

Effects of Congenital Heart Disease Treatment on Quality of Life



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With rising survival rates of patients with congenital heart disease (CHD), functional health variables have become the key aspect in treatment evaluation. The effectiveness of various treatment options on the health-related quality of life (HRQoL) and the objectively measured exercise capacity as peak oxygen uptake (VO₂ peak) remains rather unclear and hence, its investigation is the primary aim of this study. Data from 1014 patients (≥14-years-old, various CHD) were retrospectively reviewed. The patients had completed at least twice the SF-36 questionnaire on HRQoL prior to a cardiopulmonary exercise test. Each patient was assigned to 1 of 4 treatment groups (i.e., surgery, catheter intervention, drug therapy, and surveillance) according to the received treatment between the baseline and the follow-up examination. After 4.0 ± 2.2 years of follow-up, patients with surgery and catheter intervention showed an increase in the physical summary score of HRQoL as compared to the other treatment groups (p < 0.001). This effect remained also significant in a multivariable model accounting for anthropometric and baseline data. No significant differences in the mental summary score of HRQoL and the VO₂ peak were evident between the different treatment groups in the multivariable model. No significant correlation was found between the changes in HRQoL and VO₂ peak over time. In conclusion, despite insignificant changes in aerobic capacity, adolescents and adults with CHD report better physical HRQoL following surgery and catheter intervention compared to the other treatment options. HRQoL and exercise capacity need to be considered concurrently in the evaluation of adolescents and adults with CHD. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1163–1168)

Diagnostic and therapeutic improvements in the field of congenital heart disease (CHD) have led to a decrease in infant mortality and a growing number of adolescents and adults with CHD.¹ As a result, the key aspect for the evaluation of their health-care outcomes is not mortality anymore, but other variables associated with functional health, such as exercise capacity and patient-reported health-related quality of life (HRQoL). Recent studies^{2–5} have examined HRQoL and its relation with objective measurements like cardiopulmonary exercise test (CPET) variables in patients with CHD.^{6–8} Furthermore, HRQoL is widely used in studies exploring the effectiveness of treatment methods from the patient's point of view. However, with a few exceptions,^{9–11} existing studies have a cross-sectional design. Most of them investigate only children and they usually focus on a single treatment method, mostly related to a specific surgical or interventional procedure.^{11–17} To fill this gap, this paper presents the results of a retrospective longitudinal study conducted on a fairly large cohort of adolescents and adults with CHD, which aims to evaluate the effectiveness of different treatment options in terms of

induced changes in patient-reported HRQoL and objectively measured exercise capacity. The overall goal of the study is to serve as an orientation for health-care decisions to both physicians and patients.

Methods

We reviewed patients from our tertiary outpatient department for CHD, who were referred for a CPET from June 2001 to June 2016. The CPET is a routine follow-up examination for all patients in our clinic, especially those with moderate and complex CHD. Patients included in our study had a wide spectrum of different CHD diagnoses. All patients filled the German version of the SF-36 questionnaire on quality of life^{18,19} with a 4-week window prior to their CPET.

In order to investigate changes over time, we retrospectively selected 2 CPET examinations with the associated SF-36 questionnaires per patient, based on the following criteria: (1) at the time of each examination the patient had to be 14 years or older, as the SF-36 questionnaire is only evaluated for this age group; (2) each examination had to be separated by a minimum of 12 months from any previous heart surgery or catheter intervention, in order to avoid the influence of short-term side effects of these procedures; and (3) the 2 examinations had to be at least 12 months apart. Each included patient was assigned to 1 of 4 groups, according to the received treatment in the time period between the baseline and the follow-up examination. The 4 treatment groups were: heart surgery, catheter intervention, change in medication, and no change in treatment.

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Depending on their condition at the baseline examination, the patients were categorized into 3 severity grades (simple-moderate-complex), according to the classification of the American College of Cardiology (ACC) by Warnes et al²⁰ For the quantitative evaluation HRQoL, we used the Medical Outcomes Study 36-item short form (SF-36, New England Hospital Inc., Boston, MA).²¹ This questionnaire consists of 36 items which can be answered in approximately 5 to 10 minutes by choosing 1 of the 2 to 6 response options. One item of the questionnaire refers to the self-reported health transition within the last 12 months. The remaining 35 items refer to the patient's preceding 4 weeks and build eight health scales, which finally form 2 summary scales: the Physical Health Summary and the Mental Health Summary. The scores of the summary scales have a mean value of 50 and a standard deviation of 10. Higher scores mean better HRQoL. All patients completed the SF-36 questionnaire before performing the CPET without any external assistance.

