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Original Article

Predictors of health-related quality of life in children with chronic heart disease

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Abstract *Objective:* Chronic paediatric heart disease is often associated with residual symptoms, persisting functional restrictions, and late sequelae for psychosocial development. It is, therefore, increasingly important to evaluate the health-related quality of life of children and adolescents with chronic heart disease. The aim of this study was to determine medical and socio-demographic variables affecting health-related quality of life in school-aged children and adolescents with chronic heart disease. *Patients and methods:* The Pediatric Cardiac Quality of Life Inventory was administered to 375 children and adolescents and 386 parental caregivers. Medical information was obtained from the charts. The socio-demographic information was provided by the patients and caregivers. *Results:* Greater disease severity, low school attendance, current cardiac medication, current parental employment, uncertain or limited prognosis, history of connection to a heart–lung machine, number of nights spent in a hospital, and need for treatment in a paediatric aftercare clinic independently contributed to lower health-related quality of life (self-report: $R^2 = 0.41$; proxy-report: $R^2 = 0.46$). High correlations between self-reports and parent-proxy reports indicated concordance regarding the evaluation of a child's health-related quality of life. *Conclusions:* Beyond medical treatment, integration into school is important to increase health-related quality of life in children and adolescents surviving with chronic heart disease. Regular screening of health-related quality of life is recommended to identify patients with special needs.

Keywords: Chronic paediatric heart disease; health-related quality of life; predictive factors; self-report and parent-proxy report

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Chronic heart disease (CHD) comprises a heterogeneous group of diseases characterised by a structural heart defect.[1] They are the most common single-organ malformations,[2] with an incidence of six to eight in every 1000 live births.[3,4] Over the past few decades, new surgical techniques and advances in cardiopulmonary bypass, intensive care, cardiac catheterisation, non-invasive imaging, and medical therapies have reduced mortality dramatically, resulting in a growing proportion of patients reaching adolescence and adulthood.[5–9] Survival and objective assessment of heart functioning do not reflect the entire impact of CHD and its

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treatment.[10] Survivors are at risk of a variety of physical and psychosocial problems, such as stigmatisation due to large incisions in the chest,[11] developmental and motor dysfunctions, neurocognitive deficits, residual injuries, persisting functional restrictions,[2,12–18] behavioural and emotional problems,[5,11–13,19–23] long-term sequelae for psychosocial development,[4,20,24–30] and, by extension, of reduced health-related quality of life.[31–34] This development leads to a steadily increasing need to assess health-related quality of life.[22,35]

Health-related quality of life is a multidimensional construct including physical, psychological, and social well-being and functioning.[28,31] There is no linear relationship between physical health and health-related quality of life. Chronic somatic diseases manifest a disease-specific organic dysfunction, leading to specific subjective complaints. They, in turn, impact the patient's general well-being and functioning. More precisely, physical symptoms may impair the patient's psychological and social well-being and functioning; therefore, viewed together, these aspects can help increase an overall understanding of the disease.[36–38]

Thus, multiple factors have to be considered when investigating health-related quality of life in children with CHD.[11] Previous health-related quality of life studies in patients with CHD described psychological,[1,32,39] psychosocial,[5,24,30] and medical variables[29,40] separately and their impact on health-related quality of life as well as specific dimensions of health-related quality of life.[5,10,27,28,31,32,34,41,42] Health-related quality of life,[33,43,44] emotional and psychological functioning,[42] and psychosocial adjustment were investigated as outcomes after different invasive treatments,[9,33,43,44,45] or patients with different diagnoses were compared.[46] Predictors and associated factors of psychosocial well-being were examined.[32,44] *Drakouli et al*[37] *found in a systematic review that patients' quality of life was associated with more severe cardiac lesions. Children reported diminished quality of life after cardiac surgery concerning physical, psychosocial, emotional, and school functioning. The most important determinants of children's quality of life were parental support, lower socio-economic status, limitations due to physical impairment, sense of coherence, and finally the level of the child's everyday anxiety and depression*. A very small proportion of studies investigated medical variables predicting health-related quality of life at school age and beyond.[40] Utens et al[44] identified several medical variables such as number of heart operations, hypothermia, duration of pregnancy, % oxygen saturation, and age at surgical repair as significant predictors for behavioural/emotional maladjustment of school-aged children and beyond with CHD; however, the impact of these factors on health-related quality of life within a multidimensional approach is under-researched. The scope of medical and socio-demographic variables associated with health-related quality of life within a *multidimensional* approach largely remains unclear. Only a few studies have integrated medical and psychosocial variables.[38] Goldbeck et al[29] demonstrated significant effects of disease severity on health-related quality of life of children with CHD and of social disadvantages on health-related quality of life of both children and their parental caregivers.

