Published in final edited form as:

J Pediatr. 2016 March ; 170: 173–180.e4. doi:10.1016/j.jpeds.2015.10.004.

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

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Abstract

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

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*List of Pediatric Cardiomyopathy Registry Investigators is available at www.jpeds.com (Appendix).

The authors declare no conflicts of interest.

Portions of the study were presented as a poster at the World Congress of Pediatric Cardiology and Cardiac Surgery, Cairns, Queensland, Australia, June 22–24, 2009.

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.

Trial registration—[ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00005391): 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 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 $\pm$ 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 children¹⁸ 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 modeling were used to assess association between functional status and 2 clinical outcomes: time to earliest occurring of death and cardiac transplantation, and time to listing for cardiac transplantation. Scores as continuous predictors, normal vs abnormal, and tertile (to detect any nonlinearities in association) were evaluated. The primary analysis used the time of cardiomyopathy diagnosis as time zero and a sensitivity analysis used the time of the survey as time zero.

A *P*-value was considered statistically significant if less than .05. All tests, where applicable, were 2-tailed. All analyses were conducted with the Statistical Analysis System Version 9.3 (SAS Institute, Inc, Cary, North Carolina), and S-Plus 8.0 (Insightful Corp., Seattle, Washington).

Results

A total of 355 patients enrolled between October 2002 to May 2010 who were evaluated at 5 years old were included in the primary analysis. All had a FSII(R) total score, 343 had calculable CHQ Summary Scores, and 352 had a Parental Impact-Emotional score. At the time of the survey, this cohort was 11.7 ± 4.3 years old, and the first questionnaire was completed at a median 2.6 years after presentation with cardiomyopathy; 30% were assessed in the first year (Table I; available at www.jpeds.com).

Of the 355 patients, 42% of the cohort had DCM (*n* = 149), 36% had HCM (*n* = 129), and 22% had a mixed or other (eg, restrictive, arrhythmogenic) type of cardiomyopathy (*n* = 77) with multiple defined etiologies, but most patients (72%) had idiopathic disease. About two-thirds (64%) of parents or guardians listed postsecondary school education as the greatest attained educational level, and in 22% completion of high school was the greatest attained level. Total annual household income was less than \$60 000 in 46%; \$60 000–\$99 000 in 30%; and \$100 000 in 24%.

As expected, LV size and function varied by functional type of cardiomyopathy (Table I). In addition, the severity of cardiac structural abnormalities at the time of questionnaire

completion was somewhat lower than the severity at the time of presentation with cardiomyopathy. For example, the mean $\pm$ SD LV fractional shortening (LV EDD z score) in the DCM cohort was 25 ± 12 (2.8 ± 2.2) and 18 ± 10 (3.8 ± 2.4) at the times of questionnaire completion and presentation with cardiomyopathy, respectively. The mean $\pm$ SD intraventricular septal thickness z score in the HCM cohort was 3.3 ± 2.7 and 3.6 ± 2.4 at the times of questionnaire completion and presentation with cardiomyopathy, respectively.

Functioning Compared with Historical Controls

On average, CHQ Summary Scores were significantly lower than those of healthy historical controls (Table I^{14,15} and Figure 1, A): the mean Physical Summary Score was 41.7 ± 14.4 vs 53.0 ± 8.8 for controls¹² and the mean Psychosocial Summary Score was 47.8 ± 10.7 vs 51.2 ± 9.1 for controls.¹² However, 71% had a CHQ Physical Summary Score and 90% had a Psychosocial Summary Score within 2 SD of healthy historical controls (35.4 for Physical and 33.0 for Psychosocial). These percentages did not vary significantly by type of cardiomyopathy. CHQ domain scores for mental health, behavior, role/social limits emotional domain, and self-esteem did not differ from normal; however, general health, physical functioning, pain, and the emotional and time impacts of the child's health on the parent were significantly lower, indicating poorer functioning (Figure 1, B). The most extreme z scores were for the Parental Impact- Emotional scale (median ± 1.12 , IQR ± 1.90 to 0.44) and General Health Perceptions (median ± 0.78 , IQR ± 1.42 to 0.08).

