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Relationship of Patient and Medical Characteristics to Health Status in Children and Adolescents After the Fontan Procedure

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Background—After the Fontan procedure, patients are at risk for suboptimal health status related to their complex healthcare experience, physiological limitations, medical complications, and guarded long-term prognosis.

Methods and Results—In the Pediatric Heart Network cross-sectional study of Fontan survivors 6 to 18 years of age, parents completed the Child Health Questionnaire, and scores were related in multivariable analysis to patient and medical characteristics obtained from medical record review. For 537 patients (mean age at study, 11.9 years; 60% male) with a median age at Fontan of 2.8 years (range, 0.7 to 14.6 years), parent-reported patient morbidities included deficits in vision in 33%, speech in 27%, and hearing in 7%, as well as problems with attention in 46%, learning in 43%, development in 24%, behavior in 23%, anxiety in 17%, and depression in 8%. Child Health Questionnaire summary scores were significantly lower than the US population sample for Physical Functioning (mean Z score, -0.47 ± 1.19 ; $P < 0.001$) and Psychosocial Functioning (-0.28 ± 1.08 ; $P < 0.001$). Parent-reported medical conditions and long-term and current medical problems explained the greatest amount of variation in the Physical Functioning scores. Parent-reported patient conditions, including behavior, learning, anxiety, and attention problems and depression, explained the greatest amount of variation in the Psychosocial Functioning scores. Lower family income had a negative impact on both Physical and Psychosocial Functioning.

Conclusions—There are deficits in health status in children and adolescents after the Fontan procedure. Strategies to address this problem might emphasize coordinated and effective prevention, detection, and management of noncardiac and psychosocial conditions, as well as specific targeting of patients from low-income households. (*Circulation*. 2006; 113:1123-1129.)

Key Words: follow-up studies ■ Fontan procedure ■ heart defects, congenital ■ health status ■ quality of life

As mortality related to congenital heart disease continues to decline, the focus of clinical care has turned to morbidity and quality of life. Health status has various domains, related primarily to physical functioning and psychosocial aspects.¹ It may be affected by many factors, including medical history, current medical morbidity, perceptions, reactions and adaptations to health-related problems, available resources, and opportunities to deal with those problems, as well as the patient's psychosocial milieu and support systems.²

poor health status. These patients are subjected to a complex and prolonged medical experience. They have diminished exercise tolerance imposed by their cardiovascular physiology.^{3,4} Moreover, Fontan patients may have important and debilitating morbidities⁵ and have a guarded long-term prognosis. We therefore sought to characterize health status and its sociodemographic and medical determinants in this high-risk population.

Clinical Perspective p 1129

Patients with functional single ventricle who have undergone the Fontan procedure may be especially predisposed to

Methods

The Fontan Cross-Sectional Study was performed by the Pediatric Heart Network. The Pediatric Heart Network, which consists of 7 pediatric cardiac centers in the United States and Canada, a data

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The online-only Data Supplement can be found at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.576660/DC1>.

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coordinating center at the New England Research Institutes, and the Pediatric Heart Network chair, performs multicenter clinical studies with funding from the National Heart, Lung, and Blood Institute of the National Institutes of Health. The primary aim of the Fontan Cross-Sectional Study was to assess the correlation between measures of health status, ventricular function, and exercise performance in children and adolescents who have survived a Fontan procedure. The present analysis and report focus only on the data collected from the medical record review and the parent report health status questionnaire. All 7 centers obtained local Institutional Review Board or Ethics Committee approval before initiating the study, and written informed consent was obtained for all subjects from either a parent or a legal guardian or from the subject if of legal age. Subject assent was also obtained per local guidelines.

Study Subjects

Eligible patients were identified by a preliminary medical record review of all children who had undergone a Fontan procedure and were currently followed up at 1 of the 7 centers. Study subjects were eligible if they were 6 to 18 years of age at the time of enrollment; had undergone a Fontan procedure at least 6 months before initial study testing; and agreed to have an echocardiogram, to complete a parent report health status questionnaire, and to have blood testing within 3 months of enrollment at one of the study centers. Exclusion criteria included the presence of a noncardiac medical or psychiatric disorder that would prevent successful completion of planned study testing or would invalidate the results of study testing. Additional criteria included ongoing or planned participation in another research protocol that would conflict with the present study, lack of reading fluency by the primary caregiver in English or Spanish, and pregnancy at the time of enrollment or pregnancy planned before the completion of study testing.