After completing the SF-36 questionnaire, all patients underwent a symptom-limited CPET on a bicycle in an upright position.^{7,11} Patients had a 3-minute warm-up with unloaded cycling, followed by a ramp-wise increase of load with 5, 10, 15, 20, or 30 W/min, depending on the expected physical capacity of each individual as estimated by the supervising investigator. The aim was that patients reach a total exercise time of 8 to 12 minutes after warm-up. The CPET featured a breath-by-breath gas exchange analysis using a metabolic chart. Peak oxygen uptake (peak $\dot{V}O_2$) was defined as the highest mean uptake of any 30-second interval during exercise. Excluded from this study were all patients, who did not meet the exercise effort criteria on the CPET as described previously,²² that is patients with peak heart rate $\leq 85\%$ combined with peak respiratory exchange ratio (peak RER) ≤ 1.05 and peak oxygen saturation (peak SpO_2) $\geq 90\%$.

In January 2010, our laboratory switched the CPET equipment from *Vmax 229* to *Encore 29* (both Becton Dickinson, Franklin Lakes, NJ). The latter measured slightly higher values of the peak $\dot{V}O_2$ (about 5%) than the former. Therefore, specifically for the investigation of the changes in peak $\dot{V}O_2$, we excluded the patients whose baseline examination was before January 2010 and the follow-up examination was after that date. Thus, the number of patients included in the analysis concerning changes in peak $\dot{V}O_2$ was reduced to n = 469.

Demographic data of the study population are presented in Table 1. The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Ethical approval was waived due to the retrospective nature of the study. All patients gave written informed consent.

The analysis of all collected data was performed with the Statistical Package for Social Sciences (SPSS version 22.0.1, SPSS Inc., Chicago, IL). Due to the size of our study population, it was assumed that the examined variables were normally distributed and the results were reported as the mean value and the associated standard deviation. We analyzed 3 outcome variables: the overtime changes in the 2 summary components of HRQoL (physical summary score and mental summary score), as well as the overtime changes in peak $\dot{V}O_2$. We performed paired *t* tests to compare them with the associated baseline values. In order to detect differences

Table 1
Demographics

Variable	Health-related quality of life study population (n = 1014)	Peak oxygen uptake study population (n = 469)
Male	578 (57.0%)	264 (56.3%)
Female	436 (43.0%)	205 (43.7%)
Baseline severity grade		
Simple	102 (10.1%)	56 (11.9%)
Moderate	322 (31.8%)	138 (29.4%)
Complex	578 (57.0%)	269 (57.4%)
Not classified	12 (1.2%)	6 (1.3%)
Treatment		
Heart surgery	185 (18.2%)	81 (17.3%)
Catheter intervention	123 (12.1%)	69 (14.7%)
Change in medication	195 (19.2%)	104 (22.2%)
No change in treatment	511 (50.4%)	215 (45.8%)
Baseline age (years)		
Range	14.1 - 67.3	14.1 - 65.0
Median (quartile Q1, Q3)	24.4 (18.6, 31.7)	25.4 (19.1, 34.0)
Follow-up (years)		
Mean \pm standard deviation	4.0 \pm 2.2	2.8 \pm 1.3

between the grades of severity and the treatment groups in the outcome variables mentioned afore, we did an analysis of variance (ANOVA), followed by a Bonferroni post hoc analysis. Furthermore, we performed a multivariable regression analysis to investigate the influence of the following additional variables on the observed effects: sex, height, body mass, body mass index (BMI), baseline age, baseline values of each component, and follow-up duration. Finally, in order to examine the correlation between the changes in the physical/mental summary score and the changes in peak $\dot{V}O_2$, we calculated the Pearson's correlation for normally distributed variables. In all analyses, only p values of <0.05 were accepted to be significant.

Results

At baseline, the severity of the patient's defect (according to the modified ACC classification) was associated with a worse HRQoL and a reduced peak $\dot{V}O_2$, as seen in Table 2. The changes in HRQoL and peak $\dot{V}O_2$ over time did not differ significantly between the ACC severity groups.