The mean total score from the FSII(R) instrument in the cohort aged ≤ 5 years was 88.5 ± 15.0 (14.7 median 92.9), lower than the well-child norm of 96.1 ± 8.2 ($P < .001$), with no difference by type of cardiomyopathy (Table II). The CHQ Physical and Psychosocial Summary Scores were moderately correlated with the FSII(R) total score, $r = 0.52$ (95% CI 0.43 – 0.59) and $r = 0.55$ (95% CI 0.47 – 0.62), respectively (generalized additive model predicted curves in Figure 2; available at www.jpeds.com).

The FSII(R) instrument is validated for younger as well as older children. There were 245 participants who had an FSII(R) completed before age 5 years (median age 1.8 years), a median of 0.9 years after cardiomyopathy presentation. Their mean total score was 86.6 ± 18.0 (Table III). The mean total score of all participants ($N = 565$; 1 week to 18 years) was 87.1 ± 16.4 , with 41% assessed in the first year after presentation (Table III).

Multivariable Modeling: Correlates of Functioning

Multivariable modeling of the CHQ Summary Scores, CHQ Parent-Emotional scale, and FSII(R) total score in the age ≤ 5 years cohort identified several significant associations with patient and disease variables, but the adjusted R^2 ranged from 5% to only 27% (Table IV; available at www.jpeds.com). In the DCM cohort, age at diagnosis was an independent predictor, with children diagnosed at younger ages having better functional status ($P < .001$ for CHQ Physical, even after we controlled for age at time of testing). A larger LV EDD z score was associated independently with lower CHQ Physical and Psychosocial Summary Scores ($P = .001$ and $P = .03$), lower CHQ Parent-Emotional scale ($P = .03$), and lower

FSII(R) total score ($P = .001$). The FSII(R) total score was independently and positively correlated with greater parental education level ($P = .05$).

In the HCM cohort, a lower CHQ Physical Summary Score independently predicted lower level of parental education (a mean 11-point decrease if the parent did not complete high school, $P = .003$), and below normal LV EDD z score (a mean 5-point decrease if the z score was < -2 , $P = .02$). Better psychosocial functioning and better function with respect to emotional impact on parents was observed in those with greater household income (both $P = .002$). In the HCM cohort, a greater FSII(R) total score was predicted independently by younger age at diagnosis (0.7 points per earlier year of diagnosis, $P < .001$) and parental education (14.4 points greater if parental education exceeded high school, $P < .001$).

In the cohort with mixed and other types of cardiomyopathy, a greater level of parental education was a significant predictor of a greater CHQ Physical Summary Score ($P = .02$), CHQ Psychosocial Summary Score ($P = .03$) and better function with respect to the emotional impact of the child's health on the parent ($P = .02$). Older age at diagnosis was associated with a lower CHQ Physical Summary Score and lower FSII(R) total score.

Association of Functional Status with Clinical Outcomes

During a median follow-up of 4.9 years (IQR 2.2–7.6 years) in the age 5 year cohort, there were 4 deaths (1 DCM, 2 HCM, 1 other/mixed), 39 transplants (29 DCM, 2 HCM, 13 other/mixed), and 44 patients who were listed for transplant (28 DCM, 3 HCM, 15 other/mixed). For the DCM and other/mixed cohorts, both the composite of death/transplant (Table V; available at www.jpeds.com) as well as the outcome of listing for transplant were strongly associated with CHQ Physical Summary Score and FSII(R) total score ($P < .001$; data from the DCM cohort age 5 years are shown in Figure 3). For the CHQ Physical Summary Score, children with DCM and those with mixed/other phenotype who had scores in the lowest tertile were at greatest risk of death or transplant (DCM hazard ratio [HR] 12.1 vs highest tertile; 5-year event rate 37% vs 2%), and those in the upper two tertiles were at similar risk for the first 3 years after diagnosis. This association with score tertile remained significant in the DCM cohort ($P = .03$) even after we adjusted for LV EDD z score (HR 1.47 per 1 SD, 95% CI 1.19–1.82 $P = .001$) and remained significant in the mixed/other cohort ($P = .007$) even after we adjusted for LV mass z score. Listing for transplant had a similar pattern. For the FSII(R) total score, there was differing risk across all 3 tertiles for the DCM cohort ($P = .01$; HR 9.5 for lowest vs highest tertile; HR 6.2 for the middle vs highest tertile; 5-year event rates 30%, 19%, 7%, for lowest, middle, and highest tertiles) and for mixed/other phenotype patients ($P < .001$). These associations also remained significant after adjustment for cardiac status ($P = .008$ for DCM and $P < .001$ for mixed/other).