Medical Record Review

For enrolled study subjects, a detailed medical record review was performed through the use of standardized forms to abstract data on patient demographics, underlying cardiac anatomy, pre-Fontan characteristics (interim surgical and interventional catheterization procedures, complications, pre-Fontan clinical status), Fontan procedure characteristics (type of Fontan connection, fenestration, concomitant procedures, immediate complications, hospital course, and discharge status), and outcomes during follow-up after the Fontan procedure, including the most recent clinical assessment and testing.

Health Status Questionnaire

The study used the Child Health Questionnaire (CHQ) Parent Report Form (CHQ-PF50) as a generic measure of health status completed by the parent.⁶ The Parent Report CHQ, which measures the physical and psychosocial (eg, emotional, behavioral, and social) well-being of children 5 to 18 years of age, was to have been completed by a parent for all enrolled study subjects. The Parent Report CHQ measures components of physical and psychosocial functioning in 12 categories (subscales). Domains that contribute most heavily to the Physical Functioning summary score include physical functioning limitations, physical limitations on schoolwork or activities with friends, bodily pain, and general health perceptions. Domains that contribute most heavily to the Psychosocial Functioning summary score include mental health, limitations on schoolwork or activities from emotional or behavioral problems, general behavior, and self-esteem. Domains concerning the impact of the child's health on the parents' worries, concerns, and time; family activities; and family cohesion contribute to both summary scores. In addition, as part of the Parent Report CHQ that is not scored, parents are asked to indicate on a checklist if they had ever been told by a teacher, school official, doctor, nurse, or other health professional that their child had any of a list of noncardiac health conditions.

Data Analysis

Data are described as frequencies, medians with ranges, and means with standard deviations as appropriate. When data are missing, the

number of available values is given. Parent Report CHQ scores were converted to Z scores on the basis of published normative data and tested for deviation from normal with single sample *t* tests.^{6,7} CHQ summary scores of Physical and Psychosocial Functioning were related to patient and medical history variables using *t* tests, ANOVA, and linear regression analysis. Variables that showed a significant bivariable relationship ($P < 0.05$) then formed the variable set for multivariable analysis. For the purposes of multivariable analyses, missing values for predictor variables were informatively imputed and replaced with the mean of all nonmissing values. No variable was missing $> 5\%$ of values. Patient and medical history variables were grouped and entered into separate multiple linear regression analysis for each of the CHQ summary scores of Physical Functioning and Psychosocial Functioning. The overall R^2 for each regression was noted to determine the amount of variation in scores explained by each group of variables. Separate stepwise multivariable linear regression analyses were then performed for each of the CHQ summary scores of Physical and Psychosocial Functioning. Bootstrap bagging (repeated sampling and stepwise multivariable analysis of the main data set) and cluster analysis were used to guide and indicate reliability of variable selection for inclusion in the final multivariable models and to provide an assessment of reliability of variable selection. Given the large number of variables being tested, only those variables that were significant with a value of $P < 0.05$ in the final models are reported to minimize the effects of multiple comparisons. In addition, the adjusted effects of the type of Fontan connection and study site were explored in each final model. All analyses were performed with SAS/STAT software, version 9.1 of the SAS System for Windows (SAS Institute Inc).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

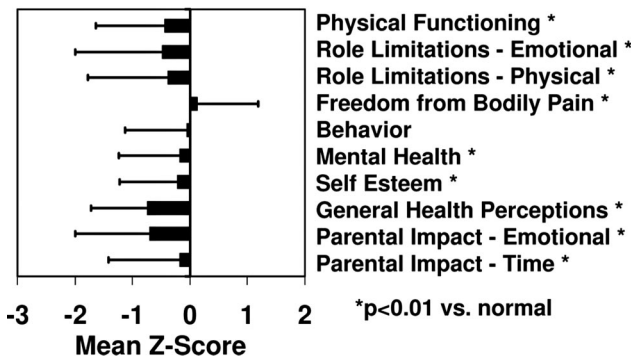
Study Participation

The records of 1078 children who had undergone a Fontan procedure were screened. Of the 831 (77%) judged potentially eligible for the study, only 644 (60%) were found to be fully eligible after being contacted. The consent rate was 85%, and 546 children were enrolled with family consent. Different proportions of enrolled patients completed each of the study tests, and 9 parents did not complete the CHQ. The present study includes 537 enrolled patients who had medical record reviews and whose parents completed the Parent Report CHQ.

