Quality of Life Among Patients With Congenital Heart Disease After Valve Replacement

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Most studies concerning valve replacement in congenital heart disease (CHD) focus on surgical morbidity and mortality. However, with the increased life expectancy of these patients, the focus shifts to quality of life (QOL). The aim of this study was to report and compare the QOL of CHD patients after valve replacement with the general population and to find factors associated with QOL. In a multicenter cross-sectional observational study of adults with CHD, QOL was measured with the RAND-36 questionnaire (a health-related QOL questionnaire, with 8 domains scoring from 0 to 100; higher scores indicate a better QOL). Functional status was measured with exercise capacity testing. Uni- and multivariable linear regression was used to find associations with QOL. In total, 324 patients with CHD and a prosthetic valve were included in this study. CHD patients with a valve replacement scored significantly lower than the general population on the general health, vitality, and social functioning domains ($P < 0.05$). On the bodily pain domain, they scored significantly higher (less pain) ($P < 0.001$). Higher NYHA class was associated with a lower QOL for all domains, reflecting the importance of functional capacity. Other variables related to aspects of QOL were age, gender, exercise capacity, and employment status. Adult patients with CHD and a prosthetic valve have lower scores on the QOL domains general health, vitality, and social functioning as compared to the general population. NYHA class was negatively associated with all QOL domains. Health care professionals should be aware of these patterns in counseling patients.

Quality of life of patients with congenital heart disease after valve replacement.

Central Message

Patients with CHD and a prosthetic valve have lower scores on 3 out of 8 of the QOL domains compared to the general population. Health care professionals should be aware of this when counseling.

Perspective Statement

This study contributes to the current knowledge and the clinical decision-making of the many congenital heart disease patients who have significant valve disease. A description of the QOL of these patients after valve replacement could help clinicians and patients in their expectations of the valvar surgery.

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INTRODUCTION

Life expectancy of patients with congenital heart disease (CHD) has improved in the last decades. Currently, there are more adults than children with CHD.[1] With the improved survival of patients having undergone surgery for CHD, quality of life (QOL) becomes more and more important in this population.[2,3] Literature has not been conclusive on the QOL of adults with CHD. Most studies conclude that adults with CHD have a reduced QOL on the physical domains as compared to the general population,[4] although there are also studies suggesting that there is no reduction of QOL compared to the general population.[5−7]

Many patients with CHD require valve replacement(s) at a certain moment in time. Current studies on adults with CHD and a prosthetic valve generally focus on the medical outcome in terms of risk of reoperations, mortality, and long-term valve functioning. The implantation of a prosthetic heart valve and its consequences could very well influence the QOL, as patients with a prosthetic heart valve encounter specific problems for example: the need for anticoagulation, the expected problems for future pregnancies (women), and the anticipated reoperations for degenerated prosthetic valves.[8] To our knowledge, data on QOL in adult patients with CHD and a prosthetic heart valve are lacking. The 2 valves that are replaced most frequently in the congenital cardiac population are the aortic and the pulmonary valves.[9]

The aim of this study is to evaluate the QOL in adult CHD patients with a history of valve replacement and to compare these results with previously reported results in the general population. In addition, we set out to investigate possible associations with QOL and the influence of valve position on QOL, using the PROStheses in Adult congenital heart VAlve disease (PROSTAVA) cohort.[10]

METHODS

Patient Population

Patients were selected from the PROSTAVA study (NTR2112). The PROSTAVA study has been designed as a cross-sectional observational study; in 2011, all patients over 18 years with a prosthetic heart valve registered in the Dutch CONgenital CORvitia (CONCOR) database[11] were approached to participate in the PROSTAVA study. The rationale and design of the PROSTAVA study have been previously described.[10] Briefly, data were retrospectively collected on demography and medical history by patient record. Data on echocardiography, cardiac magnetic resonance (CMR), blood testing, and exercise testing were collected as part of routine clinical care. Additionally, patients were asked to fill out a QOL questionnaire and a general questionnaire including questions about sport participation, educational level, and employment. The general questionnaire can be found in Supplementary file 1. Employment was self-defined by the patient according to the questions in the general questionnaire.

For this study, patients with a prosthetic valve in either the aortic valve position (AVR), pulmonary valve position (PVR), tricuspid valve position (TVR), or mitral valve position (MVR) that competed the QOL questionnaire were selected from the PROSTAVA cohort. Patients with congenital corrected transposition of the great arteries were classified as TVR. Patients who did not complete the QOL questionnaire were excluded. This study was approved by the ethical committees of all the participating centers (coordinating center University Medical Center Groningen). Informed consent was obtained from all patients.

