HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2017 March 01.

Published in final edited form as:

J Pediatr. 2016 March ; 170: 166–172.e1. doi:10.1016/j.jpeds.2015.11.016.

Assessment of Quality of Life in Young Patients with Single Ventricle after the Fontan Operation

Karen Uzark, PhD, CPNP[1], **Victor Zak, PhD**[2], **Peter Shrader, MA**[2], **Brian W McCrindle, MD, MPH**[3], **Elizabeth Radojewski, RN**[3], **James W. Varni, PhD**[4], **Kaitlyn Daniels, BSN, RN**[5], **Jill Handisides, BSN**[6], **Kevin D. Hill, MD, MS**[7], **Linda M. Lambert, MSN, FNP**[8], **Renee Margossian, MD**[6], **Victoria L. Pemberton, RNC, MS, CCRC**[9], **Wyman W. Lai, MD**[10], and **Andrew M Atz, MD**[11,*] **on behalf of the Pediatric Heart Network Investigators**

[1]University of Michigan Mott Children's Hospital, Ann Arbor, MI

[2]New England Research Institutes, Watertown, MA

[3]University of Toronto Hospital for Sick Children, Toronto, ON, Canada

[4]Texas A&M University, College Station, TX

[5]Children's Hospital of Philadelphia, Philadelphia, PA

[6]Boston Children's Hospital, Boston, MA

[7]Duke University Medical Center, Durham, NC

[8]Primary Children's Hospital, Salt Lake City, UT

[9]National Heart, Lung, and Blood Institute, Bethesda, MD

[10]Columbia University Medical Center, New York, NY

[11]Medical University of South Carolina, Charleston, SC

Abstract

Objectives—To assess self-reported quality of life (QOL) in a large multicenter cohort of adolescent and young adults surviving Fontan.

Study design—Cross-sectional. The Pediatric Quality of Life Inventory (PedsQL) was administered to 408 survivors of Fontan ages 13–25 years enrolled in the Pediatric Heart Network Fontan Follow-up Study. Subjects also completed either the Child Health Questionnaire (CHQ-87, age < 19years) or Short Form 36 (SF-36, age ≥19 years). PedsQL data were compared with

Address correspondence to: Karen Uzark, PhD, CPNP, University of Michigan Mott Children's Hospital, L2110 Women's, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5202, karenu@med.umich.edu, Telephone: 734-615-9748 FAX: 734-232-3744.

*List of Pediatric Heart Network Investigators is available at www.jpeds.com (Appendix).

The other authors declare no conflicts of interest.

Portions of the study were presented as an abstract and poster at the American Heart Association Scientific Sessions, Chicago, IL, November <dates>, 2014.

matched controls without a chronic health condition. Correlations between the measures were examined.

Results—Mean PedsQL scores for subjects receiving Fontan were significantly lower than those for the control group for physical and psychosocial QOL (P<0.001). Overall, 45% of subjects receiving Fontan had scores in the clinically significant impaired range for physical QOL with 30% in the impaired range for psychosocial QOL. For each 1 year increase in age, the physical functioning score decreased by an average of 0.76 points (p=0.004) and the emotional functioning score decreased by an average of 0.64 points (p=0.03). Among subjects ≥ 19 years of age, the physical functioning score decreased by an average of 2 points for each year increase in age (p=0.02). PedsQL scale scores were significantly correlated with conceptually related CHQ-87 (p<0.001) and SF-36 scores (p<0.001).

Conclusions—Survivors of Fontan are at risk for significantly impaired QOL which may decline with advancing age. Routine assessment of QOL is essential to inform interventions to improve health outcomes. The PedsQL allowed QOL assessment from pediatrics to young adulthood.

Trials Registration—ClinicalTrials.gov: NCT00132782.

Keywords

congenital heart disease; psychosocial; quality of life; PedsQL

Advances in medical and surgical care have dramatically improved the life expectancy of children with congenital heart disease (CHD), including children born with complex single ventricle defects who undergo the Fontan operation. Although the Fontan surgery does not provide anatomic correction, it provides separate pulmonary and systemic circulations supported by the single ventricle, allowing an increasing number of patients to reach adulthood and the opportunity for a productive life. However, greater knowledge of psychosocial morbidity and the potential impact of the Fontan operation on overall quality of life (QOL) and functioning are essential to improving outcomes in this patient population.

QOL is a multidimensional construct which includes physical, psychological, and social functioning, consistent with the World Health Organization's (WHO) definition of health.[1] Furthermore, the WHO has emphasized that QOL is a subjective experience, defined as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns."[2] QOL measurement however, has been fraught with many conceptual and methodological issues.[3] It is often incorrectly used as a generic label to describe a range of physical, health status, and psychosocial variables, including objective observations by others reflecting their standards. Past studies have often relied on parental report, are limited by small sample size/single center design, are restricted to a specific age-group, or use different measures across age-groups.[4–10] No longitudinal follow-up of QOL has been reported in patients with Fontan physiology as they move through childhood to young adulthood, perhaps in part reflecting the lack of an available self-report QOL measurement instrument that spans the age range of this growing population of survivors of Fontan.

Our aims were to describe self-reported QOL in a large multicenter cohort of adolescent and young adult patients following the Fontan operation as measured by the Pediatric Quality of Life Inventory (PedsQL), and to examine the correlation between the PedsQL and related conceptual functional domains (Physical and Psychosocial/Mental functioning) as measured on the Child Health Questionnaire (CHQ-87) in patients < 19 years of age and the Short-Form Health Survey (SF-36) in patients 19 years of age and older.