Previous studies on health-related quality of life are limited due to small sample size[28,34,45,47] and the use of non-specific psychometric instruments such as generic quality-of-life instruments or screening instruments for behavioural problems.[28,31,33,34,43,44,47] *These instruments, however, have limitations when aiming at specific psychosocial and physical sequelae of somatic diseases.*[5,11] On the basis of the available information, only one study so far has used a disease-specific health-related quality of life instrument – Pediatric Cardiac Quality of Life Inventory – to assess health-related quality of life of children with CHD. *Another disease-specific quality of life questionnaire is the PedsQL™ 3.0 Cardiac Module.*[48] *Compared with this measure, the Pediatric Cardiac Quality of Life Inventory focusses even more on the physical and psychosocial impact of heart diseases. As expected, the external validity of the original and German versions of the Pediatric Cardiac Quality of Life Inventory correlate with disease severity, and accordingly the measures are sensitive for disease-specific burdens and functional restrictions*.[49,50] Marino et al[38] found that the factors worse executive functioning, gross motor ability, and symptoms of anxiety and depression significantly predicted lower Pediatric Cardiac Quality of Life Inventory scores, and they appear to be key health-related quality of life drivers in survivors with complex CHD. Further investigations including other potential factors that impact health-related quality of life and multiple informants are needed.[31,33]

This study aimed to extend our knowledge on the long-term development of children and adolescents with CHD. The objectives were to identify medical and socio-demographic determinants of health-related quality of life in children and adolescents with CHD, and to investigate the concordance of patients' self-reports and parents' proxy reports.

Materials and methods

Study design

This study was conducted between 2010 and 2012, and was part of a cross-sectional, multicentre study in eight German centres and one Swiss centre for paediatric cardiology. Patients aged between

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8 and 17 years with either acquired heart disease or congenital heart disease and fluent in German were eligible. The questionnaires were completed by patients and their parental caregivers at the clinic or at home. The research protocol was approved by the Institutional Review Board at the University of Ulm, Germany. Informed consent was obtained from all individual participants included in the study.

Study sample

Altogether, 676 children and adolescents with heart disease as well as their parental caregivers who attended the medical centres and fulfilled inclusion criteria were approached to participate in this study. In the end, 375 children and adolescents (response rate 56.1%) and 386 parents (response rate 57.7%) participated in the present study. There were no significant differences in medical and socio-demographic characteristics between responders and non-responders. Table 1 gives the participants' socio-demographic and socio-economic characteristics. Table 2 gives the participants' medical characteristics.

Measures

Health-related quality of life. The Pediatric Cardiac Quality of Life Inventory is a disease-specific questionnaire for children and adolescents.[4,50] For this study, the original American-English versions were translated into German using international guidelines for the cross-cultural translation and validation of patient-reported outcomes.[51] The German versions showed high internal consistencies (*Cronbachs'* α between 0.92 and 0.95).[49] For test–re-test reliability determination, a subgroup of children and adolescents with heart disease, who were outpatients in the first assessment, as well as parents whose children with heart disease were outpatients in the first assessment, were re-assessed after 4–6 weeks. If any significant life event or change in clinical status had occurred between the two time points, these questionnaires were excluded from this analysis. The test–re-test reliability was sufficient with correlations between $r_{tt} = 0.73$ and 0.93.[49] The children's version (ages 8–12) comprises 27 items on three dimensions: impact of disease, psychosocial impact, and emotional environment. The adolescent version (age 13 and above) comprises 38 items on corresponding dimensions. The two subscales impact of disease and psychosocial impact can be added to a total score, indicating overall health-related quality of life.

Medical and socio-demographic information. Medical variables were collected through a medical case report form filled out by the responsible physician, based on the patient's medical charts; furthermore,

Table 1. Socio-demographic information of the study participants.

	Patient reports (n = 375)		Parent reports (n = 386)	
Age in years (mean, SD, span)	M = 12.93, SD = 2.89, 8–18 years		M = 12.82, SD = 2.85, 8–18 years	
Patient gender				
Male	212	(56.2%)	220	(56.7%)
Female	162	(43.5%)	165	(43.1%)
Not reported	1	(0.3%)	1	(0.3%)
Participating caregivers				
Mothers			318	(82.3%)
Fathers			55	(14.4%)
Other (foster mother, foster father, stepmother, sister, or grandmother)			6	(1.5%)
Not reported			7	(1.8%)
Parent education				
<10 years school			245	(63.8%)
⩾10 years school			135	(35.0%)
Not reported			6	(1.55%)
Current parental employment				
Full time			112	(29.2%)
Part time			190	(49.2%)
Not employed			72	(18.5%)
Not reported			12	(3.1%)
Age of child at diagnosis				
Before birth			42	(11.0%)
Within the 1st year of life			236	(61.3%)
After the 1st birthday			96	(24.6%)
Not reported			12	(3.1%)

Socio-demographic information of subjects based on parent reports

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Table 2. Medical information of the subsamples.