QOL Questionnaire

QOL was measured as health-related QOL and was defined as the individuals' perceived effect of health status on multidimensional physical and mental well-being. To assess health-related QOL, we used the Dutch version of the Medical Outcome Study 36-item General Health Survey (RAND-36), comparable with the ShortForm36 (SF36).[12] The freely available RAND-36 was selected because of the available Dutch reference population. The RAND-36 is a self-administered, health-related QOL questionnaire. It consists of 36 questions of which 35 questions are divided into the following 8 domains of QOL: physical functioning (the extent to which physical activities are limited), physical role limitations (the extent to which physical health interferes with daily activities), bodily pain (the presence and intensity of pain and its effect on normal activities), general health (a person's evaluation of their health status), vitality (the extent to which one feels energetic), social functioning (the extent to which normal social activities are limited), emotional role limitations (the extent to which emotional problems interfere with daily activities), and mental health (general mental health problems). From the last question, a ninth domain on health change (change in health over the past year) can be calculated. Since patients in this study do not have a similar follow-up duration, we did not analyze this domain. RAND-36 scores were converted to the 8 domain scales ranging from 0 to 100 according published guidelines.[12] Higher scores on the domains indicate a better QOL. Patients were asked to fill in the questionnaire at home and return it through regular mail. QOL scores in our cohort were compared with the reference scores from the Dutch manual of the RAND-36. The reference group consists of 1063 persons over 18 years of age, from the northern part of the Netherlands, with a mean age of 44.1 (range 18−89) years.[12,13]

Exercise Capacity Testing

Treadmill or an upright bicycle ergometer was used for the determination of exercise capacity, according to local routine

clinical care protocol (Bruce, 10, 15 Watt program). After a short-unloaded warm-up period, workload was increased step-wise, based on age, sex, height, and weight aiming for an exercise duration of 6−8 minutes. Patients were permanently monitored with ECG, blood pressure, and oxygen saturation during the test. Symptoms onset prompted the end of the test. Achieved workload was determined as either the maximum oxygen capacity (VO_{2peak} [mL/min/kg]) or the maximum workload (W_{peak} [watts]), depending on the hospitals resources. Predicted exercise levels were calculated with the Wasserman/Hansen equation for predicted maximum oxygen (VO_{2pred}) uptake,[14] and for predicted workload (W_{pred}) as described by Ascoop et al.[15] To evaluate exercise capacity, we used the percentage of predicted exercise capacity (PPEC). This was calculated by dividing the achieved exercise level by the predicted exercise levels.

Echocardiography

To determine left and right ventricular function, left ventricular ejection fraction (LVEF) and tricuspid annular plane systolic excursion were determined using routine 2-dimensional and M-mode echocardiography. When image quality was sufficient, LVEF (%) was measured using Simpson's rule. In order to take into account the function of the valve, valve regurgitation and peak gradient were evaluated. An obstructed aortic or pulmonary prosthetic valve was defined as a peak gradient ≥36 mm Hg over the pulmonary or aortic valve (ie, similar or more than moderate stenosis).[16−18] Valvar regurgitation was quantified according to current guidelines into 4 classes: no regurgitation, mild, moderate, and severe regurgitation.[16]

Cardiac Magnetic Resonance Imaging

CMR imaging was performed for the assessment of ventricular stroke volume and ventricular ejection fraction for both ventricles. CMR protocols and acquisitions used for assessment of ventricular volume have been previously described by our group in detail.[19,20]

Statistical Analysis

Normally distributed continuous variables are presented as means and standard deviations, not normally distributed continuous variables are presented as medians, inter quartile ranges, and ranges. Categorical variables are presented in absolute numbers and percentages. The different subscales of the RAND-36 questionnaire are presented as means and standard deviations even if not normally distributed, to give a uniform representation of the data. The Dutch reference group on the RAND-36 was also reported in means and standard deviations.[13] If patients had repeated valve replacements in one position, the last implanted valve was considered for analyses. A single sample t test against a hypothesized mean was used for the comparison with the Dutch reference group, since for the reference group only means and standard deviations were available.

An independent sample t test was used to compare AVR and PVR patient groups. Dichotomous variables were compared using the Fisher's exact test. Ordinal variables were compared using the Mann-Whitney U test. The sample size of our studies allows the use of parametric testing, even though some of the parameters are skewed.[21,22] Associations with QOL were determined for the entire cohort. Uni- and multivariable linear regression analyses were used to study the association between QOL subcategories and patient and valve characteristics. Variables were selected based on previous literature as well as reasonable influence on QOL, including educational level, interval between implantation and questionnaire, valve type, valve position (AVR, PVR, combined PVR and AVR), age, gender, number of sternotomies, sport activity, employment, PPEC, valve functioning, tetralogy of Fallot, aortic stenosis, Marfan syndrome, and NYHA class.[5] MVR and TVR patients were not taken into account due to the limited number of patients in these groups. All variables that were associated on univariable analyses, with one of the outcome parameters with $P < 0.10$, were included in the multivariable analysis. Models were selected using backward elimination. Multivariable analysis was used to adjust for multiple factors that are highly correlated, including initial diagnosis and procedural group. A P value of <0.05 was considered significant. For all statistical analysis, IBM SPSS Statistics version 23 was used.