METHODS

The Pediatric Heart Network Fontan Cross-Sectional Study (Fontan 1) characterized a multi-institutional cohort (7 sites) of 546 survivors after the Fontan procedure, ages 6 to 18 years at enrollment.[11]. From this original cohort, patients who were alive with a Fontan circulation were approached for enrollment in the Fontan Follow-up Study (Fontan 2) from 2009–2011[12] and are the subjects of this study. Changes in functional health status from Fontan 1 to Fontan 2 as well as predictors of these changes in this patient cohort have been previously reported.[12] The protocol was approved by each center's institutional review board and informed consent was obtained.

To assess QOL, patients completed the Pediatric Quality of Life Inventory (PedsQL) 4.0 Generic Core Scales[13] and the PedsQL Cardiac Module.[14, 15] The 23-item PedsQL Core scales encompass Physical, Emotional, Social, and School/Work functioning. Items are linearly transformed to a 0-to-100 scale, so that higher scores indicate better QOL. Parallel Child, Teen, and Young Adult versions of the PedsQL have been developed with similar content and wording across forms to facilitate evaluation of differences across and between age groups as well as longitudinal tracking. To create a Psychosocial Health Summary score, the mean of the Emotional, Social, and School/Work functioning scales is computed. The reliability and validity of the PedsQL Generic Core Scales have been demonstrated in healthy and patient populations.[13, 16–18] The PedsQL Cardiac Module has 6 scales related to symptoms, treatment barriers (for patients on medications), perceived physical appearance, treatment anxiety, cognitive problems, and communication. Formatting and scoring are the same as the PedsQL Generic Core Scales. Validity and reliability for 8 to 18 year olds has been demonstrated.[14]

Patients < 19 years old completed the Child Health Questionnaire (CHQ)-CF87, the same measure administered to patients 10–18 years of age in Fontan 1. The CHQ assesses functional health status across a range of areas related to physical, mental, and social domains.[19] The scale domain scores range from 0 to 100, with higher scores indicating better function.

In patients ≥ 19 years of age, functional health status was measured using the Short-Form Health Survey version 2 (SF-36). The 36-item SF-36 is a multi-purpose, short-form health survey. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based Physical and Mental Health component summary measures.[20] The reliability and the validity of the SF-36 health survey have been established.[21, 22]

Data analyses

Descriptive statistics for demographic and clinical variables are reported as means and standard deviation or medians with interquartile range (IQR) for continuous variables and frequencies/proportions for categorical variables. Patient characteristics and PedsQL Scale and summary scores were compared between adolescents (< 19 years old) and young adults (≥ 19 years of age) using appropriate statistical tests (Student's t-test for means, Wilcoxon ranked-sum test for medians, or Fisher Exact test for frequencies). PedsQL Scale and summary scores were also compared with an age, sex, and race/ethnicity matched healthy children sample from the PedsQL database. The healthy comparison group was comprised of 342 subjects from the PedsQL healthy children database which is composed of children and young adults without a chronic health condition[16, 17] and included 242 subjects < 19 years old and 100 subjects 19–25 years of age. Comparisons were repeated after adjustments for minor differences in age and sex and showed no significant differences from unadjusted values. Adjusted values are reported. For each individual scale and the psychosocial health summary score, we report the frequency of scores greater than one standard deviation below the general pediatric population sample mean, the cutoff score for significantly impaired QOL.[16] Individual item analysis with ranking was performed to identify the most significant problems or lowest mean scores within PedsQL Core and Cardiac Module scales. Unadjusted linear regression models were used to test the association between each of the PedsQL Scale scores and age. Regression analyses were used to test the association of PedsQL Scales with income, maternal education, and sex. Spearman correlation coefficients were calculated to test the association between the PedsQL scores and the corresponding CHQ-CF87 and SF-36 scores. Effect sizes were designated as small (0.10–0.29), medium (0.30–0.49), and large (≥ 0.50).

RESULTS

Of 427 subjects enrolled in Fontan 2 in 2009–2011, 408 (96%) completed the PedsQL. In addition to the PedsQL, 255 adolescents < 19 years old completed the CHQ and 153 young adults 19–25 years of age completed the SF-36. Demographic and key patient characteristics for subjects receiving Fontan are summarized in Table I. The mean age at Fontan 2 enrollment was 18.4 ±3.4 years. The mean follow up time after Fontan surgery was 15.2 ±3.4 years. Young adult patients were more likely than adolescents to have an atriopulmonary connection. There were no significant differences in demographic characteristics between the subjects receiving Fontan and the healthy comparison sample except that among subjects < 19 years old, the subject group receiving Fontan was somewhat older (mean age 16.2±1.6 years) than the healthy group (mean age 15.0 ±1.1 years), P <0.001.

Young adults receiving Fontan had significantly lower PedsQL scores related to Physical Functioning (P=0.02), heart problems/symptoms (P=0.01) and treatment barriers (P=0.002) in comparison with adolescents with Fontan. Overall mean PedsQL scores for subjects with Fontan were significantly lower than those for the healthy controls for physical and psychosocial QOL, including emotional, social, and School/work QOL (all P<0.001). In the young adults receiving Fontan (Table II), PedsQL scores for Total, Physical, and Social

QOL were significantly lower than the healthy comparison group (all P <0.001), but there were no significant differences related to Psychosocial, Emotional or School/work functioning scores. Overall, 45% of subjects with Fontan had Physical Functioning Scores > 1 standard deviation below the population sample mean, the cutoff point for significantly impaired QOL in the general pediatric population (Table III). In 30% of subjects receiving Fontan, Psychosocial Health Summary scores were consistent with significantly impaired psychosocial QOL. Emotional functioning was least likely to be significantly impaired (20%) with more frequent impairment noted for Social Functioning (27%) and School/Work Functioning (31%).