	Patient reports (n = 375)		Parent reports (n = 386)	
Type of clinic				
Paediatric CHD clinic	101	(27.2%)	105	(27.4%)
Cardiac centre (surgery)	242	(64.1%)	253	(65.1%)
Paediatric aftercare clinic	32	(8.7%)	28	(7.4%)
Treatment setting*				
Outpatient	257	(68.6%)	265	(68.7%)
Inpatient	113	(30.1%)	116	(30.0%)
Not reported	5	(1.3%)	5	(1.3%)
Type of HD*				
Single ventricle	39	(10.3%)	44	(10.3%)
Two ventricle	269	(72.0%)	278	(72.0%)
Cardiac arrhythmia	29	(7.7%)	28	(5.7%)
Acquired HD	18	(4.7%)	16	(5.1%)
Other	13	(4.3%)	13	(3.4%)
Not reported	7	(1.8%)	7	(3.4%)
Severity of heart dysfunction*				
NYHA-class I, no symptoms, no limitation	263	(69.9%)	272	(70.3%)
NYHA-class II, mild symptoms	88	(23.7%)	92	(24.1%)
NYHA-class III, marked limitation	13	(3.4%)	11	(2.8%)
NYHA-class IV, severe limitations	7	(1.8%)	7	(1.8%)
Not reported	4	(1.1%)	4	(1.0%)
Medical prognosis*				
Good	261	(69.4%)	266	(68.7%)
Uncertain	106	(28.5%)	112	(29.2%)
Limited	3	(0.8%)	3	(0.8%)
Not reported	5	(1.3%)	5	(1.3%)
Approach to treatment*				
Non-corrective	64	(17.2%)	67	(17.4%)
Curative normal cardiovascular condition	204	(54.1%)	212	(54.6%)
Curative with limited functions	58	(15.8%)	58	(15.4%)
Palliative	25	(6.6%)	25	(6.4%)
Not reported	24	(6.3%)	24	(6.2%)
Heart transplantation*				
Yes	25	(6.6%)	24	(6.1%)
No	349	(93.1%)	360	(93.3%)
Not reported	1	(0.3%)	2	(0.5%)
Cardiac pacemaker**				
Yes			44	(11.5%)
No			330	(85.4%)
Not reported			12	(3.1%)
Need for further surgery(s)*				
Yes	36	(9.8%)	32	(8.5%)
Probably	121	(31.9%)	127	(32.6%)
No	168	(44.9%)	181	(46.9%)
Not reported	50	(13.5%)	46	(12.0%)
History of connection to a heart–lung machine**				
Yes			222	(57.7%)
No			148	(38.2%)
Not reported			16	(4.1%)
Current cardiac medication*				
Yes	145	(38.5%)	146	(37.7%)
No	229	(61.2%)	239	(62.1%)
Not reported	1	(0.3%)	1	(0.3%)
Total number of nights in hospital due to CHD**				
None			43	(11.3%)
One			60	(15.4%)
2–5			108	(28.2%)
6–20			63	(16.2%)
>20			103	(26.7%)
Not reported			9	(2.3%)

*Medical information of subjects based on physician reports

**Medical information of subjects based on parent reports

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the physicians evaluated the current health status (NYHA-class) and the medical prognosis. The NYHA classification system gives the classification of cardiac insufficiency and is widely used to characterise the severity of cardiac disease.[17,20] Prognosis was acquired as subjective assessments by the physicians and estimated to be good, uncertain, or limited. Socio-demographic and socio-economic data were provided by the caregivers and the children or adolescents themselves by means of a self-constructed questionnaire.

Statistical analysis

Descriptive analyses were performed for each medical and socio-demographic variable. To meet the current standards in quality of life assessment, the Pediatric Cardiac Quality of Life Inventory total raw scores were transformed linearly into a scale ranging from 0 to 100, with higher values indicating good health-related quality of life.

χ^2 tests were computed to investigate differences in terms of disease severity depending on different settings of medical care delivery, such as paediatric CHD clinic, cardiac centre for surgery, and paediatric aftercare clinic.

To explore the impact of each separate predictor variable, the hypothesised medical and socio-economic predictor variables were tested on the Pediatric Cardiac Quality of Life Inventory total score separately by bivariate analyses; t-tests for independent samples were used for variables with two characteristics. Between-group effect sizes were computed using *Cohen's* d. Univariate analysis of variances were performed for variables with more than two characteristics. The medical or socio-economic variables were used as independent variables, and the health-related quality of life total score was used as a dependent variable. A significance level of $\alpha = 0.05$ was applied (two-sided).

We calculated two separate regression models for parent-reported and self-reported quality of life scores to estimate associations between potential predictors and outcomes. The relationship between CHD and health-related quality of life was explored by multilinear regression analysis with a stepwise inclusion procedure of independent variables (Table 3), *which had been pre-selected on the basis of findings from previous studies*.[5,29,37,52] The Pediatric Cardiac Quality of Life Inventory total score was used as a dependent variable. To estimate associations between each characteristic of the potential predictors, ordinal scaled variables were dichotomised for linear regression analysis. Characteristics of type of clinic, approach to treatment, need for further surgery, severity of heart dysfunction, children's age at diagnosis, number of nights spent in hospitals, parental education, and current parental employment were coded into 0, 1. Independent variables that met the significance criterion of $p < 0.10$ were entered in multivariate analyses. Those with $p < 0.05$ remained in the final multivariate model. Estimations of model-explained variation were determined by R^2 statistics.