Functional status was not significantly associated with clinical outcome in the HCM cohort age 5 years; however, among the 545 participants of all ages (median follow-up 3.8 years), there were more deaths and transplants: 46 in the DCM cohort, 11 in the HCM cohort, and 24 in the mixed/other phenotype cohort. Patients with HCM had a 6-fold increased risk of death/transplant ($P = .004$) if the FSII(R) total score was in the abnormal range, compared with those with a score in the normal range.

The CHQ and FSII(R) administration in the age 5 year cohort occurred an average of 2.6 years after cardiomyopathy diagnosis. A sensitivity analysis that modeled time to death/transplant from the time of survey completion revealed associations that were very similar to those identified by the primary analysis.

Discussion

Although cardiomyopathy has associated impairment, many children are able to function within the normal range. It is notable, however, that these 343 children, at a mean age of 8.6 years, had a mean CHQ Physical Summary Score of 41.7 (median 46.0) that was lower what has been reported for children with congenital heart disease of similar or older ages. The 546 Pediatric Heart Network Fontan study participants⁶ had a mean parent-reported score of 45.3; 66 teens with repaired tetralogy of Fallot⁷ had a mean score of 49.4, and 47 children with thoracic organ transplants²⁰ had a median score of 50.6. Typically, a difference of 3–5 points in CHQ Summary Scores is considered clinically significant. Therefore, in children, cardiomyopathy imposes physical limitations that are greater than other cardiac conditions. In children with DCM, this is likely related to heart failure symptomatology and associated repeat hospitalizations.

Psychosocial functioning as measured by the CHQ parent report was closer to the normal mean (47.8 for PCMR vs 51.2 for healthy children), although still lower. Functioning in this realm is similar to that of survivors of Fontan⁶ (mean 47.2), adolescents with tetralogy of Fallot⁷ (mean 50.6), and children who have undergone thoracic organ transplant²⁰ (median 51.5).

The FSII(R) is designed to measure overall well-being in children with chronic illnesses, and during development it was shown to be correlated with hospitalization days.¹⁴ The mean total score of the entire PCMR cohort (87.1, median age 6.6 years) was lower than that of the healthy controls studied by Stein et al¹⁴ (mean 96.1), and similar to the mean score (86.8) of a cohort of chronically ill children. There are few reports of the FSII(R) being administered to children with cardiac conditions. The mean FSII(R) total score in 53 survivors of congenital diaphragmatic repair survivors²¹ (median age 8 years) was 91; however, the mean total score in the subset of those with concurrent clinical problems was 89, more similar to the PCMR cohort.

Although the distribution of FSII(R) scores revealed a ceiling effect, that is, was skewed toward better functioning with fewer children having very low scores than seen with the CHQ, we identified a moderate positive correlation (>0.5) between the CHQ Physical Summary Score and the broader-based FSII(R). The coefficient of variation for the 2 instruments is roughly similar; therefore, these results do not suggest that one instrument is necessarily preferable over the other for use as an outcome measure. However, the FSII(R) is validated for use in children <5 years of age, and the CHQ is not appropriate for younger children.¹³

In our study, we found that functional status, whether physical or psychosocial/emotional, was correlated with age at diagnosis as well as SES and the child's echocardiographic

profile. However, the percentage of variation explained by the models derived for each cardiomyopathy phenotype ranged from 8% to 27% for the CHQ Physical Summary Score and FSII(R) total score, and from 5% to 15% for the CHQ Psychosocial Summary Score and Parental Impact-Emotional scale. McCrindle et al²² found that echocardiographic predictors yielded an adjusted R^2 of only 7% for the CHQ Physical Summary Scores obtained from pediatric survivors of Fontan. Nevertheless, it is interesting that larger LV size (in patients with DCM) in our study was a significant predictor of not only worse physical functioning in cardiomyopathy, but of the emotional impact of the child's health on parents. Furthermore, the independent correlations of greater levels of education and income with better psychosocial functioning of the child and lessened impact on parents indicate that families in need of greatest support may be identified by measures of SES regardless of the severity of the child's cardiomyopathy.