Regarding HRQoL in the total group of patients (n = 1014), there were overall no significant changes in the physical and mental summary scores over time. Between the treatment groups, significant differences were detected, as seen in Table 3. More specifically, patients with surgery and catheter intervention showed an increase in the physical summary score compared to the patients who received no change in treatment (Bonferroni post hoc analysis p <0.001 and p = 0.005, respectively). This effect remained significant even after performing a multivariable regression analysis, for the additional effects of age, sex, pacemaker status, body mass, body height, body mass index, baseline values of the outcome variables, and follow-up duration. On the contrary, no significant differences between the treatment groups were evident in the mental summary score in the multivariable model.

Table 2

Baseline physical and mental summary score of health related quality of life (n=1014) and baseline peak oxygen uptake (n = 469) according to baseline severity grade

	Simple	Moderate	Complex	p value ANOVA*
Baseline physical summary score	55.24 ± 4.94	52.85 ± 6.62	50.65 ± 8.08	<0.001
Baseline mental summary score	52.35 ± 7.70	49.44 ± 9.46	51.49 ± 8.44	0.001
Baseline peak oxygen uptake	38.14 ± 9.80	30.80 ± 9.10	25.44 ± 8.41	<0.001

Values presented as mean ± standard deviation.

* ANOVA= Analysis of variance (comparing the 3 severity groups).

Regarding exercise capacity (n = 469), peak $\dot{V}O_2$ significantly deteriorated in total over time. The differences detected between the treatment groups were not significant any more after performing the aforementioned multivariable regression analysis (Table 3).

In patients with a CPET the changes of HRQoL in the physical summary score did not correlate with the changes in peak $\dot{V}O_2$ (r = 0.074, p = 0.109). The same applies to the correlation between the changes in the mental summary score and those in peak $\dot{V}O_2$ (r = 0.027, p = 0.561) (Figure 1).

Discussion

This study showed that adolescents and adults with CHD rated their physical HRQoL better after surgery and catheter intervention compared to the other treatment options, although this effect was not apparent in the objectively measured exercise capacity estimated by the peak $\dot{V}O_2$.

Patients with CHD are admittedly a quite heterogeneous group, as there is a great variety of diagnoses and grades of severity. In our analysis, we saw that the severity of the patient's condition has an influence on the baseline scores of most investigated components of HRQoL. This is consistent with part of the existing literature and especially with

the review studies of Pteropouli et al² and Kahr et al,³ which suggest that more complex conditions are associated with poorer HRQoL, mainly with regard to its physical components. It is noteworthy that other studies report contrasting results, as they were not able to show a definitive relation between CHD complexity and HRQoL.^{23,24} Under-scoring our results, more complex defects have been also associated with worse exercise capacity in existing literature.²⁵ Despite significant differences at baseline, our data show that the changes of HRQoL and peak $\dot{V}O_2$ over time do not differ between the different severity groups. As this was a longitudinal study, and we were interested in the changes of the investigated variables in the course of time, we decided not to split our study population into subgroups, but to look at all patients as 1 large cohort with the common general characteristic of CHD. Although in this way it was not possible to investigate the effects of specific interventions or drugs, the followed approach can serve as a comprehensive orientation framework for physicians and patients, independent of the specific condition, and its severity.

According to our results, surgery, and catheter intervention lead to a significantly better physical summary score of HRQoL compared to the other treatment options. This finding is consistent with the results of several follow-up

Table 3

Physical and mental summary score of health related quality of life (n = 1014) and peak oxygen uptake (n = 469) according to the 4 treatment groups

	Total	Heart surgery	Catheter intervention	Change in medication	No change in treatment	p value ANOVA*
Physical summary score						
baseline	51.83 ± 7.49	49.65 ± 8.55	50.90 ± 7.57	49.05 ± 8.95	53.91 ± 5.63	
follow-up	51.67 ± 7.83	51.14 ± 7.64	52.27 ± 7.04	48.76 ± 9.28	52.82 ± 7.17	
Changes	-0.17 ± 7.38	1.49 ± 8.76 [†]	1.37 ± 6.49 [†]	-0.29 ± 8.01	-1.09 ± 6.61	<0.001 [‡]
Mental summary score						
baseline	50.86 ± 8.78	49.87 ± 8.74	50.89 ± 8.43	48.79 ± 10.36	51.99 ± 8.03	
follow-up	51.06 ± 8.60	50.19 ± 8.28	50.87 ± 9.01	50.60 ± 9.09	51.59 ± 8.41	
changes	0.20 ± 9.11	0.32 ± 9.79	-0.02 ± 9.51	1.81 ± 9.38	-0.40 ± 8.60	0.038 [§]
peak oxygen uptake (ml/kg/min)						
baseline	28.58 ± 9.84	25.21 ± 8.20	26.33 ± 7.41	24.25 ± 8.49	32.66 ± 10.14	
follow-up	27.38 ± 9.42	24.34 ± 8.07	26.68 ± 8.41	23.35 ± 8.44	30.71 ± 9.51	
changes	-1.19 ± 5.07	-0.88 ± 4.49	0.35 ± 4.01	-0.90 ± 4.28	-1.95 ± 5.78	0.008 [¶]