Patient and Clinical Characteristics

The table found in the online Data Supplement summarizes the frequencies and distributions of sociodemographic and medical history. Medical history before the Fontan procedure was complex; ≥ 2 cardiac surgeries were performed in 80% of subjects, and at least 1 interventional cardiac catheterization was done in 47%. Postoperative complications after the Fontan procedure were frequent; 40% of subjects had a postoperative length of hospital stay of ≥ 2 weeks, and 95% were discharged on at least 1 medication (mean number of medications, 3.7). During follow-up from the Fontan procedure to the study date, 23% of patients had at least 1 cardiac surgery, and 48% had at least 1 interventional cardiac catheterization, with 23% having at least 1 Fontan-related complication. At the time of enrollment in the present study, most patients (89%) were taking at least 1 daily medication, and the mean number of current medications was 2.4.

CHQ Domain



Domain scores from the Parent Report CHQ. Width of the bars represents the mean; error bars represent 1 SD (shown in only 1 direction for simplicity, although all statistical testing was 2 sided).

Health Status From the Parent Report CHQ

The Z scores of the domain and summary scores are presented in the Figure. Summary scores were significantly lower than the US population sample for both Physical Functioning (mean Z score, -0.47 ± 1.19 ; $P < 0.0001$) and Psychosocial Functioning (mean Z score, -0.28 ± 1.08 ; $P < 0.0001$). For all domains, scores of Fontan patients were significantly worse than those of the US population sample, except for the domains of Freedom From Bodily Pain, which was significantly better, and Behavior, which was not significantly different.

Frequencies of responses from the questions about noncardiac health conditions from the Parent Report CHQ, together with reported frequencies from a US population sample,⁶ are given in Table 1. The frequency of all conditions was higher in the

Fontan patients than the US population sample, except for problems with allergies.

Variable Groups and Their Relation to CHQ Summary Scores

Individual multivariable regressions were performed for both the CHQ Physical and Psychosocial Functioning summary scores for groups of variables as defined in the table in the Data Supplement. In addition, the bivariable relationship between each variable and each summary score is also given in the Data Supplement table. The R^2 , or proportion of variance in the scores explained by each group of variables, is shown in Table 2. The greatest amount of variation in the Physical Functioning summary score was explained by parent-reported noncardiac conditions in the patient and long-term and current medical problems noted in the medical record. For Psychosocial Functioning summary scores, the parent-reported noncardiac conditions in the patient predominated. Nonmedical patient characteristics had a small influence on both Physical and Psychosocial Functioning summary scores, whereas pre-Fontan procedure status and Fontan procedure characteristics had a small influence on Physical Functioning summary scores only.

Independent Factors Associated With CHQ Summary Scores

Multivariable regression modeling was performed for the CHQ summary scores, with the reliability of variable selection assessed by bootstrap bagging. For Physical Functioning summary scores, 11 variables were independently significant, with an overall model R^2 of 0.40, or 40% of the variation in scores explained. The medical variables associated with poorer Physical Functioning summary scores are shown in Table 3. These

TABLE 1. Patient Noncardiac Health Problems Reported by the Caregiver Completing the Parent Report CHQ

Condition	n	Value (%)	Reference, %†	Relationship to (P)*	
				Physical Functioning Summary Score	Psychosocial Functioning Summary Score
Asthma	524	76 (15)	12	<0.001	0.002
Non-asthma respiratory problems	532	58 (11)	4	<0.001	0.005
Allergies	529	87 (16)	18	<0.001	0.15
Orthopedic problems	530	60 (11)	3	<0.001	0.49
Sleep problems	530	52 (10)	2	<0.001	<0.001
Vision problems	535	178 (33)	20	0.05	0.18
Speech problems	534	142 (27)	12	<0.001	<0.001
Deafness	533	37 (7)	4	0.60	0.05
Problems with anxiety	530	89 (17)	5	<0.001	<0.001
Depression	533	45 (8)	5	0.01	<0.001
Developmental delay	535	129 (24)	3	<0.001	<0.001
Problems with attention	533	246 (46)	19	0.01	<0.001
Learning problems	534	225 (42)	12	<0.001	<0.001
Behavior problems	533	123 (23)	15	0.007	<0.001

*Probability value from linear regression of physical and psychosocial summary scores, respectively, on each variable by itself. The direction of all significant associations was such that the presence of the health condition was associated with lower (worse) Summary Scores.

