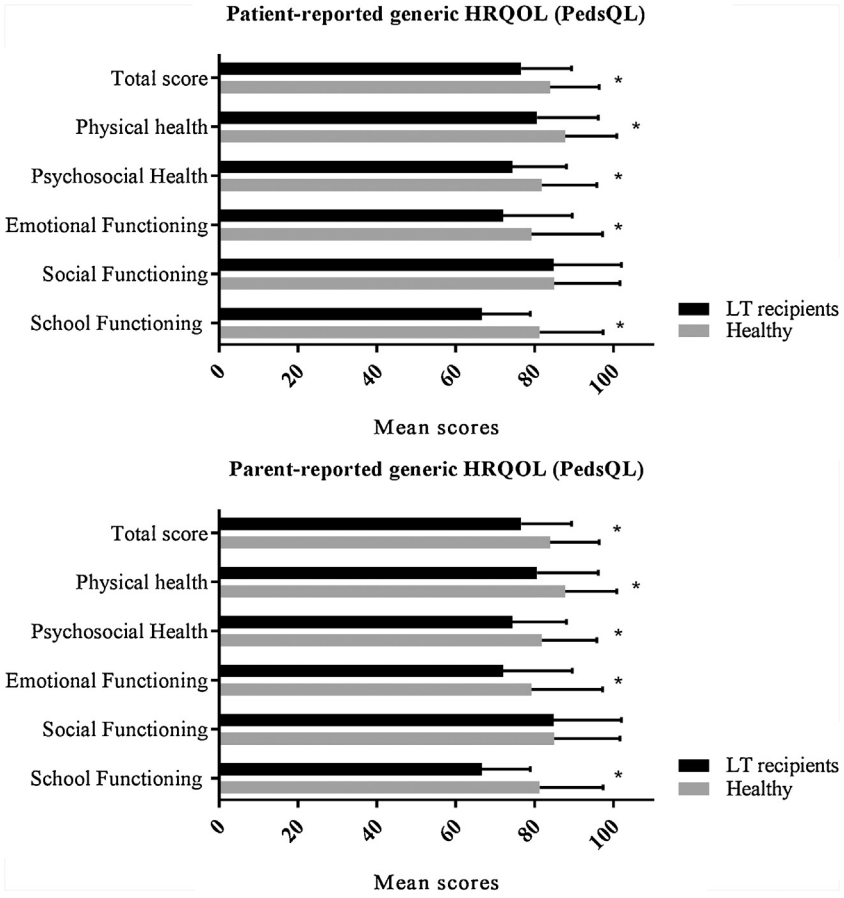

Figure 1 Mean Histograms depicting mean PedsQL TM 4.0 Generic Core (PedsQL) total and subdomain scores for pre-adolescent liver transplant (LT) recipients with Biliary Atresia (BA) and healthy population Mean Total, Physical Health, Psychosocial Health, Emotional and School functioning patient and parent-reported scores were significantly lower ($P < .001$) in liver transplant recipients with biliary atresia, compared to the healthy comparison population.

cohort. Biliary ($n = 11$ anastomotic stricture and $n = 9$ other) complications were identified in 20 (29%) children. Re-transplantation occurred in 4 cases, three of them within 30 days from first LT and one after 4.9 months from first LT.

At least one episode of biopsy-proven acute cellular rejection (BPAR) was reported for 20 (29%) of LT recipients. Five children were reported to have histologic evidence of chronic graft rejection. Post-transplant lymphoproliferative disorder was diagnosed in two children, within one and three years post-LT respectively.

Medications post-LT

Study participants were taking a median of 3 medications at time of HRQOL assessment (interquartile range 2-3 medications). Forty-five (64%) participants were on immunosuppression monotherapy ($n = 41$ tacrolimus; $n = 3$ sirolimus and $n = 1$ steroids), with the remainder on polytherapy ($n = 23$ on two, and $n = 2$ on three, immunosuppressant medications). Amongst patients on polytherapy, tacrolimus with steroids was the most common combination in 11 (44%) patients. There were no patients off immunosuppression.

Non-immunosuppressive medication utilization was reported in 56 (80%) of all LT recipients, which was comprised of: magnesium supplements ($n = 23$); anti-bacterial agents ($n = 18$); ursodeoxycholic acid ($n = 12$); vitamin D ($n = 7$); other vitamin or mineral supplements ($n = 13$); anti-hypertensive medication ($n = 6$); proton pump inhibitors ($n = 3$); anti-seizure medication ($n = 1$) and others ($n = 2$).

Clinical characteristics (ALT, GGT and platelets), days since last hospitalization and previous history of BPAR were not different between LT BA recipients on immunosuppression monotherapy vs. those on polytherapy (data not shown).