Individual item analysis revealed the most common problems reported as “often” or “almost always” included getting out of breath during sports activity or exercise (35%), having to rest more than friends (28%), difficulty running (26%), fast heart beat (15%), difficulty doing sports or exercise (22%), not being able to do things others could do (18%), trouble sleeping (16%), worrying about what will happen (16%), not liking people to see scars (16%), and difficulty explaining heart problem to others (21%).

There were significant associations between Physical Functioning scores and both age and sex (Table IV). For each 1 year increase in age, the predicted Physical Functioning score decreased by an average of 0.76 points (p=0.004). The predicted mean Physical Functioning score was 6.9 points higher for males than females (P<0.001). Among subjects ≥ 19 years of age, for each 1 year increase in age, the Physical Functioning score decreased by an average of 2 points (P=0.02), and the average Physical Functioning score was 9.2 points higher in males than females (P=0.005). There was no significant association between Physical Functioning scores and household income or maternal education. There were no differences in physical functioning scores related to type of Fontan among young adults, mean scores 71.8 ± 20.4 in atriopulmonary connection versus 71.4 ± 20.3 in total cavopulmonary connections. There was a significant correlation between PedsQL Physical Functioning and Psychosocial Health Summary scores for all subjects (r=0.71, P<0.001), among adolescents < 19 years (r=0.67, P<0.001), and among young adults (r=0.77, P<0.001).

Psychosocial Health Summary scores (Table IV) were significantly associated with household income (P=0.04), especially among subjects ≥ 19 years age (P=0.006). There was no significant association between Psychosocial Health Summary scores and subject age, sex, or maternal education. There was also no significant difference related to type of Fontan. Among all subjects, there was a significant association between Emotional Functioning scores and both age (P=0.03) and sex (P=0.002) with males having an average score 6.2 points higher than females. For each 1 year increase in age, the Emotional Functioning score decreased by an average of 0.64 points (P=0.03). There was no significant association between Social Functioning scores and sociodemographic characteristics. Among all subjects, school/work functioning was significantly associated with household income (P=0.007) as well as with maternal education (P=0.008).

In patients < 19 years of age, the relationship between QOL as measured by the PedsQL and related conceptual functional domains (Physical and Psychosocial/Mental functioning scores) as measured by the Child Health Questionnaire (CHQ-87) was examined. All

CHQ-87 scores were significantly correlated with each of the PedsQL scores, P<0.001. There was a strong correlation between the two physical functioning scores, r=0.75. There was also a strong correlation between the PedsQL Psychosocial Health Summary score and the Behavior (r=0.66), Mental Health (r=0.66), and Self-Esteem scales (r=0.60) of the CHQ-87.

In subjects ≥ 19 years old, for whom the CHQ-87 is not a valid measure, the relationship between QOL as measured by the PedsQL and related conceptual functional domains (Physical and Psychosocial/Mental scores) as measured by the SF-36 were also examined. All SF-36 scores were significantly correlated with each of the PedsQL scores, P<0.001. There were strong correlations between PedsQL Physical Functioning scores and SF-36 Physical Functioning, (r=0.77) and the SF-36 Aggregated Physical Scores, r=0.68. There was a medium to strong correlation between the PedsQL Psychosocial Health Summary and the SF-36 Mental Health score (r=0.59, P<0.001) and SF-36 Aggregated Mental score (r=0.53, P<0.001). The SF-36 Mental Health scores were more highly correlated with the PedsQL Emotional Functioning scale (r=0.59) than with the Social Functioning scale (r=0.40).

DISCUSSION

Adolescents and young adults with Fontan circulation describe lower physical and psychosocial QOL than the healthy population without a chronic health condition, with lower physical functioning, more symptoms (heart problems), and more perceived treatment barriers reported by young adults than the adolescent age group. Lower self-reported physical and psychosocial QOL is also consistent with parent-reports of functioning in these domains on the CHQ in this same patient group,[12] and with pediatric and adult self-reports in patients receiving Fontan previously reported in Denmark and the Netherlands,[4, 23] as well as in patients with other chronic health conditions.[7] Deficits in physical health or functional status[6, 24] and depression[24] have also been reported in the single ventricle population. Furthermore, in this cross sectional sample, age group comparisons and the linear regression model suggest that physical QOL may diminish with advancing age. Although there was no significant association between type of Fontan and physical functioning scores as previously reported[7], older patients in our cohort were more likely to have had an atriopulmonary connection which was reported to be associated with a significantly higher incidence of developing a new arrhythmia requiring treatment, perhaps partly explaining the association between older age and greater treatment related problems[12]. Male subjects receiving Fontan reported significantly higher scores for physical functioning, similar to findings in healthy populations, perhaps reflecting different gender expectations.[17, 25] Psychosocial QOL was strongly correlated with physical functioning in our study. Although the majority of patients with Fontan report a good psychosocial QOL, overall psychosocial QOL was impaired in nearly one in three patients. In spite of lower physical functioning in the young adults, overall psychosocial functioning was not worse in older patients. Young adults had lower social functioning than their healthy counterparts, but their emotional functioning was not significantly different from their peers, perhaps suggesting the majority had learned how to cope with their physical limitations. Diminished social functioning and problems with social cognition have been recognized in patients with