†From Reference 6.

TABLE 2. Proportion of Variance (Model R^2) in Summary Scores Explained in Multivariable Analysis by Various Groups of Variables

Group of Variables†	Relationship to (Model R^2)*	
	Physical Functioning Summary Score	Psychosocial Functioning Summary Score
Nonmedical patient, caregiver, and family factors	0.12	0.09
Underlying cardiovascular anatomy	0.01	0.03
Pre-Fontan status and risk factors	0.07	0.02
Fontan procedure factors	0.07	0.03
Immediate post-Fontan medications	0.02	0.01
Long-term outcomes, procedures, and current medications	0.17	0.04
Caregiver-reported current medical conditions for the patient	0.26	0.33

*From multiple linear regression analysis.

†For variables included in each group, see Data Supplement Table.

included a greater patient weight at Fontan procedure, fenestration not performed at Fontan procedure, other surgical procedures performed at Fontan procedure, arrhythmias occurring during follow-up, and a greater number of current medications at study enrollment. Additional noncardiac variables that were independently significant in the model included the noncardiac medical conditions of asthma, nonasthma respiratory problems, orthopedic problems, and learning problems. In addition, a parent not working because of the patient's health and lower family income were significantly associated with lower scores. After these significant factors were controlled for, there was no significant relationship with type of Fontan connection ($P=0.81$) or study site ($P=0.63$).

A similar multivariable regression model determined independent factors significantly associated with poorer Psychosocial Functioning summary scores (Table 4). The overall R^2 for this model was 0.34, and significant independent factors included the presence of behavior and learning problems, anxiety and attention problems, depression, and lower family income. After these significant factors were controlled for, there was no significant relationship with type of Fontan connection (trend toward higher

scores with atriopulmonary and intracardiac lateral tunnel connections, $P=0.06$) or with study site ($P=0.11$).

Discussion

Summary

We noted that child and adolescent survivors of the Fontan procedure had important deficits in many domains of health status, primarily in Physical Functioning domains. The presence of noncardiac medical problems had the greatest impact on physical functioning health status scores, whereas few cardiac-specific factors were associated. For Psychosocial Functioning health status scores, problems with learning, behavior, attention, anxiety, and depression significantly lowered scores and were more prevalent in the Fontan patients than in a US population sample. Lower family income had a negative impact on both physical and psychosocial functioning.

Quality of Life

Quality of life is difficult to conceptualize, particularly in children, and has been defined as follows: "Rather than being a description of patients' health status, quality of life is a reflection

TABLE 3. Independent Factors Associated With Lower CHQ Physical Functioning Summary Scores*

Variable	Estimate (SE)	<i>P</i>	Reliability, %†
Higher patient weight at Fontan	-0.2 (0.1)	0.01	61
Fenestration not performed at Fontan	-3.3 (0.9)	<0.001	74
Other surgical procedures performed at Fontan	-3.1 (0.8)	<0.001	86
Arrhythmias occurring during follow-up	-3.0 (1.1)	0.008	60
Higher number of current medications	-1.0 (0.3)	0.002	72
Current presence of			
Asthma	-4.2 (1.2)	<0.001	82
Nonasthma respiratory problems	-9.9 (1.5)	<0.001	100
Orthopedic problems	-6.5 (1.4)	<0.001	91
Learning problems	-4.1 (0.9)	<0.001	79
Parent not working because of patient's health	-10.1 (1.8)	<0.001	96
Lower family income	-0.6 (0.3)	0.04	56

*From multivariable general linear regression modeling; overall model $R^2=0.40$. Missing values for Physical Functioning Summary Scores were not imputed; therefore, analysis relates to 511 patients.

†From bootstrap bagging analysis.

TABLE 4. Independent Factors Associated With Lower CHQ Psychosocial Functioning Summary Scores*

Variable	Estimate (SE)	P	Reliability, %†
Current presence of			
Behavior problems	-6.3 (1.1)	<0.001	100
Learning problems	-4.2 (1.0)	<0.001	98
Problems with anxiety	-4.0 (1.2)	0.003	82
Problems with attention	-3.3 (1.0)	0.001	80
Problems with depression	-4.2 (1.6)	0.007	79
Lower family income	-0.9 (0.2)	<0.001	86

*From multivariable general linear regression modeling; overall model R²=0.34. Missing values for Psychosocial Functioning Summary Scores were not imputed; therefore, analysis relates to 511 patients.