Ideal survivor status

Complete data for assessment of ''ideal'' LT survivor status were available for 64 LT recipients, with 23(36%) meeting all thirteen criteria required for acquisition of an ''ideal'' survivor status. The remaining subjects were not considered an ''ideal'' survivor due to the need for additional medications ($n = 26$), allograft instability ($n = 12$) and presence of immunosuppression-induced comorbid conditions ($n = 3$).

Sports participation

A total of 65 (93%) LT recipients completed the patient survey. Forty (60%) LT recipients reported regular participation

Table 2 Predictors of patient-reported Health-Related Quality of Life in LT recipients (aged 8—12 years) ($n = 70$).

	PedsQL				PeLTQL			
	Unadjusted β coefficient (SE)	*P*-value	Adjusted β coefficient (SE)	*P*-value	Unadjusted βcoefficient (SE)	*P*-value	Adjusted β coefficient (SE)	*P*-value
''Ideal'' survivor status								
Ref. = ideal survivor								
Non-ideal survivor	1.66	.63			−3.73	.37		
Immunosuppression regimen								
Ref. = monotherapy								
Combined regimen	−2.46	.44			−8.93	.02	−7.52	.06
Number of medications	−1.26	.29			−1.56	.30		
Sports (team and/or individual)								
Ref. = participation in sports								
Non-participation	-0.35	.91			−1.11	.78		
Country's child well-being rank status								
Ref. = lower 1/3	—				—			
mid 1/3	3.03	.35			−7.37	.06	−4.67	.25
upper 1/3	6.97	.28			2.98	.64	4.9	.44
							$R^2 = .075$; F for change in $R^2 = .045$	

Ref.: reference.

in team sports, 28(42%) in individual sports and 12 (18%) in both. Eighteen (27%) LT recipients reported no regular sports practice other than gymnastics at school.

HRQOL assessment

Median PedsQL Total Scores were 77.17 (IQR: 65.9—85.86) on the patient-report ($n = 69$) and 79.13 (IQR: 64.13—87.22) on the parent report ($n = 68$), with higher scores indicating better HRQOL. Total PedsQL Scores were more than one deviation below the mean score of the general population in 30% (21/69) of children and 29% (20/68) of parents, indicating an at-risk status for impaired overall HRQOL [22]. Overall, pediatric LT recipients and their parents reported significantly lower PedsQL Total Scores and physical health, emotional functioning and school functioning subdomain scores, compared with North-American healthy children (Fig. 1). Most effect sizes were in the small to medium range (0.20—0.79). The largest effect sizes were found in the comparison of the school functioning subdomain [22]. Overall, among the study cohort there was good agreement between patient- and parent-reported total PedsQL Scores (ICCs 0.72, 95% confidence interval 0.59, 0.82).

Median PeLTQL Total Score was 77.1 (IQR: 67.83—85.81) on the patient report ($n = 68$) and 78.56 (IQR: 69.17—86.15) on the parent report ($n = 68$). Lower scores were obtained for the coping and adjustment subdomain (see Table, Supplemental Digital Content 1). There was a moderate agreement between patient- and parent- reported total PeLTQL scores (ICCs 0.57, 95% confidence interval 0.38, 0.71). ICCs were also used to assess differences in capturing HRQOL between 68-paired PedsQL and PeLTQL patient-reports, with poor to fair agreement between the two HRQOL tools observed (ICCs 0.31, 95% confidence interval 0.07, 0.74).

Factors Associated with HRQOL

Univariate linear regression analysis was performed to understand the relationship between patient-reported total PedsQL and PeLTQL Scores and the following independent variables among LT recipients: ''ideal'' survivor status of LT, total number of medications, immunosuppression monotherapy and sports (team and/or individual) participation (Table 2). In univariate analysis, immunosuppression polytherapy (≥ 2 immunosuppressant drugs) at the time of HRQOL assessment was associated with lower PeLTQL Scores, but not with generic (PedsQL) HRQOL Scores. However, this did not remain statistically significant after adjusting for disparities in children's country of residence well-being in the multivariate analysis.

Separate analyses were conducted for total PedsQL and PeLTQL parent-proxy-reports. Sports practice was identified as a potential predictor of parent-reported PedsQL in the univariate analysis but this did not remain significant when entered in a multiple model adjusting for disparities in children's country of residence well-being.

Discussion

BA is the most common indication for pediatric LT worldwide. This is the first multi-center international, cross-cultural study to utilize both validated pediatric LT-specific

as well as generic HRQOL instruments to assess HRQOL in a homogeneous cohort of pre-adolescent BA patients, who underwent LT as an infant. Our study demonstrates lower PedsQL Scores in pre-adolescent LT recipients with BA compared to the healthy population [22], with diminished physical and psychosocial function, especially in the area of school function. These results are in line with findings of previous studies investigating HRQOL in pediatric LT recipients using the same instrument [7,30]. The finding of low PeLTQL coping and adjustment subdomain score, according to the disease-specific PeLTQL instrument in this current study, supports clinical teams harnessing efforts towards targeted interventions aimed at promoting positive coping responses in the pediatric LT population, towards enhancing better long-term outcomes.

