Health-Related Quality of Life and Functional Status Are Associated with Cardiac Status and Clinical Outcome in Children with Cardiomyopathy

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Objectives To measure the health-related quality of life (HRQOL) and functional status of children with cardiomyopathy and to determine whether they are correlated with sociodemographics, cardiac status, and clinical outcomes.

Study design Parents of children in the Pediatric Cardiomyopathy Registry completed the Child Health Questionnaire (CHQ; age ≥5 years) and Functional Status II (Revised) (age ≤18 years) instruments. Linear and Cox regressions were used to examine hypothesized associations with HRQOL.

Results The 355 children evaluated at ≥5 years (median 8.6 years) had lower functioning (CHQ Physical and Psychosocial Summary Scores 41.7 ± 14.4 and 47.8 ± 10.7) than that of healthy historical controls. The most extreme CHQ domain score, Parental Impact-Emotional, was one SD below normal. Younger age at diagnosis and smaller left ventricular end-diastolic dimension z score were associated independently with better physical functioning in children with dilated cardiomyopathy. Greater income/education correlated with better psychosocial functioning in children with hypertrophic and mixed/other types of cardiomyopathy. In the age ≥5 year cohort, lower scores on both instruments predicted earlier death/transplant and listing for transplant in children with dilated and mixed/other types of cardiomyopathy ($P < .001$). Across all ages (n = 565), the Functional Status II (Revised) total score was 87.1 ± 16.4, and a lower score was associated with earlier death/transplant for all cardiomyopathies.

Conclusions HRQOL and functional status in children with cardiomyopathy is on average impaired relative to healthy children. These impairments are associated with older age at diagnosis, lower socioeconomic status, left ventricular size, and increased risk for death and transplant. Identification of families at risk for functional impairment allows for provision of specialized services early in the course of disease. *(J Pediatr 2016;170:173-80)*.

Trial registration ClinicalTrials.gov: NCT00005391.

The rate of mortality of cardiomyopathy-related heart failure in children exceeds that of the combined mortality of all childhood cancers.[1,2] Nevertheless, data from the Pediatric Cardiomyopathy Registry (PCMR) have demonstrated that many children survive with chronic illnesses related to cardiomyopathy.[3-5] Chronic illnesses impact functional status and may be some of the most important determinants of quality of life. Although there are prospective studies of the health-related quality of life (HRQOL) of children with congenital heart disease[6,7] and noncardiac conditions,[8-10] few have studied children with cardiomyopathy.[11,12] Such information may be useful for counseling, identifying families in need of special services, and in the planning of clinical management strategies.

We sought to: (1) measure the HRQOL and functional status of children with cardiomyopathy and compare it with that of healthy historical controls; (2) determine whether sociodemographic factors and concurrent echocardiographic measures of left ventricular (LV) size and function are correlated with functioning, thus establishing a surrogate relationship between functional and

CHQ	Child Health Questionnaire
DCM	Dilated cardiomyopathy
EDD	End-diastolic dimension
FSII(R)	Functional Status II (Revised)
HCM	Hypertrophic cardiomyopathy
HR	Hazard ratio
HRQOL	Health-related quality of life
LV	Left ventricular
PCMR	Pediatric Cardiomyopathy Registry

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cardiac outcomes; (3) examine the association between validated measures of HRQOL and functional status; and (4) assess whether HRQOL and functional status predict clinical outcomes. We hypothesized that poorer HRQOL and functional status would be associated with a shorter time to listing for cardiac transplant as well as for mortality and transplant.