CHD[26] with perceived social support identified as a positive and potentially modifiable predictor of QOL in adolescents and adults with Fontan or other CHD.[24, 27–30]

Our data support a significant relationship between QOL and functional status related to both physical and psychosocial functioning. Both concepts, QOL or well-being and functioning, are now considered essential aspects of health, reflected in individual experience.[31] Functioning is generally thought to be more objective compared with the more subjective category of well-being or QOL.[31] Functional status is often affected by health status and may have a significant impact on QOL, at least with respect to physical functioning, though the relationship to psychosocial functioning has been less clear. In patients < 19 years of age, we found high intercorrelations between QOL as measured on the PedsQL and functional status related to physical and psychosocial functioning as measured utilizing the CHQ-87. In older subjects, there was also a strong correlation between QOL as measured on the PedsQL Physical Functioning scale and functional status related to Physical Functioning on the SF-36. The PedsQL Psychosocial Health Summary Score demonstrated medium to high intercorrelations with the SF-36 Aggregated Mental score, as reported in the healthy sample described by Varni and Limbers[16] with the SF-8.

QOL related to physical functioning was perceived as significantly impaired by approximately 50% of young adults with Fontan. In addition, our data demonstrate impaired psychosocial QOL in approximately one in three patients with Fontan, especially related to social functioning. Although psychosocial QOL is significantly related to physical functioning in these patients, it should be noted that physical and especially psychosocial QOL is often not related to clinical indicators of disease severity.[27, 32–34] Weak associations between functional status (CHQ -87 scores) and echocardiographic results, cardiac magnetic imaging results, and serum brain natriuretic peptide levels in patients post Fontan have been found[33, 35, 36]. Studies suggest that exercise prescription or rehabilitation and avoidance of unnecessary exercise restriction may improve exercise capacity and psychosocial QOL.[37, 38] Recent reports also suggest the potential for pulmonary vasodilators to improve exercise performance in children and young adults with Fontan circulation,[39, 40] however the impact on QOL has not been examined.

Finally, the data support the validity of the PedsQL across the age-span from 13–25 years. The measure distinguished between healthy individuals and patients with Fontan and was significantly correlated with similar functional health status domains in adolescents and young adults. Several studies have expanded the use of the PedsQL Young Adult to persons older than 25 years of age with and without chronic health conditions, supporting the reliability and validity in older patients,[41,42] emphasizing the value of the instrument especially for those transitioning from childhood to adulthood and for longitudinal assessment.

The strengths of this study include the multi-site, large sample size, self-reporting rather than proxy-reporting, and use of a single validated instrument with normative data across a wide age span. Study limitations are related to the cross-sectional design and potential survivor bias. Minimal concurrent objective data regarding disease severity precluded examinations of associations with clinical data.

Survivors of Fontan are at risk for significantly impaired QOL which may worsen with advancing age. Improvement in both QOL and functioning are important outcomes in young patients with chronic health conditions. The PedsQL allowed QOL assessment from pediatrics to young adulthood. Longitudinal studies are needed to further elucidate changes in QOL over time and to evaluate the impact of targeted interventions, including promotion of physical activity and social support, to improve outcomes.

Acknowledgments

Supported by the National Heart, Lung, and Blood Institute (HL068269, HL068270, HL068279, HL068281, HL068285, HL068292, HL068290, HL068288). This work is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health/ National Heart, Lung, and Blood Institute. J.V. holds the copyright and the trademark for the PedsQL™ and receives financial compensation from the Mapi Research Trust, which is a nonprofit research institute that charges distribution fees to for-profit companies that use the Pediatric Quality of Life Inventory™. He did not receive compensation for this project.

Abbreviations

CHD	congenital heart disease
CHQ	Child Health Questionnaire
PedsQL	Pediatric Quality of Life Inventory
QOL	quality of life
SF-36	Short-Form Health Survey

REFERENCES

1. World Health Organization. Geneva, Switzerland: World Health Organization; 1948. Constitution of the World Health Organization basic document.
2. Szabo, S. (WHOQOL Group). The World Health Organization Quality of Life (WHOQOL) assessment instrument. In: Spiker, B., editor. Quality of Life in Clinical Trials. Philadelphia, PA: Lippincott-Raven Publishers; 1996. p. 355-362.
3. Moons P, Van Deyk K, Budts W, De Geest S. Caliber of quality-of-life assessments in congenital heart disease: a plea for more conceptual and methodological rigor. Arch Pediatr Adolesc Med. 2004; 158:1062–1069. [PubMed: 15520344]
4. Idorn L, Jensen AS, Juul K, Overgaard D, Nielsen NP, Sorensen K, et al. Quality of life and cognitive function in Fontan patients, a population-based study. Int J Cardiol. 2013; 68:3230–3235. [PubMed: 23632112]
5. Lambert LM, Minich LL, Newburger JW, Lu M, Pemberton VL, McGrath EA, et al. Parent-versus child-reported functional health status after the Fontan procedure. Pediatrics. 2009; 124:e942–e949. [PubMed: 19841109]
6. Manlhiot C, Knezevich S, Radojewski E, Cullen-Dean G, Williams WG, McCrindle BW. Functional health status of adolescents after the Fontan procedure -- comparison with their siblings. Can J Cardiol. 2009; 25:e294–e300. [PubMed: 19746247]
7. McCrindle BW, Williams RV, Mitchell PD, Hsu DT, Paridon SM, Atz AM, et al. Relationship of patient and medical characteristics to health status in children and adolescents after the Fontan procedure. Circulation. 2006; 113:1123–1129. [PubMed: 16490823]
8. Overgaard D, Schrader AM, Lisby KH, King C, Christensen RF, Jensen HF, et al. Patient-reported outcomes in adult survivors with single-ventricle physiology. Cardiology. 2011; 120:36–42. [PubMed: 22094965]