A paired sample t-test was computed to examine differences in mean scores of self-reported and parent-proxy health-related quality of life ratings, patients and parents. A significance level of $p < 0.05$ was applied (two-sided).

Statistical analyses were performed using the software programme IBM Statistical Package for the Social Sciences (SPSS) for Windows Version 21.0.

Results

Disease severity differences depending on different settings of medical care delivery

The following variables were tested: type of heart disease, approach to treatment, heart transplantation, assessment of severity of heart dysfunction via NYHA classification system, physicians' subjective assessment of medical prognosis, current cardiac medication, number of nights spent in hospitals due to heart disease, cardiac pacemaker, need for further surgery, as well as school attendance over the previous 4 weeks. χ^2 Tests showed significant differences with regard to disease severity of heart disease in children treated in a paediatric CHD clinic, cardiac centre for surgery, and a paediatric aftercare clinic ($p < 0.01$).

Factors predicting health-related quality of life

The impact of each hypothesised predictor variable was indicated by bivariate associations with the Pediatric Cardiac Quality of Life Inventory total score (Table 3). Most hypothesised predictor variables indicated that patients with mild disease severity obtained significantly higher Pediatric Cardiac Quality of Life Inventory total scores than patients with at least moderate disease severity. Owing to the known impact[43] of health-related quality of life, predictor variables that failed significant associations were not excluded from regression analysis.

According to the first regression model, 42% of the variance in self-reported health-related quality of life (total score) was explained by investigated variables (adjusted $R^2 = 0.41$; $F(5,253) = 36.59$, $p < 0.001$). According to the second regression model, 47% of the variance in parent-reported health-related quality of life was explained (adjusted $R^2 = 0.46$; $F(9,266) = 26.57$; $p < 0.001$). Higher Pediatric Cardiac Quality of Life Inventory total scores were predicted by NYHA-class I and NYHA-class II as

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Table 3. Group comparisons of variables impacting health-related quality of life (as indicated by the Pediatric Cardiac Quality of Life Inventory total scores).

	Self-reports						Parent reports					
Variables	**n**	**Mean**	**SD**	**t/F**	**p**	**d**	**n**	**Mean**	**SD**	**t/F**	**p**	**d**
t-Tests for independent samples												
Treatment setting												
Outpatient	208	83.44	13.17	6.22	<0.001	0.85	213	81.62	14.06	7.16	<0.001	0.98
Inpatient	88	71.58	15.71				90	67.03	17.06			
Medical prognosis												
Good	215	83.28	12.91	5.87	<0.001	0.83	219	81.77	13.55	7.32	<0.001	1.06
Uncertain or limited	81	71.27	16.61				85	66.05	17.91			
Current cardiac medication												
No	191	84.49	12.32	7.03	<0.001	0.83	200	82.95	13.26	8.31	<0.001	1.08
Yes	108	72.08	15.84				107	67.31	16.88			
Heart transplantation												
Yes	13	68.27	14.94	−2.92	0.004	0.83	16	59.80	14.30	−4.55	<0.001	1.17
No	286	80.46	14.72				289	78.38	15.98			
History of connection to a heart–lung machine												
Yes	170	78.97	15.51	−1.92	0.055	0.23	181	73.72	17.84	−5.27	<0.001	0.59
No	118	82.44	14.37				123	83.06	13.05			
Treatment with cardiac pacemaker												
Yes	33	74.10	18.36	−2.20	0.034	0.49	37	70.69	19.20	−2.78	0.006	0.49
No	256	81.40	14.32				271	78.58	15.73			
School attendance in the previous 4 weeks												
Yes	187	85.03	12.19	7.02	<0.001	0.94	200	82.45	13.71	7.30	<0.001	0.94
No	104	72.28	16.14				108	68.35	17.37			
Parental education												
<10th grade	183	79.79	15.99	−0.59	0.557	0.07	196	77.51	16.33	0.17	0.868	0.02
>10th grade	109	80.87	13.66				111	77.18	17.33			
ANOVAs												
Type of clinic												
Paediatric CHD clinic	201	83.04	14.18	13.72	<0.001		207	81.36	15.05	19.17	<0.001	
Cardiac centre (surgery)	80	75.29	14.97				83	70.81	17.10			
Paediatric aftercare clinic	27	71.00	16.07				27	67.02	16.00			
Approach to treatment												
Non-corrective	45	83.13	13.70	8.64	<0.001		55	82.03	15.59	14.70	<0.001	
Curative normal cardiovascular condition	169	82.62	13.05				172	80.12	14.36			
Curative with limited functions	48	74.42	16.93				48	68.01	16.44			
Palliative	17	69.36	11.92				15	62.74	14.96			
Need for further surgeries												
No	137	83.53	13.93	8.57	<0.001		152	82.44	14.08	16.70	<0.001	
Probably	92	77.93	14.62				95	71.80	17.81			
Yes	30	73.25	13.78				26	70.00	16.69			
Severity of heart dysfunction												
NYHA-class I	216	84.47	11.89	55.41	<0.001		218	82.39	12.97	51.20	<0.001	
NYHA-class II	70	70.78	15.10				75	67.75	16.48			
NYHA-class III or IV	14	56.43	13.21				13	53.28	14.46			

