Cross-Sectional Analysis of Health-Related Quality of Life in Pediatric Liver Transplant Recipients

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Objective To investigate the distribution of health-related quality of life in pediatric liver transplant recipients compared with a normative population.

Study design This cross-sectional, multicenter study was conducted at select centers. Patients between 2 and 18 years of age, surviving liver transplantation by at least 12 months, were eligible. Parent/guardian fluency in English or Spanish was required. Children ≥8 years and parents of all children completed the age-appropriate versions of the PedsQL 4.0 (Mapi Research Institute, Lyon, France). Scores were compared with a sample of healthy children (n = 3911) matched by age group, sex, and race/ethnicity and with a sample of pediatric patients with cancer receiving chemotherapy and/or radiation.

Results Participants included 65% (873/1339) of eligible patients. Mean age was 8.17 ± 4.43 years, and 55% were female. The total and subscale scores of PedsQL 4.0 were lower than in healthy children ($P < .001$), with effect sizes for self-report ranging from −0.25 for Emotional Functioning to −0.68 for School Functioning. Patients and their parents reported better physical functioning than patients with cancer but similar social and school functioning. Correlations between parent and self-reports were in the moderate agreement range.

Conclusions Pediatric liver transplant recipients and their parents report lower health-related quality of life than control subjects with some domains equal to children receiving cancer therapy. *(J Pediatr 2010;156:270-6)*.

Liver transplantation is expected not only to prolong life and reverse the consequences of end-stage organ failure but also to result in a health state that is desirable and a marked improvement from the pretransplant condition. In considering all aspects of health, physicians must examine not only physical outcomes but also psychosocial outcomes including mental health, behavior, and role function. Health-related quality of life (HRQOL) is a multidimensional measurement of health outcomes that includes assessment of physical, psychosocial, and functional status. HRQOL can be measured directly from the patient's perspective or in situations in which the patient is unable to adequately respond, from the perspective of an involved proxy, such as a parent. Liver transplantation is typically performed in children as a treatment for life-threatening complications of liver disease with an expected improvement in HRQOL status as a secondary objective. However, a full understanding of HRQOL in children after liver transplantation will help to better define overall outcomes for this group, set expectations for health care providers and parents, and identify areas of functional deficits that might be improved with focused interventions.

The purpose of this study was to use a well-validated instrument to measure HRQOL in patients included in the Studies of Pediatric Liver Transplantation (SPLIT) Registry, the largest assembled cohort of pediatric liver transplant recipients in North America.[1] Previous reports have suggested that HRQOL in patients who have survived liver transplantation is not equal to healthy children, but these reports have not been large or comprehensive enough to truly define this population.[2-7] This report includes data from the majority of children who have survived liver transplantation at 22 North American transplant centers during the past 10 years. As such, it provides the broadest perspective of health outcomes in this population yet described and renders a snapshot of the pediatric liver transplant survivor experience in the current era.

HRQOL	Health-related quality of life
ICC	Intraclass correlations
SAPS	School Attendance and Performance Survey
SCHIP	State Children's Health Insurance Program
SPLIT	Studies of Pediatric Liver Transplantation

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Methods

Twenty-two centers elected to participate in this ancillary study to the SPLIT Registry. Patients between 2 and up to 18 years of age, recipients of liver transplantation, and survivors of at least 12 months after transplant were eligible. Patients and parents/guardians were also required to be fluent in English or Spanish. Children who were not maintaining regular medical follow-up with their transplant center and recipients of combined organ transplants were also excluded. The study was approved by the institutional review boards at participating centers, and written informed consent was obtained from parents or guardians before participation. Assent was obtained from children as required by individual institutions.

We used the 23-item PedsQL 4.0 (Mapi Research Institute, Lyon, France) Generic Core Scales, which encompass: (1) Physical Functioning (8 items), (2) Emotional Functioning (5 items), (3) Social Functioning (5 items), and (4) School Functioning (5 items), and were developed through focus groups, cognitive interviews, pretesting, and field testing measurement development protocols. The instrument takes approximately 5 minutes to complete.[8] Participating families of children age 6 and older also completed the School Attendance and Performance Survey (SAPS) that is administered as part of the routine clinical data collected for the SPLIT registry.