It is interesting to note that LV EDD was an independent predictor of physical and psychosocial functioning, but LV function, although critical physiologically and what one might presume would be independently related to HRQOL, was not. The strong predictive power of LV size is likely attributable to its lower measurement error: LV EDD has intra- and interobserver reproducibility that is four times greater than that of LV fractional shortening, which is a function of two measurements.²³ This may be an important design consideration when selecting laboratory outcome measures for a trial.

Our hypothesis that impaired functional status would be associated with more rapid development of adverse clinical outcomes was confirmed. Furthermore, this association existed even with adjustment for cardiac status. The children in our study had a median of 4.9 years of follow-up after diagnosis, and the follow-up on average extended more than two years past the time of functional status assessment. Children with DCM who were in the lowest tertile of physical functioning were at 12 times the risk of death or transplant compared with children in the upper tertile, with a corresponding large difference in 5-year event rates (37% vs 2%). This association also was observed with respect to listing for transplant. The mixed/other cardiomyopathy phenotype group had event rates that were roughly similar to those of the DCM cohort and also correlated with CHQ Physical Summary Score and the FSII(R) total score. These findings are important from a research perspective in that these validated instruments, at least in the pediatric population with cardiomyopathy, may be able to serve as surrogate measures of clinical outcome when designing a trial that may not be of sufficient duration to observe a large number of clinical events. Indeed, there are now pharmaceutical trials in patients with heart failure where quality of life is the primary, rather than secondary, outcome.²⁴ Our findings are important from a clinical perspective in that they suggest that children at greatest risk of clinical decline can be identified by these measures and warrant increased monitoring; and that formal functional status measurement should be integrated into prognostic assessment, similar to such increasing practice in adult care.²⁵ Uzark et al²⁶ demonstrated the clinical utility of such assessment in the setting of a pediatric cardiology clinic.

Our findings should be interpreted in light of some limitations. Although the PCMR sample is larger than most single-center studies, the sizes of the cardiomyopathy phenotype subgroups for the CHQ were still relatively small, and some statistical associations may not

have been detected that could have clinical relevance. In particular, our analysis of clinical outcomes was limited for the HCM cohort, which had only 3 clinical events in the CHQ analysis and 11 in the full cohort. The low percentage of variation explained in our predictive models indicates that other variables either not measured or not analyzed contribute to a child's functional status. Such variables may include growth measures,²⁷ medications, and concurrent noncardiac illnesses.²² It is also important to note that the CHQ instrument is designed to assess only children age 5 years and older; therefore, the reported CHQ results may not be generalizable to children living with cardiomyopathy at younger ages. Finally, we caution that the assessments presented here are based on parental report. Although their association with clinical outcome cannot be dismissed, self-reports of functioning by children are at somewhat higher levels than that of their parents.^{28,29}

Importantly, the most impaired domain identified in our pediatric population with cardiomyopathy was the emotional impact of the child's illness on the parents. Families at risk for functional impairment can be identified, and a multidisciplinary integrated care model, including the provision of specialized social services early in the course of disease, should be considered.

Acknowledgments

Supported by the National Heart, Lung, and Blood Institute (NHLBI; R01 HL HL53392). The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the NHLBI.

We thank the participating centers for subject recruitment and follow-up data collection. We also thank the Children's Cardiomyopathy Foundation for their ongoing support of the Pediatric Cardiomyopathy Registry's research efforts.

Glossary

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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Appendix

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Figure 1.

A, CHQ Parent Report Summary Scores (N = 343) by functional type of cardiomyopathy.

Overall Summary Scores were 41.7 ± 14.4 for Physical (raw score -0.83 ± 1.44 , median -0.40) and 47.8 ± 10.7 for Psychosocial (raw score -0.22 ± 1.07 , median -0.05). **B**, CHQ Parent Report Scales: Median z scores, overall cardiomyopathy cohort. *P* values from signed rank test indicate whether the cardiomyopathy cohort median differs from the healthy norm of $Z = 0$.