Children's age at diagnosis				4.87	0.008				3.88	0.022	
Before birth	34	72.69	20.72			41	71.60	19.62			
Within the 1st year of life	185	81.26	13.28			190	77.39	16.44			
After the 1st birthday	73	81.09	15.88			75	80.55	14.88			
Total number of nights in hospital because of HD				6.8	<0.001				12.48	<0.001	
None	32	86.89	10.34			37	84.95	11.53			
One	50	86.54	13.87			51	87.53	11.18			
2–5	90	80.94	14.27			85	77.83	14.84			
6–20	43	76.58	17.37			51	71.29	17.95			
>20	77	75.69	14.09			86	71.82	17.90			
Current parental employment				0.28	0.754				2.05	0.130	
Full time	85	81.30	12.75			94	75.77	16.83			
Part time	150	79.80	16.02			160	79.36	15.60			
Not employed	56	79.94	16.02			52	75.25	17.62			

ANOVA = analysis of variance

well as no history of a connection to a heart–lung machine and total number of nights spent in a hospital (once). Lower Pediatric Cardiac Quality of Life Inventory total scores were associated with no school attendance during the previous 4 weeks, current cardiac medication, current parental employment, unsure or limited prognosis, total number of nights spent in a hospital (6–20), and treatment in a paediatric aftercare clinic. All predictor variables indicated that patients with mild disease severity obtained significantly higher Pediatric Cardiac Quality of Life Inventory total scores than patients with at least moderate disease severity. The results of the final prediction models are presented in Table 4.

Comparison between self-reports and parent-proxy ratings

Paired t-tests showed significant mean differences between self-reports and parent-proxy ratings of health-related quality of life ($n = 249$, $t = 2.73$, $p < 0.01$). Children and adolescents reported significantly better health-related quality of life ($M = 80.3$, $SD = 15.1$) than their parents ($M = 78.7$, $SD = 15.8$). There was a strong correlation between self-reported and parent-reported health-related quality of life ($r_{sp} = 0.82$, $p < .001$).

Discussion

This study investigated the health-related quality of life of children and adolescents with CHD in a clinical population with on average mild-to-moderate disease severity. Participants of the study were diverse regarding their specific diagnosis and their demographic and socio-economic characteristics. The validity of the study findings is strengthened by a large sample size, multicentre recruitment, and the use of a disease-specific measure with good psychometric properties.

As expected and consistent with the literature,[52,53] CHD severity as indicated by NYHA classification, treatment history, current treatment, and medical prognoses were significantly associated with health-related quality of life. Among the psychosocial factors, patients' school attendance was, independently of other factors, associated with health-related quality of life, both from the patients' and their parents' perspectives; moreover, parent reports indicated an additional effect of hospitalisation on their children's health-related quality of life.

The need for frequent medical treatment and the limited psychosocial functioning due to CHD are known to interrupt school attendance. Days off school not only impair academic education and performance but are also associated with social isolation from healthy peers.[54] Frequency and duration of inpatient

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Table 4. Prediction of health-related quality of life outcomes by multiple variables.

Variables	n	Pediatric Cardiac Quality of Life Inventory total score			
		t	β	p	Adjusted R^2
Predictors of self-reported health-related quality of life					
NYHA-class I	259	6.27	0.75	<0.001	
NYHA-class II	259	3.25	0.38	0.001	
School attendance in the previous 4 weeks	259	−6.16	−0.31	<0.001	
Current cardiac medication	259	−2.56	−0.14	0.01	
Current parental employment (part-time)	259	−1.99	−0.10	0.47	0.41
Predicators of parent-reported health-related quality of life					
NYHA-class I	276	4.82	−0.50	<0.001	
NYHA-class II	276	2.82	0.27	0.005	
School attendance in the previous 4 weeks	276	−4.97	−0.24	<0.001	
Current medication	276	−2.92	−0.15	0.004	
Uncertain or limited prognosis	276	−2.71	−0.15	0.007	
History of connection to a heart–lung machine	276	2.48	0.11	0.014	
Number of nights spent in a hospital (once)	276	2.58	0.12	0.01	
Number of nights spent in a hospital (6–20)	276	−2.44	−0.11	0.015	
Treatment in a paediatric aftercare clinic	276	−2.14	−0.10	0.034	0.46

treatments as well as type and intensity of medical interventions – for example, medication and connection with a heart–lung machine – predict poorer health-related quality of life.[19,55,56] From the available literature, it is known that children and adolescents especially with complex CHD display poorer school performance because of many hospital stays and neuropsychological dysfunction.[56] School problems and learning difficulties increase with disease severity.[31] Owing to physical impairments, some children with CHD are less involved in school activities. They do not participate fully in or are excluded from classroom activities. They do not become members of the class.[30] This is associated with the risk of a negative impact on health-related quality of life.