Eligible patient and parent or guardian dyads were recruited during a routine follow-up visit at their transplant center between June 30, 2005, and June 30, 2008. The parent/guardian and patient (if age 8 or older) completed 1 of 4 age-specific versions of the PedsQL 4.0. Three of the 22 centers supplemented recruitment by mail. Overall, fewer than 50 patients included in the sample completed the survey by mail. Past as well as present demographic and clinical data for participating patients were extracted from the SPLIT database.

The primary outcomes measure was the total PedsQL 4.0 score from the child self-report survey for children age 8 to 18 years. Secondary outcomes measures included the PedsQL 4.0 Total Score from the parental survey for children age 2 up to 18 years and the PedsQL 4.0 Summary Scores for Physical and Psychosocial Health from the parental and self-report survey. These outcomes were compared with a sample of healthy children (n = 3911) randomly matched by age group, sex, and race/ethnicity to the liver transplant sample, using the SPSS statistical software random sample case selection command.[9] The sample of healthy children was derived from the PedsQL 4.0 Generic Core Scales initial field test (n = 329, 8.4%),[8] a State Children's Health Insurance Program (SCHIP) evaluation (n = 2199, 56.2%),[10] and from a school-based study within the San Diego Unified School District (n = 1383, 35.4%).[11]

We also compared the outcomes of the liver transplant group with a sample of children with cancer. The cancer group was chosen for this comparison because it represented a high level of medical disability that would be familiar to most pediatricians and provided a lower anchor to the spectrum of chronic disease in childhood. The pediatric cancer sample was derived from the PedsQL 3.0 Cancer Module field test[12] and included 183 patients, 105 with self-report and 180 with parent report results. The sample included pediatric patients with cancer, receiving cancer treatment (chemotherapy and radiation), with acute lymphocytic leukemia (n = 118, 64.5%), brain tumors (n = 8, 4.4%) non-Hodgkin lymphoma (n = 9, 4.9%), Hodgkin lymphoma (n = 6, 3.3%), Wilms tumor (n = 7, 3.8%), and other cancers (n = 35, 19.1%). The size of the cancer sample precluded random matching to the liver transplant sample.

Statistical Analysis

The feasibility of the PedsQL 4.0 Generic Core Scales as an outcome measure for pediatric patients receiving liver transplant was determined from the percentage of missing values for each item.[13] Scale internal consistency reliability was determined by calculating Cronbach coefficient α.[14] Scales with reliabilities of $\geq$0.70 are recommended for comparing patient groups, and a reliability criterion of 0.90 is recommended for analyzing individual patient scale scores.[15,16] Range of measurement was based on the percentage of scores at the extremes of the scaling range, that is, the maximum possible score (ceiling effect) and the minimum possible score (floor effect).[13] Construct validity was determined using the known-groups method.[15] In this study, independent-samples *t* tests were used to compare groups differing in known health status (pediatric patients receiving liver transplant, the sample of healthy children, and the sample of cancer patients) on the PedsQL 4.0 Generic Core Scales. The overall Type I error rate was maintained at 0.05 by the Hochberg adjustment for multiple comparisons.[17] This adjustment was made separately for child report and parent proxy report. Mann-Whitney *U* tests were performed to validate results obtained from parametric analyses. To determine the magnitude of the differences, effect sizes were calculated.[18] Effect sizes for differences in means are designated as small (0.20), medium (0.50), and large (0.80) in magnitude.[18] Comparisons of the distribution and range of demographic and clinical variables between eligible participants and nonparticipants were conducted by χ^2 and Kruskal-Wallis as appropriate. Agreement between child self-report and parent proxy report was determined through Intraclass Correlations (ICC).[19,20] Intraclass correlations are designated as $\leq$0.40 as poor to fair agreement, 0.41 to 0.60 as moderate agreement, 0.61 to 0.80 as good agreement, and 0.81 to 1.00 as excellent agreement.[21,22] Statistical analyses were conducted using SAS version 8.02 and SPSS Version 15.0 for Windows (Microsoft Inc., Redmond, Washington).[9]

Results

There were 1339 patients eligible during the study period, and 873 (65%) children participated. At the time of this analysis, there were 331(25%) patients who were still eligible and