Figure 2. Correlation between FSII(R) total score and **A**, CHQ Physical Summary Score (Spearman $R = 0.52$, 95% CI 0.43–0.59) and **B**, CHQ Psychosocial Summary Score (Spearman $R = 0.55$, 95% CI 0.47–0.62).

Figure 3.

Freedom from clinical outcome in children with dilated cardiomyopathy with HRQOL assessment at age 5 years, all $P < .001$. Curves are truncated at 8 years. **A**, Time to death/cardiac transplantation by CHQ Physical Summary Score tertile. There were 14, 8, and 2 events in the lowest, middle, and highest tertile, respectively. **B**, Time to listing for cardiac transplantation by CHQ Physical Summary Score tertile. There were 15, 8, and 4 events in the lowest, middle, and highest tertile, respectively. **C**, Time to death/cardiac transplantation by FSII(R) Total Score tertile. There were 14, 9, and 2 events in the lowest, middle, and highest tertile, respectively. **D**, Time to listing for cardiac transplantation by FSII(R) Total Score tertile. There were 15, 10, and 3 events in the lowest, middle, and highest tertile, respectively.

Table 1

FSII(R) total score* for PCMR Functional Status study participants, by age at assessment

Variable	All	Dilated	Hypertrophic	Mixed/Other	P value [†]
First assessment, all participants	N = 565	N = 272	N = 183	N = 110	
Median age at diagnosis of cardiomyopathy, y	1.9	1.1	5.3	4.1	<.001
Median age at functional status assessment, y	6.6	5.5	11.3	6.9	<.001
Median time from diagnosis to functional status assessment, y	1.4	1.2	2.1	1.1	.04
FSII(R) total score					.82
Mean ± SD	87.1 ± 16.4	86.2 ± 18.2	87.9 ± 14.6	88.3 ± 14.2	
Median (IQR)	92.9 (78.6, 100)	92.9 (78.6, 100)	92.9 (78.6, 100)	92.9 (78.6, 100)	
First assessment at age <5 y	N = 245	N = 143	N = 60	N = 42	
Median age at diagnosis of cardiomyopathy, y	0.4	0.5	0.5	0.4	.99
Median age at functional status assessment, y	1.8	1.7	2.2	2.4	.51
Median time from diagnosis to functional status assessment, y	0.9	0.9	1.0	0.9	.84
FSII(R) total score					.71
Mean ± SD	86.6 ± 18.0	86.9 ± 18.7	85.5 ± 17.2	87.1 ± 17.0	
Median (IQR)	96.4 (78.6, 100)	96.4 (82.1, 100)	92.9 (73.2, 100)	96.4 (78.6, 100)	
First assessment at age ≥ 5 y	N = 355	N = 149	N = 129	N = 77	
Median age at diagnosis of cardiomyopathy, y	8.6	5.6	11.1	9.2	.003
Median age at functional status assessment, y	12.0	10.6	14.1	10.4	<.001
Median time from diagnosis to functional status assessment, y	2.6	3.3	2.8	1.9	.05
FSII(R) total score					.55
Mean ± SD	88.5 ± 14.7	86.8 ± 17.1	89.4 ± 12.9	90.2 ± 11.8	
Median (IQR)	92.9 (82.1, 100)	92.9 (78.6, 100)	96.4 (82.1, 100)	96.4 (82.1, 100)	

* Well-child FSII(R) 14-item total score mean ± SD is 96.1 ± 8.2. All groups differ from the historical well-child mean, $P < .001$. The historical ill-child FSII(R) mean ± SD is 86.8 ± 15.7.¹⁴[†] P value from Kruskal-Wallis test.