9. Pike NA, Evangelista LS, Doering LV, Eastwood JA, Lewis AB, Child JS. Quality of life, health status, and depression: comparison between adolescents and adults after the Fontan procedure with healthy counterparts. J Cardiovasc Nurs. 2012; 27:539–546. [PubMed: 21912272]
10. Saliba Z, Butera G, Bonnet D, Bonhoeffer P, Villain E, Kachaner J, et al. Quality of life and perceived health status in surviving adults with univentricular heart. Heart. 2001; 86:69–73. [PubMed: 11410565]
11. Anderson PA, Sleeper LA, Mahony L, Colan SD, Atz AM, Breitbart RE, et al. Contemporary outcomes after the Fontan procedure: a Pediatric Heart Network multicenter study. J Am Coll Cardiol. 2008; 52:85–98. [PubMed: 18598886]
12. Atz AM, Zak V, Mahony L, Uzark K, Shrader P, Gallagher D, et al. Survival Data and Predictors of Functional Outcome an Average of 15 Years after the Fontan Procedure: The Pediatric Heart Network Fontan Cohort. Congenit Heart Dis. 2015; 10:e30–e42. [PubMed: 24934522]
13. Varni JW, Seid M, Kurtin PS. PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. Medical Care. 2001; 39:800–812. (2001). [PubMed: 11468499]
14. Uzark K, Jones K, Burwinkle TM, Varni JW. The Pediatric Quality of Life Inventory™ in children with heart disease. Prog Pediatr Cardiol. 2003; 18:141–149.
15. Uzark K, Jones K, Slusher J, Limbers CA, Burwinkle TM, Varni JW. Quality of life in children with heart disease as perceived by children and parents. Pediatrics. 2008; 121:e1060–e1067. [PubMed: 18450848]
16. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr. 2003; 3:329–341. [PubMed: 14616041]
17. Varni JW, Limbers CA. The PedsQL 4.0 Generic Core Scales Young Adult Version: feasibility, reliability and validity in a university student population. Journal of Health Psychology. 2009; 14:611–622. [PubMed: 19383661]
18. Varni JW, Limbers CA. The Pediatric Quality of Life Inventory: measuring pediatric health-related quality of life from the perspective of children and their parents. Pediatr Clin North Am. 2009; 56:843–863. [PubMed: 19660631]
19. Landgraf, J.; Abetz, L.; Ware, J. The Child Health Questionnaire (CHQ): a User's Manual. Boston, MA: The Health Institute, New England Medical Centre; 1996.
20. Ware, JE.; Kosinski, M.; Keller, SK. SF-36 Physical and Mental Health Summary Scales: A User's Manual. Boston, MA: The Health Institute; 1994.
21. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care. 1993; 31:247–263. [PubMed: 8450681]
22. Ware JE Jr. SF-36 health survey update. Spine (Phila Pa 1976). 2000; 25:3130–3139. [PubMed: 11124729]
23. van den Bosch AE, Roos-Hesselink JW, Van Domburg R, Bogers AJ, Simoons ML, Meijboom FJ. Long-term outcome and quality of life in adult patients after the Fontan operation. Am J Cardiol. 2004; 93:1141–1145. [PubMed: 15110207]
24. Pike NA, Evangelista LS, Doering LV, Koniak-Griffin D, Lewis AB, Child JS. Clinical profile of the adolescent/adult Fontan survivor. Congenit Heart Dis. 2011; 6:9–17. [PubMed: 21269408]
25. Jorngarden A, Wettergen L, von Essen L. Measuring health-related quality of life in adolescents and young adults: Swedish normative data for the SF-36 and the HADS, and the influence of age, gender, and method of administration. Health Qual Life Outcomes. 2006; 4:91. [PubMed: 17140436]
26. Bellinger DC. Are children with congenital cardiac malformations at increased risk of deficits in social cognition? Cardiol Young. 2008; 18:3–9. [PubMed: 18093362]
27. Kovacs AH, Saidi AS, Kuhl EA, Sears SF, Silversides C, Harrison JL, et al. Depression and anxiety in adult congenital heart disease: predictors and prevalence. Int J Cardiol. 2009; 137:158–164. [PubMed: 18707776]
28. Rose M, Kohler K, Kohler F, Sawitzky B, Fliege H, Klapp BF. Determinants of the quality of life of patients with congenital heart disease. Qual Life Res. 2005; 14:35–43. [PubMed: 15789939]