Values presented as mean ± standard deviation.

* ANOVA: Analysis of variance (comparing the 4 treatment groups).

[†] Still significantly better in multivariable model.

[‡] Statistically significant difference between "heart surgery" and "no change in treatment" (p <0.001) as well as "catheter intervention" and "no change in treatment" (p = 0.005) in Bonferroni post hoc analysis.

[§] Statistically significant difference between "change in medication" and "no change in treatment" (p = 0.024) in Bonferroni post hoc analysis.

[¶] Statistically significant difference between "catheter intervention" and "no change in treatment" (p = 0.006) in Bonferroni post hoc analysis.

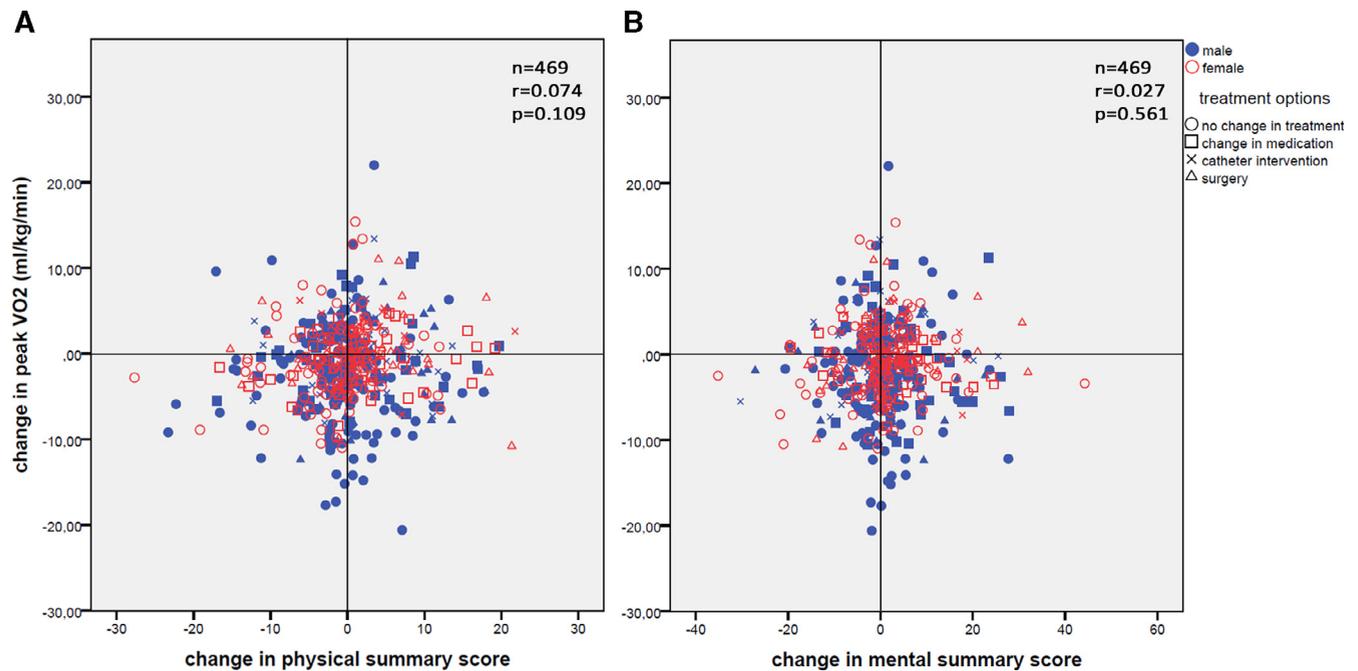


Figure 1. Correlation between changes in exercise capacity (peak $\dot{V}O_2$) and changes in A) physical summary score and B) mental summary score of health related quality of life peak $\dot{V}O_2$ = peak oxygen uptake (ml/kg/min).