Table II

Characteristics of 355 participants age 5 years in the PCMR Functional Status study

Characteristic	All	DCM	HCM	Mixed or other type of cardiomyopathy
N	355	149	129	77
Male, n (%)	208 (59)	74 (50)	92 (71)	42 (53)
Age at diagnosis of cardiomyopathy, y [*]	8.6 (1.4, 13.5)	5.7 (0.4, 12.5)	11.1 (3.8, 14.3)	9.2 (3.3, 13.4)
Age at CHQ completion, y [*]	12.0 (7.4, 15.8)	10.6 (6.4, 15.1)	14.1 (10.7, 16.3)	10.4 (6.7, 15.6)
Time from diagnosis to CHQ completion, y [*]	2.6 (0.8, 5.3)	3.4 (0.8, 5.9)	2.8 (1.1, 5.1)	1.9 (0.4, 4.9)
Follow-up time of nontransplanted survivors, y [*]	4.9 (2.2, 7.6)	5.0 (2.5, 7.4)	5.0 (2.4, 8.4)	3.0 (1.7, 6.5)
Race/ethnicity, n (%)				
White, non-Hispanic	208 (59)	76 (51)	86 (67)	46 (60)
Black, non-Hispanic	60 (17)	30 (20)	16 (12)	14 (18)
Hispanic	71 (20)	33 (22)	24 (19)	14 (18)
Other	17 (5)	10 (7)	3 (2)	3 (4)
Congestive heart failure at time of diagnosis of cardiomyopathy, n (%)	112 (33)	90 (61)	3 (2)	19 (25)
Unknown, n	4	2	2	0
Etiology, n (%)				
Idiopathic	257 (72)	104 (70)	90 (70)	63 (82)
Inborn error of metabolism	10 (3)	5 (3)	2 (2)	3 (4)
Malformation syndrome	7 (2)	0 (0)	5 (4)	2 (3)
Familial isolated cardiomyopathy	52 (15)	13 (9)	32 (25)	7 (9)
Myocarditis	29 (8)	27 (18)	0 (0)	2 (3)
Currently married, n (%)	251 (71)	104 (71)	93 (72)	54 (71)
Unknown, n	3	2	0	1
Total household income, n (%)				
<\$40 000	115 (33)	52 (36)	38 (30)	25 (33)
\$40 000–\$79 000	109 (31)	46 (32)	38 (30)	25 (33)
\$80 000	125 (36)	47 (32)	52 (41)	26 (34)
Unknown, n	6	4	1	1
Highest education of caregiver, n (%)				
Some high school	45 (13)	26 (18)	13 (10)	6 (8)
High school graduate	77 (22)	29 (20)	31 (24)	17 (23)
Some college/vocational	108 (30)	45 (31)	39 (31)	24 (32)
Bachelor's/postgraduate	116 (34)	45 (31)	44 (35)	27 (36)
Unknown, n	9	4	2	3
LV echocardiographic measurements [†]				
Fractional shortening, %	-	24.6 ± 11.5	44.7 ± 9.6	31.8 ± 10.4
Ejection fraction, % [‡]	-	41.6 ± 15.1	67.4 ± 10.1	53.0 ± 13.1
End-diastolic posterior wall thickness to EDD ratio	-	0.14 ± 0.09	0.28 ± 0.13	0.20 ± 0.10
End-diastolic septal:posterior wall thickness ratio	-	1.02 ± 0.28	1.64 ± 0.87	1.11 ± 0.22

Characteristic	All	DCM	HCM	Mixed or other type of cardiomyopathy
Echocardiographic LV z scores [§]				
EDD	-	2.8 ± 2.2	-1.5 ± 2.0	0.6 ± 2.4
Fractional shortening	-	-3.9 ± 4.6	4.5 ± 4.0	-0.8 ± 4.2
Ejection fraction	-	-3.7 ± 2.5	0.8 ± 1.8	-1.6 ± 2.1
End-diastolic posterior wall thickness	-	-0.8 ± 2.4	1.7 ± 2.7	0.1 ± 2.5
End-diastolic septal thickness	-	-0.9 ± 1.8	3.3 ± 2.7	0.3 ± 2.0
Mass	-	1.2 ± 2.2	2.1 ± 2.4	0.8 ± 2.3
End-diastolic posterior wall thickness to EDD ratio [*]	-	-2.1 (-2.8, -0.9)	2.4 (0.4, 4.8)	-0.7 (-1.6, 1.6)
End-diastolic septal:posterior wall thickness ratio [*]	-	-0.33 (-1.03, 0.41)	1.5 (-0.1, 4.6)	0.0 (-0.6, 1.0)

Summary statistic is mean ± SD unless otherwise noted.