Methods

The Functional Status Study of the PCMR collected HRQOL and functional status data (referred to as the survey) from pediatric patients with cardiomyopathy followed at 12 US pediatric cardiac centers. Inclusion criteria for the study required that the patient meet the PCMR criteria for the diagnosis of cardiomyopathy (dilated cardiomyopathy [DCM]; hypertrophic cardiomyopathy [HCM]; or mixed/other type),[13] be 18 years or younger at the time of the survey, and that the patient had not undergone previous heart transplantation. A patient is deemed eligible for the PCMR if strict quantitative echocardiographic criteria are met with the use of measurements of LV dimensions, wall thickness, and function, or the pattern of cardiomyopathy conforms to a defined semiquantitative pattern. Patients also are eligible if the diagnosis is confirmed by autopsy or tissue analysis; or the investigator has submitted other compelling evidence of cardiomyopathy. The PCMR excludes patients with cardiomyopathy that is secondary to another condition.[13] Additional exclusion criteria for functional status assessment were neuromuscular disease, such as Duchenne muscular dystrophy, which can affect functional status, and lack of reading fluency by the parent in both English and Spanish. The instruments were available for completion in English and Spanish.

Functional status data were collected from children (≤18 years) of all ages. The primary analysis in this report uses only the first completed questionnaire of each type from each participating family of a child age at least 5 years of age (the minimum age for which both instruments are validated) at the time of questionnaire completion. A secondary analysis reports the Functional Status II (Revised), or FSII(R),[14] scores from all participants (infancy to age 18 years). This report does not include any data collected after cardiac transplantation.

Institutional Review Board approval was obtained at all participating centers. Implied consent was used for the first phase of the study and was defined as voluntary completion and return of the questionnaires by the child's parent or guardian. In the second phase of the study, which included additional measures not part of this report, 93% completed the informed consent.

Clinical data were abstracted from the medical record by a team of trained data collectors with the use of standardized case report forms. The two standardized and validated instruments used to measure HRQOL and overall functional health status were the 50-item Child Health Questionnaire (CHQ) Parent Report for children 5-18 years of age[15,16] and the 14-item version of the FSII(R) questionnaire.[14] All questionnaires were self-administered by the parent or surrogate annually. The parent also reported the greatest achieved educational level, race, marital status, and income.

The overall findings of the CHQ are described by Physical and Psychosocial Summary Scores, which range from 0 to 100. The CHQ also assesses 14 health concepts: (1) physical functioning; (2) role/social-physical; (3) role/social emotional; (4) role/social behavioral; (5) bodily pain; (6) general behavior; (7) mental health; (8) self esteem; (9) general health perceptions; (10) changes in health; (11) parental impact-emotional; (12) parental impact-time; (13) family activities; and (14) family cohesion. These scales are expressed as z scores (number of SDs from a mean of zero for a healthy comparison group). The 14-item version of the FSII(R) yields a total score, which has a maximum value of 100. The FSII(R) captures physical and emotional functioning but does not assess pain, social, or role functions. Greater CHQ Summary Scores and FSII(R) scores indicate better functioning.

Statistical Analyses

Continuous variables are summarized as mean ± SD and median with IQR. Body-surface area was calculated from height and weight according to the Haycock formula.[17] LV end-diastolic dimension (EDD), LV posterior wall thickness, septal thickness, and LV mass were expressed as z scores relative to the distribution of these measurements vs body surface area in healthy children[18] and LV fractional shortening and ejection fraction were expressed as the z score relative to age.[19] Echocardiographic measurements analyzed as concurrent correlates of functional status were obtained a median of 1 month before the survey, and 75% of the measurements defined as concurrent were obtained within 9 months. Group classification was based on the functional type of cardiomyopathy at the time of diagnosis of cardiomyopathy.

Mean echocardiographic z scores were compared with a mean of zero using a one-sample *t* test. CHQ Summary Scores and FSII(R) total scores were compared against the mean for healthy children[14,15] via a Wilcoxon signed rank test, and the scores by functional type of cardiomyopathy were compared using the Kruskal-Wallis test. The percentage abnormal (>2 SD from the healthy mean) was compared with an exact test. Spearman correlation and generalized additive modeling was used to assess association between the CHQ and FSII(R).

Stepwise multivariable linear regression was used to examine the association between demographic and clinical predictors (with the exception of LV ejection fraction, etiology, and race) and 4 outcomes: CHQ Physical and Psychosocial Summary Scores, the CHQ Parental Impact-Emotional scale, and FSII(R) total score. Annual household income for 54 cases was imputed with a regression of income on parental education level and marital status. Kaplan-Meier estimation and Cox proportional hazards