Significant associations between different settings for the provision of medical care and patients' health-related quality of life could be demonstrated. Children participating in inpatient paediatric aftercare programmes show significantly greater disease severity as well as significantly lower health-related quality of life, compared with children treated in paediatric CHD clinics and cardiac centres for surgery. It seems that the history of medical treatment and disease severity has a major influence on health-related quality-of-life estimations. Especially children and adolescents participating in inpatient paediatric aftercare programmes undergo more different invasive treatments, and show poorer manifestations of medical variables such as NYHA-class III or IV; therefore, this finding might constitute a selection effect and might reflect different levels of exposure to medical stressors such as hospital stay and associated traumatic experiences according to medical interventions[19,47] in children and adolescents with CHD.

Our study shows that patients and parents have very similar perceptions of patients' health-related quality of life. A high correlation between self-reports and parent reports could be demonstrated. Previous studies of children with CHD found significant differences[33,34] as well as rather low-to-moderate correlations between self-reports and parent reports.[28,47] It cannot be ruled out that caregivers and children were aware of each other's evaluation of health-related quality of life when responding to their own questionnaire, although the instructions advised patients and parents to fill in the questionnaires independently. It may be that parents and children in our study population have similar perceptions owing both to a strong empathy of parents with their child's situation and to the close connection between them during medical consultations and daily care.

The limitations of our study have to be considered when interpreting and generalising the findings. Our study sample only comprised a small proportion of severely ill children and adolescents. *In addition, there is broad empirical evidence for the impact of parental psychological well-being on their children's psychological adaptation.*[57,58] *Parents of children with CHD show high levels of anxious and depressive symptoms, for example, among parents of children with cystic fibrosis,*[59] *and traumatic symptoms, for example, after cardiac surgery.*[60] *Owing to limited resources, we were not able to assess these parental variables. Thus, further research should include more children with a severe disease and should also consider parental symptoms such as anxiety, depression, or post-traumatic stress.*

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Conclusions

Children and adolescents with CHD can benefit from integration into school. Multiprofessional care teams are highly recommended to address the comprehensive needs of children and adolescents with CHD and consider and monitor their health-related quality of life when planning and evaluating medical treatment and psychosocial interventions. In future, the use of health-related quality of life as an additional outcome variable in clinical studies, as recommended, for example, by the Food and Drug Administration[61] for clinical trials, will probably extend our knowledge on the effects of interventions for children and adolescents with CHD.

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

Ethical Standard

The authors assert that all procedures contributing to this work comply with ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (Institutional Review Board at the University of Ulm, Germany).