†From bootstrap bagging analysis.

of the way that patients perceive and react to their health status and to other, nonmedical aspects of their lives.”⁸ Strict adherence to this definition precludes quantitative assessment and application in larger population-based studies because assessment must necessarily include personal and qualitative evaluation. No criterion standard for the assessment of quality of life currently exists. In addition, controversy exists as to terminology, definition, conceptualization, and measurement. This makes any assessment of validity problematic; if one cannot agree on the concept being measured, then it cannot be certain that the designed assessment tool is truly measuring that concept. What we believe we have measured using the CHQ is the magnitude of perceived overall functioning as affected by health-related issues, which we have equated with the term health status.

Assessment of Health Status

The assessment of health status in children has only recently gained attention and importance, with increasing understanding of its conceptualization and measurement.^{1,9-13} Generic measures are useful for comparing patient groups with each other and with normal subjects, and the CHQ has been used extensively for this purpose.⁶ Disease-specific measures identify areas of specific concern and may be of greater use in assessing changes in health status over time and in response to interventions; these have only recently been considered for congenital

heart disease.¹⁴ Furthermore, parents and their children may differ in assessments of the child’s health status.¹⁵⁻¹⁷ In this study of children 6 to 18 years of age, the Parent Report CHQ was used because the Child Report CHQ is not applicable to children <10 years of age.

Issues in Fontan Patients

The overall CHQ summary scores in our population were significantly below normal. They were also below those reported in other cardiac patients and pediatric chronic disease patients, except for children and adolescents with automatic implantable cardiofibrillators (Table 5).¹⁸⁻²⁴ The reasons why these patients scored so poorly are unclear, although the high prevalence of associated medical problems may have been a contributing factor. Neurodevelopmental outcomes are a common concern in Fontan patients, particularly for those with underlying hypoplastic left heart syndrome, and may contribute to poor health status.^{25,26} Wernovsky et al²⁷ reported results of IQ and achievement testing in a cohort of Fontan patients ranging from 3 to 41 years of age. They noted normal cognitive outcome and academic function in the majority, but the average performance was below normal, particularly for those with underlying hypoplastic left heart syndrome and use of circulatory arrest for procedures before Fontan. In contrast, Goldberg et al²⁵ noted lower cognitive scores for the those children who had the Fontan procedure and who had underlying hypoplastic left heart syndrome, but they also noted that overall scores were within the normal range. Difficulties in academic ability and achievement among children and adolescents with congenital heart disease have been associated with lower psychosocial functioning. In a cohort of 8-year-old children who had neonatal arterial switch operation for transposition of the great arteries, worse psychosocial functioning scores were associated with lower full-scale, verbal, and performance IQ scores, as well as worse academic achievement.¹⁹

Factors Affecting Health Status

Although as yet incompletely studied in children, the determinants of diminished health status have previously been studied in adults with congenital heart disease.²⁸⁻³¹ As shown by van den Bosch et al,³² adult patients who had undergone a Fontan

TABLE 5. Studies of Health Status in Children and Adolescents Using the Parent Report CHQ Questionnaire

Report	Study Subjects	Physical Functioning Summary Score	Psychosocial Functioning Summary Score
Landgraf et al ⁶	Healthy US subjects	53.0	51.2
Present study	Fontan patients	45.3	47.2
Walker et al ¹⁸	Cardiology outpatients	51.5	52.3
Dunbar-Masterson et al ¹⁹	ASO for TGA patients	54.0	49.7
Hirshfeld et al ²⁰	Transplant patients	50.6	51.5
DeMaso et al ²¹	Adolescents with AICDs	39.1	46.2
Wake et al ²²	Diabetic adolescents	48.3	47.6
Friedlander et al ²³	Overweight children	56.3	51.3
Klassen et al ²⁴	ADHD children	56.6	38.2

ASO indicates arterial switch operation; TGA, transposition of the great arteries; AICDs, automatic implantable cardiofibrillators; and ADHD, attention deficit hyperactivity disorder. Scores represent mean or median.

procedure scored significantly lower than normal in the domains of physical functioning, mental health, and general health perception. However, Saliba and colleagues³³ showed that in adult patients with univentricular hearts, those <23 years of age scored better than older patients for health and dysfunction measures. Rose et al² showed that the physical component of general health status was largely related to the level of cardiopulmonary functioning, whereas psychosocial aspects were more related to depressive symptomatology and adequacy of social support. A qualitative study by Claessens et al³⁴ suggested that “feeling different” was a central theme related to psychosocial concerns and was a key factor in the perceived impact of the disease on the patient’s daily life.