One third of our international BA patient population met the definition of an ''ideal'' LT survivor, which is comparable to what was previously reported in a cross-sectional North-American study [14]. We found no association between achieving an ''ideal'' LT survivor composite and PeLTQL or PedsQL Scores, underscoring the fact that outcome after pediatric LT encompasses multi-faceted domains beyond common currency biochemical and physiological values typically evaluated in follow-up of this patient population. Given achievement of steady improvements in graft and patient survival after LT, the spotlight is now appropriately focusing on patient-reported outcome, and the availability of well-validated HRQOL tools will arm health care professionals to continue to hear the patient voice in order to identify at-risk patients.

The effect of modifiable factors on HRQOL after pediatric LT has been scarcely investigated. Our study strategically targeted a pre-adolescent cohort of LT recipients, in whom transition of responsibility of medication taking from parents to patients themselves has typically not yet occurred, in order to characterize early determinants of HRQOL that might impact adherence during adolescence [31]. Immunosuppression monotherapy emerged from the univariate analyses as a factor associated with higher disease-specific HRQOL Scores (PeLTQL) but not of generic HRQOL Scores (PedsQL). This may be explained by the PeLTQL capturing the unique concerns of the pediatric LT population, in contrast to the PedsQL with its strong focus on the measurement of functional aspects of HRQOL as a generic instrument [32,33]. A simplified immunosuppression therapy (monotherapy) may be theorized to be less disruptive to a child's activities of daily living, associated with less medication-induced side effects, or simply the reflection of differing immunosuppression protocols practices between participating study sites, all of which could ultimately affect the HRQOL of LT recipients. The fact that no association was found between type of immunosuppression regimen and parent-reported PeLTQL, could be related to the fact that parents are more likely to understand the role of immunosuppression in ensuring durable long-tern graft outcomes. Clearly, a better understanding of the longitudinal relationship between immunosuppression regimens and medication burden and HRQOL as transition of responsibility for medication taking occurs during adolescence is needed.

The psychosocial health benefits of sports participation are evident among children and adolescents, including self-esteem, positive social interactions, and a reduction in depressive symptoms [34]. Recently, the protective effect of sports participation on the HRQOL of a nationally representative sample of Australian pre-adolescents was reported, based on parent-reported PedsQL measures [18]. Although we confirmed an association between sports participation and parent-reported PedsQL in our study sample univariate analyses, we found no association between sports participation and child self-reported PedsQL. It is possible that parents have a different perception of sports as being beneficial as compared to a child's perception. We also considered whether this finding might be dependent on the high proportion of pre-adolescents engaged in sports activity among our relatively small sized sample. While more research is encouraged to further explore the effects of sports participation on HRQOL in the LT population, one must not forget of its known positive psychosocial health benefits and that a healthy lifestyle should always be promoted as part of the post-LT follow-up care.

Our study was strengthened by its international design across six different European countries and Canada and the homogeneity of non-modifiable demographic characteristics of the study sample such as age at LT or underlying disease. We targeted children with BA in receipt of a LT before the age of 2 years in an attempt to minimize the effect on HRQOL of potential confounders such as extra-hepatic comorbidities (only 2 patients in our cohort were reported to have BA with associated structural malformations), age or interval between LT and HRQOL assessment. Certain limitations of this study should be noted. Firstly, the relatively small sample size may be contributory to the lack of associations between immunosuppression monotherapy and sports and HRQOL on the multivariate analyses. It should also be noted that this study includes a sample of potentially healthier patients followed in specialized pediatric LT programs in academic institutions, six of them enrolled in the EPTLN/Enpr-EMA network. However, despite this potential selection bias, also present in many studies investigating HRQOL, our cohort reported poorer HRQOL compared to the age-matched norms and thus HRQOL would be more likely to be overestimated rather than underestimated.

In summary, this multi-center study confirms the feasibility of assessing HRQOL in a pediatric cohort of LT recipients with cross-culturally adapted versions of the PedsQL and PeLTQL. Our findings of impaired HRQOL outcomes in LT recipients highlight the need to advocate for psychological support for this vulnerable population [35,36]. Larger and longitudinal studies should be designed to further assess the benefits of simplified immunosuppressive regimens on HRQOL, which might be beneficial in reducing rates of non-adherence and risk of graft loss reported in the adult LT population [37,38]. Future studies should also investigate the added benefits of sports participation on LT recipients' HRQOL. These data would support the development of strategies directed towards achieving best survival and HRQOL outcomes after pediatric LT.

Disclosure of interest

The authors declare that they have no competing interest.

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