studies, which focused on specific surgical/interventional procedures for different congenital heart defects. For instance, in an extensive longitudinal study, Mohr et al⁹ showed that the majority of the patients report improved subjective general health after surgical or transcatheter aortic valve replacement. In addition, according to a longitudinal study of Müller et al,¹¹ percutaneous pulmonary valve implantation leads to significant improvements mostly in the physical domains of HRQoL. Cross-sectional studies on patients with CHD after heart surgery end up with conflicting conclusions. Namely, a number of them^{15–17} present very good HRQoL scores compared to standard population, while others^{13,26–28} report poor HRQoL after open heart surgery. Note that these studies have a cross-sectional design and compare the HRQoL of the patients with that of healthy references. Consequently, they do not allow any solid conclusions regarding the actual effects of these procedures in patients with CHD over time. This observation underlines the need for more longitudinal studies evaluating specific surgical and interventional procedures.

As HRQoL is a subjective evaluation of health and well-being from the patient's point of view, we decided to include as a secondary outcome parameter in our study the objective measurement of exercise capacity, which is considered to be a significant but weak cofactor of HRQoL.⁸ Our study did not show any significant influence of the different treatment options on the changes of peak $\dot{V}O_2$ over time. The changes in peak $\dot{V}O_2$ did not even correlate with the changes in the physical/mental summary scores of HRQoL as reported by the patients. This confirms previously published results by Ehlert et al,⁷ based on a smaller sample of 182 patients, which suggest that changes in patient-reported HRQoL do not correspond adequately with changes in the objectively measured exercise capacity in

patients with CHD. This implies that HRQoL is independent of improvement or worsening of exercise capacity in patients with CHD. This might be attributed to a great extent to these patients being used to their exercise capacity limitations, since they grew up and lived their whole lives in this state. Since the interplay of expectations and experience is a major determinate of HRQoL,²⁹ it is likely that in CHD patients who probably do not have high expectations with regard to their exercise capacity, HRQoL is not substantially affected by limitations in this domain. Other components, and not exercise capacity, are probably weighed more in the determination HRQoL in these patients.

The SF-36 questionnaire, which we chose for the evaluation of HRQoL, is a generic instrument, which can be used across age, disease, and treatment group.³⁰ In contrast to more disease-specific instruments, which essentially evaluate a patient's self-reported health status, the SF-36 does not focus only on disease specific symptoms, but also on other aspects of HRQoL. Nevertheless, it may be too general for the precise detection of small changes. Being aware of this limitation, we included a fairly large cohort of patients (n=1014), so that clinically relevant fluctuations should have been clearly detected.

Regarding further limitations of this study, our institution is a tertiary referral center for patients with congenital heart disease of any age. This led to a referral bias, over-representing patients with severe defects (see Table 1). However, this group of patients is the most challenging one in the cohort of adolescents and adults with congenital heart disease. A referral bias based on the indication for a CPET can be excluded, as CPET is a routine examination in the surveillance of patients in our institution and was not performed exclusively in cases of worsening of the health condition or to support treatment decisions. In addition, a bias

towards a healthier patient sample cannot be ruled out, as those not surviving to a follow-up investigation and those with a major neurological deficit, not being able to complete the SF-36 form, were excluded. However, this holds true for all four investigated treatment groups. As discussed above, the study is not designed to evaluate specific interventions or drugs but types of treatment in general and it cannot be precluded that the patients' specific congenital heart defect may have determined the treatment group by indication to a large extent. Another potential limitation in the interpretation of the results of this study is the difference in follow up time between the total study population and the subgroup included in peak $\dot{V}O_2$ analysis.

To conclude, adolescents, and adults with CHD report better physical HRQoL after surgery and catheter intervention compared to the other treatment options. This effect could not be detected by the objectively measured exercise capacity. Therefore, the need for parallel assessment of patient-reported HRQoL and objectively measured outcome such as exercise capacity is imperative in the evaluation of individual patients with CHD. This holds also true for cross-sectional studies as well as treatment studies on adolescents and adults with CHD.

Disclosures

The authors report no relationships that could be construed as a conflict of interest for the current study.

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Supplementary materials

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