29. Silva AM, Vaz C, Areias ME, Vieira D, Proenca C, Viana V, et al. Quality of life of patients with congenital heart diseases. Cardiol Young. 2011; 21:670–676. [PubMed: 21729509]
30. Teixeira FM, Coelho RM, Proenca C, Silva AM, Vieira D, Vaz C, et al. Quality of life experienced by adolescents and young adults with congenital heart disease. Pediatr Cardiol. 2011; 32:1132–1138. [PubMed: 21710181]
31. Krasuska M, Riva S, Fava L, von Mackensen S, Bullinger M. Linking quality-of-life measures using the International Classification of Functioning, Disability and Health and the International Classification of Functioning, Disability and Health-Children and Youth Version in chronic health conditions: the example of young people with hemophilia. Am J Phys Med Rehabil. 2012; 91:S74–S83. [PubMed: 22193314]
32. Grigioni F, Carigi S, Grandi S, Potena L, Coccolo F, Bacchi-Reggiani L, et al. Distance between patients' subjective perceptions and objectively evaluated disease severity in chronic heart failure. Psychother Psychosom. 2003; 72:166–170. [PubMed: 12707484]
33. McCrindle BW, Zak V, Breitbart RE, Mahony L, Shrader P, Lai WW, et al. The relationship of patient medical and laboratory characteristics to changes in functional health status in children and adolescents after the Fontan procedure. Pediatr Cardiol. 2014; 35:632–640. [PubMed: 24264999]
34. Karsdorp PA, Everaerd W, Kindt M, Mulder BJ. Psychological and cognitive functioning in children and adolescents with congenital heart disease: a meta-analysis. J Pediatr Psychol. 2007; 32:527–541. [PubMed: 17182669]
35. Atz AM, Zak V, Breitbart RE, Colan SD, Pasquali SK, Hsu DT, et al. Factors associated with serum brain natriuretic peptide levels after the Fontan procedure. Congenit Heart Dis. 2011; 6:313–321. [PubMed: 21435188]
36. McCrindle BW, Zak V, Sleeper LA, Paridon SM, Colan SD, Geva T, et al. Laboratory measures of exercise capacity and ventricular characteristics and function are weakly associated with functional health status after Fontan procedure. Circulation. 2010; 121:34–42. [PubMed: 20026781]
37. Rhodes J, Curran TJ, Camil L, Rabideau N, Fulton DR, Gauthier NS, et al. Impact of cardiac rehabilitation on the exercise function of children with serious congenital heart disease. Pediatrics. 2005; 116:1339–1345. [PubMed: 16322156]
38. Takken T, Hulzebos HJ, Blank AC, Tacken MH, Helders PJ, Strengers JL. Exercise prescription for patients with a Fontan circulation: current evidence and future directions. Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation. 2007; 15:142–147.
39. Giardini A, Balducci A, Specchia S, Gargiulo G, Bonvicini M, Picchio FM. Effect of sildenafil on haemodynamic response to exercise and exercise capacity in Fontan patients. Eur Heart J. 2008; 29:1681–1687. [PubMed: 18534975]
40. Goldberg DJ, French B, McBride MG, Marino BS, Mirarchi N, Hanna BD, Wernovsky G, Paridon SM, Rychik J. Impact of oral sildenafil on exercise performance in children and young adults after the fontan operation: a randomized, double-blind, placebo-controlled, crossover trial. Circulation. 2011; 123:1185–1193. [PubMed: 21382896]
41. Limperg PF, Haverman L, van Oers HA, van Rossum MA, Maurice-Stam H, Grootenhuis MA. Health related quality of life in Dutch young adults: psychometric properties of the PedsQL generic core scales young adult version. Health Qual Life Outcomes. 2014; 12:1–9. [PubMed: 24382363]
42. Robert RS, Paxton RJ, Palla SL, Yang G, Askins MA, Joy SE, et al. Feasibility, reliability, and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Cancer Module, and Multidimensional Fatigue Scale in long-term adult survivors of pediatric cancer. Pediatr Blood Cancer. 2012; 59:703–707. [PubMed: 22302778]

Appendix

Additional Pediatric Heart Network Investigators includes (*no longer at the institution listed):

National Heart, Lung, and Blood Institute--Gail Pearson, MD, ScD, Mario Stylianou, PhD, Jonathan Kaltman, MD, Victoria Pemberton, RNC, MS

Data Coordinating Center--New England Research Institutes: Lynn Sleeper* (ScD), Steven Colan, MD, Dianne Gallagher, MS*, Victor Zak, PhD, Peter Shrader,* MA

Protocol Chair--Lynn Mahony, MD (University of Texas Southwestern Medical Center, Dallas, TX)

Clinical Site Investigators--Boston Children's Hospital (Boston, MA): Jane Newburger, MD, MPH (Principal Investigator), Roger Breitbart, MD, Carolyn Dunbar-Masterson, RN, MS, Jill Handisides, BSN, Lisa-Jean Buckley, Bethany Trainor, RN, BSN*; Children's Hospital of New York (New York, NY): Wyman W. Lai, MD (Principal Investigator), Rosalind Korsin, RN; Children's Hospital of Philadelphia (Philadelphia, PA): Robert Shaddy, MD, J William Gaynor, MD, Stephen M Paridon, MD(Principal Investigators), Kaitlyn Daniels, BSN, Tonia Morrison, MSM, CCRC, Nicole Mirarchi, RN*; Duke University (Durham, NC): Jennifer S. Li, MD (Principal Investigator), Piers Barker, MD, Mingfen Xu, MSN; Medical University of South Carolina, J. Philip Saul, MD *(Principal Investigator), Andrew M. Atz, MD, Patricia Infinger, CCRP, Ann Harvey Frampton, BS*; Primary Children's Hospital (Salt Lake City, UT): LuAnn Minich, MD (Principal Investigator), Richard Williams, MD, Linda Lambert MSN, cFNP; University of Toronto, Hospital for Sick Children (Toronto, Ontario, Canada): Brian McCrindle, MD (Principal Investigator), Elizabeth Radojewski, RN, Svetlana Khaikin, RN, MPH, Patricia Walter; RN, BScN. Cincinnati Children's Hospital Medical Center, (Cincinnati, OH): Bradley Marino, MD*, Karen Uzark, PhD, CPNP*