References

1. Karsdorp PA, Everaerd W, Kindt M, Mulder BJM. Psychological and cognitive functioning in children and adolescents with congenital heart disease: a meta-analysis. J Pediatr Psychol 2007; 32: 527–541.
2. Lindinger A, Schwedler G, Hense H-W. Prevalence of congenital heart defects in newborns in Germany: results of the first registration year of the PAN Study (July 2006 to June 2007). Klin Pädiatr 2010; 222: 321–326.
3. Hoffmann JL, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002; 39: 1890–1900.
4. Marino BS, Shera D, Wernovsky G, et al. The development of the pediatric cardiac quality of life inventory: a quality of life measure for children and adolescents with heart disease. Qual Life Res 2008; 17: 613–626.
5. Marino BS, Lipkin PH, Newburger JWPG, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. Circulation 2012; 126: 1143–1172.
6. Marino BS, Tomlinson RS, Drotar D, et al. Quality-of-life concerns differ among patients, parents, and medical providers in children and adolescents with congenital and acquired heart disease. Pediatrics 2009; 123: e708–e715.
7. Lindberg L, Olsson AK, Jogi P, Jonmaker C. How common is severe pulmonary hypertension after pediatric cardiac surgery. J Thorac Cardiovasc Surg 2002; 123: 1155–1164.
8. Wren C, O'Sullivan JJ. Survival with congenital heart disease and need for follow up in adult life. Heart 2001; 85: 438–443.
9. Politi P, Pinccinelli M, Poli PF, et al. Ten years of 'extended' life: quality of life among heart transplantation survivors. Transplantation 2004; 78: 257–263.
10. Mussatto KA, Tweddell J. Quality of life following surgery for congenital cardiac malformations in neonates and infants. Cardiol Young 2005; 15 (Suppl 1): 174–178.
11. Nousi D, Christou A. Factors affecting the quality of life in children with congenital heart disease. Health Sci J 2010; 4: 94–100.
12. Apitz J. Pädiatrische Kardiologie: Erkrankungen des Herzens bei Neugeborenen, Säuglingen, Kindern und Heranwachsenden. Steinkopff, Darmstadt, 1998.
13. Alden B, Gilljam T, Gillberg C. Long-term psychological outcome of children after surgery for transposition of the great arteries. Acta Paediatr 1998; 87: 405–410.
14. Bellinger DC, Rappaport LA, Wypij D, Wernovsky G, Newburger JW. Patterns of developmental dysfunction after surgery during infancy to correct transposition of the great arteries. Dev Behav Pediatr 1997; 18: 75–83.
15. Hirose Y, Ichida F, Oshima Y. Developmental status of young infants with congenital heart disease. Pediatr Int 2007; 49: 468–471.
16. Holm I, Fredriksen PM, Fosdahl MA, Olstad M, Vollestad N. Impaired motor competence in school-aged children with complex congenital heart disease. Arch Pediatr Adolesc Med 2007; 161: 945–950.
17. Hoppe UC, Böhm M, Dietz R, et al. Leitlinien zur Therapie der chronischen Herzinsuffizienz. Z Kardiol 2005; 94: 488–509.
18. Mahle WT, Clancy RR, Moss EM, Gerdes M, Jobes DR, Wernovsky G. Neurodevelopmental outcome and lifestyle assessment in school-aged and adolescent children with hypoplastic left heart syndrome. Pediatrics 2000; 105: 1082–1089.
19. Connolly D, McClowry S, Hayman L, Mahony L, Artman M. Posttraumatic stress disorder in children after cardiac surgery. J Pediatr 2004; 144: 480–484.
20. Goldbeck L, Seitz D. Angeborene Herzerkrankungen. In: von Hagen C, Schwarz HPH, (eds) Psychische Entwicklung bei chronischer Krankheit im Kindes- und Jugendalter, 1st edn. W. Kohlhammer, Stuttgart, 2009: 83–96.
21. Goldberg S, Simmons RJ, Newman J, Campbell K, Fowler RS. Congenital heart disease, parental stress, and infant-mother relationships. J Pediatr 1991; 119: 661–666.
22. Hövels-Gürich HH, Konrad K, Wiesner M, et al. Long term behavioral outcome after neonatal arterial switch operation for transposition of the great arteries. Arch Dis Child 2002; 87: 506–510.
23. Hövels-Gürich HH, Konrad K, Skorzenski D, et al. Long-term behavior and quality of life after corrective cardiac surgery in infancy for tetralogy of Fallot or ventricular septal defect. Pediatr Cardiol 2007; 28: 346–354.
24. Birkeland A-L, Rydberg A, Hägglöf B. The complexity of the psychosocial situation in children and adolescents with heart disease. Acta Paediatr 2005; 94: 1495–1501.
25. Bjorbaekmo W, Engelsrud G. 'I am almost like a fish': an investigation of how children with congenital heart disease experience and perform movement in daily life. Child Care Health Dev 2008; 34: 781–788.
26. Brosig CL, Mussatto KA, Kuhn EM, Tweddel JS. Psychosocial outcomes for preschool children and families after surgery for complex congenital heart disease. Pediatr Cardiol 2006; 28: 255–262.