^{*} Median (IQR).

[†] Echocardiographic measurement closest to time of functional status assessment was used (median 1 mo before assessment).

[‡] LV ejection fraction sample sizes were 269 for All, 125 for DCM, 87 for HCM, and 57 for mixed/other.

[§] All z scores in the DCM and HCM group significantly differ ($P < .05$) from normal ($Z = 0$). In the mixed/other group, only LV EDD, LV ejection fraction, and LV mass differ from zero.

Table III
CHQ Parent Report and FSI(R) Scores for PCMR Functional Status study participants age 5 years

Score	N	All	n	Dilated	n	Hypertrophic	n	Mixed/other	P value*
CHQ [†]									
Physical Summary Score	343	41.7 ± 14.4	143	41.3 ± 15.7	125	43.4 ± 12.0	75	39.7 ± 15.5	.46
Mean ± SD									
Median (IQR)		46.0 (32.3, 52.6)		46.6 (30.7, 52.6)		46.0 (34.4, 53.7)		43.8 (26.6, 51.6)	
Psychosocial Summary Score									.17
Mean ± SD	343	47.8 ± 10.7	143	48.1 ± 10.1	126	46.2 ± 12.0	76	49.9 ± 9.1	
Median (IQR)		49.5 (40.4, 55.8)		49.4 (40.4, 55.7)		47.4 (38.4, 55.2)		50.6 (43.6, 57.0)	
FSI(R) [‡] total score									.55
Mean SD	355	88.5 ± 14.7	149	86.8 ± 17.1	130	89.4 ± 12.9	78	90.2 ± 11.8	
Median (IQR)		92.9 (82.1, 100)		92.9 (78.6, 100)		96.4 (82.1, 100)		96.4 (82.1, 100)	

* P value from Kruskal-Wallis test.

[†] Well-child CHQ mean ± SD is 53.0 ± 8.8 for Physical and 51.2 ± 9.1 for Psychosocial summary scores.¹⁵ All values differ from the well-child mean, $P > .01$, except for the Psychosocial Summary Score of the mixed/other group.

[‡] Well child FSI(R) 14-item total score mean ± SD is 96.1 ± 8.2. All groups differ from the historical well-child mean, $P < .001$. The historical ill-child FSI(R) mean ± SD is 86.8 ± 15.7.¹⁴

Table IV
Multivariable Models for CHQ Summary Scores and FSII(R) total score (age 5 years cohort)

Outcomes	N	Adj. R ²	Variable	Slope ± SE	P value
DCM					
CHQ Physical	135	27%	Age at diagnosis, y	-1.17 ± 0.20	<.001
			LV EDD z score	-1.82 ± 0.55	.001
			LV end-diastolic posterior wall thickness z score > 2	-11.35 ± 4.68	.017
CHQ Psychosocial	139	6%	Age at diagnosis, y	-0.36 ± 0.14	.012
			LV EDD z score	-0.89 ± 0.39	.025
CHQ Parent	144	5%			
Emotional			Age at diagnosis, y	-0.04 ± 0.02	.044
z score			LV EDD z score > 2	-0.55 ± 0.23	.019
FSII(R) total	150	17%			
			Age at diagnosis, y	-0.77 ± 0.24	.002
			Parent highest educational level completed [†]	2.18 ± 1.13	.05
			LV ED posterior wall thickness:dimension ratio z score < 2	-10.36 ± 2.86	<.001
HCM					
CHQ Physical	103	11%			
			Parental education < high school graduate	-10.69 ± 3.51	.003
			LV EDD z-score < -2	-5.05 ± 2.18	.022
CHQ Psychosocial	124	7%	Annual household income category*	1.88 ± 0.58	.002
CHQ Parent	119	12%			
Emotional			Annual household income category*		
z score			LV end-diastolic posterior wall thickness z score	-0.19 ± 0.06	.002
FSII(R) total	127	19%			
			LV end-diastolic posterior wall thickness z score	-0.11 ± 0.04	.012
			Age at diagnosis, y		
			Parental education < high school graduate	-0.65 ± 0.61	<.001
				-14.41 ± 3.41	<.001
Mixed/other type of cardiomyopathy					
CHQ Physical	73	15%			
			Time from diagnosis to functional status assessment, y	1.80 ± 0.61	.005