Protocol Review Committee--Michael Artman, MD (New York University Medical Center, New York, NY); Timothy Feltes, MD (Nationwide Childrens Hospital, Columbus, OH); Julie Johnson, PharmD* (University of Florida, Gainesville, FL); Jeffrey Krischer, PhD (University of South Florida, Tampa, FL); G. Paul Matherne, MD (University of Virginia, Charlottesville, VA); Nakela Cook, MD, MPH* (National Heart, Lung, and Blood Institute, Bethesda, MD).

Data and Safety Monitoring Board--John Kugler, MD, (Children's Hospital, Omaha, NE); Chair; David Gordon, MD, PhD (National Heart, Lung, and Blood Institute, Bethesda, MD); David J. Driscoll, MD (Mayo Clinic, Rochester, MN); Mark Galantowicz, MD (Nationwide Children's Hospital, Columbus, OH); Sally A. Hunsberger, PhD (National Insitutes of Health, Bethesda, MD); Holly Taylor, PhD (Bloomberg School of Public Health, Baltimore, MD); Thomas J. Knight, JD (Anniston, AL); Catherine L. Webb, MD (University of Michigan, Ann Arbor, MI).

J Pediatr. Author manuscript; available in PMC 2017 March 01.

Table 1

Patient characteristics

Variable	Statistic	All subjects	<19 years old	≥19 years old	p*
Demographics	**N**	**408**	**255**	**153**	
Age at Fontan 2 enrollment, years	Mean±SD	18.5 ± 3.4	16.2 ± 1.6	22.3 ± 1.9	<0.001
	Median (IQR)	17.9 (15.6, 21.2)	16.1 (14.8, 17.7)	22.3 (20.6, 23.8)	<0.001
Male, %	N (%)	237 (58%)	153 (60%)	84 (55%)	0.35
Race	N (%)				0.003
White		329 (81%)	193 (76%)	136 (89%)	
Black		40 (10%)	30 (12%)	10 (7%)	
Asian		11 (3%)	11 (4%)	0 (0%)	
Other		26 (6%)	19 (8%)	7 (5%)	
Hispanic, %yes	N (%)	24 (6%)	16 (7%)	8 (5%)	0.67
Ventricular morphology	N (%)				0.07
Left		206 (50%)	121 (47%)	85 (56%)	
Right		132 (32%)	93 (36%)	39 (25%)	
Mixed		70 (17%)	41 (16%)	29 (19%)	
Fontan surgery type	N (%)				<0.001
Atriopulmonary Connection		54 (13%)	11 (4%)	43 (28%)	
TCPC Intracardiac Lateral Tunnel		239 (59%)	151 (59%)	88 (58%)	
TCPC Extracardiac Conduit		104 (25%)	89 (35%)	15 (10%)	
Other		11 (3%)	4 (2%)	7 (5%)	
Age at most recent Fontan, years	Mean±SD	3.8 ± 3.3	3.1 ± 1.7	5.1 ± 4.6	<0.001
	Median (IQR)	2.9 (2.1, 4.3)	2.7 (2.1, 3.7)	3.5 (2.4, 5.5)	<0.001
Maternal education level†	N (%)				0.94
Some high school or less		21 (6%)	15 (7%)	6 (5%)	
High school graduate or GED		76 (23%)	46 (23%)	30 (23%)	
Vocational school, some college or 2 year degree		105 (32%)	58 (28%)	47 (36%)	

Variable	Statistic	All subjects	<19 years old	≥19 years old	P*
4 year college graduate		88 (26%)	59 (29%)	29 (22%)	
Graduate degree		43 (13%)	26 (13%)	17 (13%)	
Household income†	N (%)				0.65
< $20,000		42 (12%)	26 (12%)	16 (12%)	
$20,000 – 39,999		59 (17%)	38 (18%)	21 (15%)	
$40,000 – 59,999		51 (14%)	35 (16%)	16 (12%)	
$60,000 – 79,999		53 (15%)	28 (13%)	25 (18%)	
$80,000 – 99,999		57 (16%)	33 (15%)	24 (18%)	
> $100,000		91 (26%)	57 (26%)	34 (25%)	

*P value comparing subjects <19 years old to those ≥19. P is from Student's t-test for means, Wilcoxon ranked-sum test for medians, or Fisher Exact Test for frequencies.