Congenital heart disease can also adversely affect the quality of life of the parents. Lawoko et al³⁵ reported lower quality of life, particularly among mothers, for parents of children with congenital heart disease related to feelings of distress and hopelessness and to financial concerns. Social support by the parents is important. MacPhee et al³⁶ showed that quality-of-life scores for adolescents with inflammatory bowel disease depended more on their parent’s coping styles than their own. Similarly, DeMaso et al³⁷ found that maternal perceptions were potent predictors of adjustment in school-age children with pediatric heart disease, suggesting that parental interactions are more significant predictors of emotional adjustment than medical severity.

Study Limitations

The results of this study must be viewed in light of some limitations. Because we cannot exclude an important subject selection bias, we therefore caution that the results are interpretable only for those subjects who met our defined entry criteria, most importantly those subjects followed up at major pediatric cardiac centers whose parents speak English and/or Spanish and have not had recent surgery. We would hypothesize that our entry criteria may have favored selection of subjects with better health status. The medical history data were collected from retrospective medical record review and must be viewed in light of the limitations of this data source. The use of parent or proxy report to assess health status with the CHQ has its limitations, given that parents tend to assess their children as functioning a lower level than the patients themselves. However, use of the Child Report CHQ was precluded, given the age range included, the fact that differences between parent and patient perceptions tend to quantitative rather than qualitative, and the fact that the study primarily sought to determine associations. Given the large number of variables tested, there is an issue of multiple comparisons. For that reason, only the results of multivariable associations, not bivariable analyses, are reported. In addition, the probability values for identified independent factors are, in general, highly significant, and thus might be expected to be robust. We also used bootstrapping to assess variable selection reliability, giving further evidence with regard to the robustness of the final models. We cannot confidently conclude that the Fontan patients are doing more poorly than normal because we did not simultaneously study a cohort of normal control children and because the use of the published normal data may not be relevant to our population. In addition, we do not know the clinical meaning of the magnitude of the observed deviations

from normal. We would be reluctant to conclude that the patients are doing well, given that the scores observed in our study are lower than those observed in other patients with chronic conditions (Table 5).

Study Implications

We conclude that there are deficits in health status in children and adolescents after the Fontan procedure. Strategies to address this problem might emphasize coordinated and effective prevention, detection, and management of noncardiac and psychosocial conditions, as well as specific targeting of patients from low-income households. Assessments of health status, particularly psychosocial issues, might be included in the study of these vulnerable patients for clinicians to better understand the complexities of these patients and to identify specific areas of unmet need. Clinicians need to be increasingly aware of these nonmedical morbidities and the impact they have on their patients. Opportunities and aspects of rehabilitation have, to date, received little attention in survivors of congenital heart disease; our study clearly points to a potential need.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The Fontan procedure has greatly improved overall survival of patients with cardiac anomalies associated with a functional single ventricle. Nonetheless, these survivors are at increased risk for important ongoing morbidity, mortality, and deficits in health status. Our study shows deficits in health status in children and adolescents after the Fontan procedure. These deficits are primarily in aspects of physical functioning, but other noncardiac morbidities such as vision and speech problems are prevalent in these patients. These patients are also likely to have psychosocial morbidities such as learning and behavior problems, problems with attention, and developmental delay. Strategies to address these associated morbidities might emphasize coordinated and effective prevention, detection, and management of noncardiac and psychosocial conditions and specific targeting of patients from low-income households. Assessments of health status, particularly psychosocial issues, might be included when these vulnerable patients are studied so that clinicians can better understand the complexities of these patients and identify specific areas of unmet need. Clinicians need to be increasingly aware of these medical and nonmedical morbidities and their impact on patients. Opportunities and aspects of rehabilitation have, to date, received little attention in survivors of congenital heart disease; our study clearly points to a need for improved awareness of overall health status in these vulnerable patients.