Outcomes	N	Adj. R ²	Variable	Slope ± SE	P value
CHQ Psychosocial	73	11%	Parent highest educational level completed [†]	3.31 ± 1.37	.019
			Age at diagnosis, y	−0.36 ± 0.18	.046
CHQ Parent Emotional	70	15%	Parental education < high school graduate	−8.22 ± 3.71	.030
z score			Parental education < high school graduate	−1.51 ± 0.63	.020
FSII(R) total	77	8%	LV EDD z score	0.20 ± 0.07	.006
			Age at diagnosis, y	−0.63 ± 0.23	.008

* Annual household income level categories: (1) <\$20 000; (2) \$20 000–39 000; (3) \$40 000–59 000; (4) \$60 000–79 000; (5) \$80 000–99 000; and (6) \$100 000.

[†] Highest educational level categories: (1) less than high school graduate; (2) high school graduate; (3) some college or vocational training; (4) college graduate; and (5) postgraduate education.

Table V

Cox regression modeling of time to death/cardiac transplant predicted by CHQ Physical Summary Score and FSII(R) total score (hazard ratio, 95% CI)

HR for death/transplant (95% CI)			
Cohort: Age 5 y			
CHQ Physical Summary Score	DCM (N = 143)	HCM (N = 125)	Mixed/Other (N = 75)
No. of events	24	3	14
Continuous (per 3-point increase)	0.83 (0.77–0.89)*	0.90 (0.69–1.18)	0.82 (0.74–0.91)*
Abnormal [†] (<35.4)	6.5 (2.7–14.9)*	1.3 (0.1–14.6)	8.0 (2.5–25.2)*
Tertile 1 vs 2	3.5 (1.4–8.4) [‡]	n.e.	5.0 (1.3–19.7) [‡]
Tertile 1 vs 3	12.1 (2.7–53.6) [‡]	2.1 (0.2, 23.0)	15.0 (1.8–122.3) [§]
Tertile 2 vs 3	3.5 (0.7–16.5)	n.e.	3.0 (0.3–29.0)
Cohort: age 5 y			
FSII(R) total score	DCM (N = 149)	HCM (N = 129)	Mixed/Other (N = 77)
No. of events	25	4	14
Continuous (per 5-point increase)	0.76 (0.70–0.83)*	0.85 (0.60–1.20)	0.69 (0.58–0.81)*
Abnormal [†] (<79.7)	4.9 (2.1–11.0)*	1.6 (0.2–15.6)	8.7 (2.7–27.8)*
Tertile 1 vs 2	1.5 (0.7–3.6)	0.6 (0–9.7)	8.2 (1.7–38.9) [‡]
Tertile 1 vs 3	9.5 (2.2–41.9)*	0.8 (0.1–8.4)	13.2 (2.7–64.5)*
Tertile 2 vs 3	6.2 (1.3–28.6) [‡]	1.3 (0.1–13.9)	1.6 (0.2–11.6)
Cohort: age 1 week to 18 y			
FSII(R) total score	DCM (N = 272)	HCM (N = 183)	Mixed/Other (N = 110)
No. of events	46	11	24
Continuous (per 5-point increase)	0.82 (0.77–0.87)*	0.75 (0.64–0.89)*	0.77 (0.69–0.85)*
Abnormal [†] (<79.7)	3.9 (2.1–7.0)*	6.2 (1.8–21.4) [‡]	6.1 (2.7–14.1)*
Tertile 1 vs 2	1.8 (0.9–3.5)	4.6 (0.6–37.2)	4.7 (1.4–16.1) [§]
Tertile 1 vs 3	5.7 (2.4–13.8)*	2.9 (0.8–11.3)	8.8 (2.6–30.3)*
Tertile 2 vs 3	3.2 (1.2–8.4) [§]	0.6 (0.1–6.1)	1.9 (0.4–9.4)

n.e., not estimable.

CHQ tertiles <39, 39 to <51, 51; FSII(R) tertiles <86, 86 to <100, 100.

* $P < .001$.

[†] Defined as less than 2 SD below the healthy child mean.

[‡] $P < .01$.

[§] $P < .05$.