Table 2

Comparison of PedsQL scores in Patients with Fontan and Healthy Controls

All subjects

	Fontan 2 (N=408)		Controls (N=342)		
PedsQL Score	**n**	**Mean (SE)**	**n**	**Mean (SE)**	**P**
4.0 Generic Core Scales					
Physical functioning	406	75.0 (0.8)	342	89.3 (0.8)	<0.001
Emotional functioning	406	74.4 (0.9)	342	78.1 (1.0)	<0.001
Social functioning	407	78.5 (0.9)	342	89.8 (0.9)	<0.001
School functioning	405	70.8 (0.9)	342	78.4 (1.0)	<0.001
Psychosocial heath summary	407	74.5 (0.8)	342	82.1 (0.8)	<0.001
Total score	408	74.7 (0.7)	342	84.6 (0.8)	<0.001

Subjects <19 years old

	Fontan 2 (N=255)		Controls (N=242)		
PedsQL Score	**n**	**Mean (SE)**	**n**	**Mean (SE)**	**P**
4.0 Generic Core Scales					
Physical functioning	254	76.3 (0.9)	242	90.6 (1.0)	<0.001
Emotional functioning	254	75.2 (1.2)	242	82.8 (1.2)	<0.001
Social functioning	254	78.0 (1.1)	242	92.2 (1.1)	<0.001
School functioning	254	70.5 (1.1)	242	82.0 (1.2)	<0.001
Psychosocial heath summary	254	74.6 (0.9)	242	85.7 (1.0)	<0.001
Total score	255	75.2 (0.9)	242	87.4 (0.9)	<0.001

Subjects ≥19 years old

	Fontan 2 (N=153)		Controls (N=100)		
PedsQL Score	**n**	**Mean (SE)**	**n**	**Mean (SE)**	**P**
4.0 Generic Core Scales					
Physical functioning	152	72.1 (1.3)	100	87.4 (1.6)	<0.001
Emotional functioning	152	72.1 (1.5)	100	68.2 (1.9)	0.16
Social functioning	153	78.1 (1.5)	100	86.1 (1.8)	<0.001

School/work functioning	151	70.4 (1.6)	100	71.3 (2.0)	0.66
Psychosocial heath summary	153	73.4 (1.3)	100	75.2 (1.6)	0.28
Total score	153	72.9 (1.2)	100	79.4 (1.5)	<0.001

Adjusted mean, standard error, and P value are from age-, gender-, and race-adjusted linear regression models.

Table 3

PedsQL Scores in Impaired* Range among Fontan subjects

All subjects			
Variable	**N**	**Frequency Impaired (%)**	**95% CI for Frequency**
Physical functioning	406	181 (45%)	(40% – 50%)
Emotional functioning	406	81 (20%)	(16% – 24%)
Social functioning	407	109 (27%)	(23% – 31%)
School/work functioning	405	124 (31%)	(26% – 35%)
Psychosocial health summary	407	122 (30%)	(26% – 35%)
Total score	408	152 (37%)	(33% – 42%)
Subjects <19 years old			
Variable	**N**	**Frequency Impaired (%)**	**95% CI for Frequency**
Physical functioning	254	103 (41%)	(34% – 47%)
Emotional functioning	254	51 (20%)	(15% – 26%)
Social functioning	254	65 (26%)	(20% – 31%)
School functioning	254	90 (35%)	(30% – 42%)
Psychosocial health summary	254	77 (30%)	(25% – 36%)
Total score	255	88 (35%)	(29% – 41%)
Subjects ≥19 years old			
Variable	**N**	**Frequency Impaired (%)**	**95% CI for Frequency**
Physical functioning	152	78 (51%)	(43% – 60%)
Emotional functioning	152	30 (20%)	(14% – 27%)
Social functioning	153	44 (29%)	(22% – 37%)
School/work functioning	151	34 (23%)	(16% – 30%)
Psychosocial health summary	153	45 (29%)	(22% – 37%)
Total score	153	64 (42%)	(34% – 50%)

* > 1 SD (standard deviation) demonstrates the scores that fall 1 SD below the population sample mean and represents an at-risk status for impaired health-related quality of life.

Table 4

Tests of linear association of PedsQL Scores with patient age, sex, and SES

		All subjects			Subjects <19 years old			Subjects ≥19 years old		
PedsQL Scale	**Variable**	**N**	**Slope (SE)**	**P**	**N**	**Slope (SE)**	**P**	**N**	**Slope (SE)**	**P**
Physical Functioning	Age at completion of PedsQL, yrs	406	−0.76 (0.26)	0.004	254	0.09 (0.66)	0.90	152	−2.00 (0.84)	0.02
	Sex, male	406	6.9 (1.8)	<0.001	254	5.1 (2.1)	0.02	152	9.2 (3.2)	0.005
	Household income	351		0.24	216		0.62	135		0.08
Emotional Functioning	Age at completion of PedsQL, yrs	406	−0.64 (0.30)	0.03	254	−0.84 (0.78)	0.28	152	−1.43 (0.91)	0.12
	Sex, male	406	6.2 (2.0)	0.002	254	5.6 (2.5)	0.03	152	6.9 (3.5)	0.048
	Household income	351		0.25	216		0.91	135		0.11
	Maternal education level	332		0.16	204		0.39	128		0.37
Social Functioning	Household income	352		0.26	216		0.47	136		0.08
School/Work Functioning	Household income	350		0.007	216		0.23	134		0.02
	Maternal education level	330		0.008	203		0.09	127		0.06
Psychosocial Health Summary	Sex, male	407	3.2 (1.7)	0.06	254	2.8 (2.1)	0.18	153	3.8 (2.9)	0.20
	Household income	352		0.04	216		0.80	136		0.006
	Maternal education level	333		0.06	204		0.24	129		0.36
Total Generic Score	Age at completion of PedsQL, yrs	408	−0.44 (0.23)	0.06	255	−0.12 (0.60)	0.84	153	−1.11 (0.74)	0.14
	Sex, male	408	4.5 (1.6)	0.005	255	3.8 (1.9)	0.053	153	5.4 (2.8)	0.06
	Household income	353		0.07	217		0.81	136		0.01
	Maternal education level	333		0.13	204		0.43	129		0.37

SES – socioeconomic status