27. Ekman-Joelson BM, Berntsson L, Sunnegarth H. Quality of life in children with pulmonary atresia and intact ventricular septum. Cardiol Young 2004; 15: 615–621.
28. Goldbeck L, Melches J. Quality of life in families of children with congenital heart disease. Qual Life Res 2005; 14: 1915–1924.
29. Goldbeck L, Melches J. The impact of the severity of disease and social disadvantage on quality of life in families with congenital cardiac disease. Cardiol Young 2006; 16: 67–75.
30. Granberg M, Rydberg A, Fisher AG. Activities in daily living and schoolwork task performance in children with complex congenital heart disease. Acta Paediatr 2008; 97: 1270–1274.
31. Uzark K, Jones K, Slusher J, Limbers CA, Burwinkle TM, Varni JM. Quality of life in children with heart disease as perceived by children and parents. Pediatrics 2008; 121: e1060–e1067.
32. Cohen M, Mansoor D, Langut H, Lorber A. Quality of life, depressed mood, and self-esteem in adolescents with heart disease. Psychosom Med 2007; 69: 313–318.
33. Spijkerboer AW, Utens EMWJ, De Koning WB, Bogers AJJC, Helbing WA, Verhulst FC. Health-related quality of life in children and adolescents after invasive treatment for congenital heart disease. Qual Life Res 2006; 15: 663–673.
34. Krol Y, Grootenhuis MA, Destree-Vonk A, Lubbers LJ, Koopman HM, Last BF. Health Related quality of life in children with congenital heart disease. Psychol Health 2003; 18: 251–260.
35. Berkes A, Pataki I, Kiss M, et al. Measuring health-related quality of life in Hungarian children with heart disease: psychometric properties of the Hungarian version of the Pediatric Quality of Life Inventory™ 4.0 Generic Core Scales and the Cardiac Module. Health Qual Life Outcomes 2010; 8: 14–25.
36. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA 1995; 273: 59–65.
37. Drakouli M, Petsios K, Giannakopoulos M, Patiraki E, Voutoufianaki I, Matziou V. Determinants of the quality of life in children and adolescents with CHD: a systematic review. Cardiol Young 2015; 25: 1027–1036.
38. Marino BS, Beebe D, Cassedy A, et al. Executive functioning, gross motor ability and mood are key drivers of poorer quality of life in child and adolescent survivors with complex congenital heart disease. J Am Coll Cardiol 2011; 57: E421.
39. Toren P, Horesh N. Psychiatric morbidity in adolescents operated in childhood for congenital cyanotic heart disease. J Paediatr Child Health 2007; 43: 662–666.
40. Seitz D, Borth-Bruns T, Goldbeck L. Quality of life in children after surgery on the heart-lung machine (Lebensqualität bei Kindern nach Operation an der Herz-Lungen-Maschine). Pädiat Prax 2009; 73: 621–630.
41. Menahem S, Poulakis Z, Prior M. Children subjected to cardiac surgery for congenital heart disease. Part 1: emotional and psychological outcomes. Interact Cardiovasc Thorac Surg 2008; 7: 600–604.
42. Culbert EL, Ashburn DA, Cullen-Dean G, et al. Quality of life of children after repair of transposition of the great arteries. Circulation 2003; 108: 857–862.
43. Hülser K, Dubowy K-O, Knobl H, Meyer H, Schölmerich A. Developmental outcome and psychosocial adjustment in children after surgery for congenital heart disease during infancy. J Reprod Infant Psychol 2007; 25: 139–151.
44. Utens EM, Verhulst FC, Duivenvoorden HJ, Meijboom FJ, Erdman RA, Hess J. Prediction of behavioural and emotional problems in children and adolescents with operated congenital heart disease. Eur Heart J 1998; 19: 801–807.
45. Landolt MA, Valsangiacomo Buechel ER, Latal B. Health-related quality of life in children and adolescents after open-heart surgery. J Pediatr 2008; 152: 349–355.
46. Maso DE, Beardslee DR, Silbert WR, Fyler AR, Psychological DC. Functioning in Children with cyanotic heart defects. J Dev Behav Pediatr 1990; 11: 289–294.
47. Goldbeck L, Melches J, Franz A, Voßbeck S, Lang D, Mihatsch W. Lebensqualität in Familien mit einem herzkranken Kind. Kindh Entwickl 2005; 14: 79–86.
48. Uzark K, Jones K, Burwinkle TM, Varni JW. The pediatric quality of life inventory™ in children with heart disease. Prog Pediatr Cardiol 2003; 18: 141–148.
49. Goldbeck L, Borth-Bruns T. Translating, validation, and implementation of an instrument to assess Health-related Quality of Life for children and adolescents with a chronic heart disease (Project Completion Report). Ulm University, Working Group: Behavioural Medicine. Ulm, 2013.
50. Marino BS, Tomlinson RS, Wernovsky G, et al. Validation of the pediatric cardiac quality of life inventory. Pediatrics 2010; 126: 498–508.
51. Wild D, Grove A, Martin M, et al. Principles of good practice for translation and cultural adaptation process for patient-reported outcomes (PRO) measures: report of the ISPOR Task Force Translation and Cultural Adaptation. Value Health 2005; 8: 94–104.
52. Laane KM, Meberg A, Otterstad JE. Quality of life in children with congenital heart defects. Acta Paediatr 1997; 86: 975–980.
53. Mair DD, Puga FJ, Danielsson GK. The Fontan procedure for tricuspidal aresia: early and late results of a 25-year experience with 216 patients. J Am Coll Cardiol 2001; 37: 933–939.
54. Gentles TL, Gauvreau K, Mayer J, et al. Functional outcomes after Fontan operation: factors influencing late morbidity. J Thorac Cardiovasc Surg 1997; 114: 392–403.
55. The Swedish Handicap Institute. Hjärtebarn – en lättare vardag för svårt hjärtsjuka barn (Heartchild – an easier every day life for children with complex heart disease). Joma Tryck AB, 2002.
56. Casey FA, Sykes DH, Craig BG, Power R, Mulholland HC. Behavioral adjustment of children with surgically palliated complex congenital heart disease. J Pediatr Psychol 1996; 21: 335–352.
57. Beardslee W, Versage EM, Gladstone TR. Children of affectively ill parents: a review of the past 10 years. J Am Acad Child Adolesc Psychiatry 1998; 37: 1134–1141.
58. Wiegand-Grefe S, Petermann F. Kinder psychisch erkrankter Eltern. Kindh Entwickl 2016; 25: 63–67.
59. Besier T, Born A, Henrich G, et al. Anxiety, depression, and life satisfaction in parents caring for children with cystic fibrosis. Pediatr Pulmonol 2011; 46: 672–682.
60. Franich-Ray C, Bright MA, Anderson V, et al. Trauma reactions in mothers and fathers after their infant's cardiac surgery. J Pediatr Psychol 2013; 38: 494–505.
61. Food and Drug Administration. Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims. Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, MD, 2009.