RESULTS

Baseline Characteristics

There were 385 CHD patients with a prosthetic valve included in the PROSTAVA study (Fig. 1). Sixty-one patients (15.8%) were excluded from this study because they declined to participate in the QOL study. Patients who did not participate in the QOL study were significantly younger (36.1 ± 9.9 years) and more female (68.9%) as the patients who did participate in the study. The study sample comprised 324 patients, including 127 AVR, 112 PVR, 46 PVR and AVR, 9 MVR and AVR, 16 MVR, 11 TVR, 2 TVR and PVR, and 1 PVR, AVR, and MVR patient who underwent their prosthetic heart valve surgery between May 1977 and December 2012. Mean age at study inclusion was 40.6 ± 11.9 years (range 19−70) and 35.8% was female (Table 1). In the total population, 53.6% of patients had a mechanical valve, although there were large differences between subgroups. In the AVR group mechanical valves were predominantly the valve of choice (88.7%), where in the PVR group, biological valves were predominantly used (only 13.9% mechanical valves). There were 5 patients (1.5%) with a transcatheter valve. There were 19 patients (5.8%) who had a biological valve prior to their current mechanical valve and 1 patient (0.3%) who had a mechanical valve prior to his current biological valve. For 88 patients (27.2%), the current valve was the result of a first thoracotomy. In Table 2, the functional parameters of this population are presented, showing an average LVEF of 54.6 ± 8.6%.
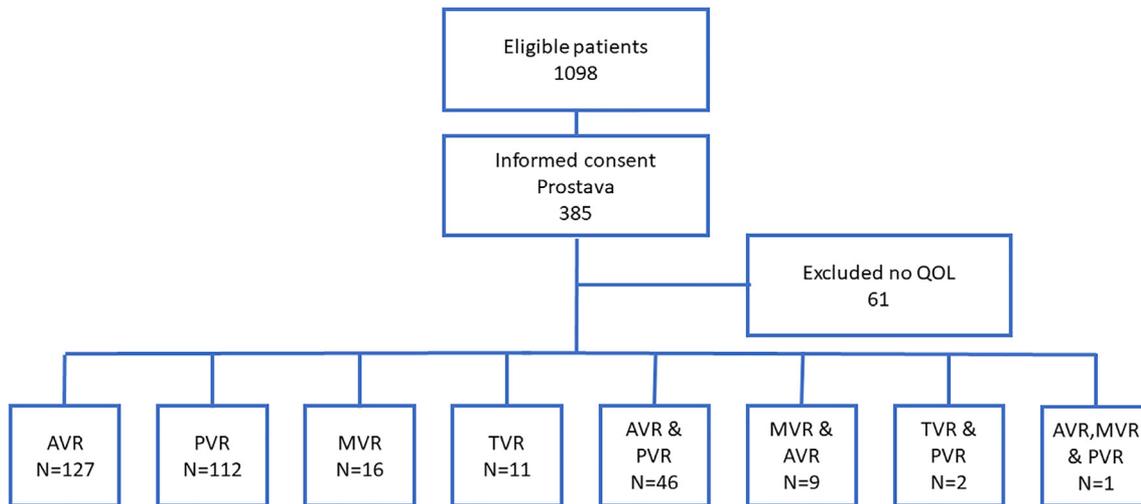
Figure 1. Flowchart of PROSTheses in Adult congenital heart VAlve disease (PROSTAVA) inclusion. AVR, aortic valve replacement; PVR, pulmonary valve replacement; TVR, tricuspid valve replacement; MVR, mitral valve replacement; QOL, quality of life questionnaire.

Comparison With the General Population

As shown in Figure 2 and Table 3, patients with CHD and a prosthetic valve scored equally to the Dutch reference population on the following domains: physical functioning, physical role performance, and mental health domains. On the following domains, the CHD group scored lower than the reference population: general health, vitality, and the social functioning scale. In contrast, on the bodily pain domain, the CHD population scored significantly higher.

Associations With QOL

We found NYHA class ≥2 to be significantly associated in the multivariable model with all domains of the RAND-36 (Table 4). Increasing age was associated with worse physical functioning. Being male was positively associated with the social functioning domain. Employment status was positively associated with the physical functioning, physical role performance, vitality, and general health domains. Increase in PPEC was associated with better physical functioning, physical role performance, social functioning, vitality, bodily pain, and general health scores (Table 4). A prosthetic valve in the AVR position was significantly associated with lower scores on physical role performance and bodily pain compared to the CHD population. A prosthetic valve in the PVR position was associated with significantly higher scores on social functioning compared to the CHD population. For both emotional functioning and mental health, the created models only explained a very limited amount of the variance, respectively 6.3% and 5.9%. In the separate analyses, we found the diagnosis Marfan associated with poorer bodily pain scores ($P = 0.05$), in contrary, TOF was associated with higher bodily pain scores ($P = 0.01$).

Valve Position

The results from our multiple regression showed that valve position was of influence on QOL score. Interestingly, both AVR and PVR had significant associations with 1 or more particular QOL domains, and therefore we performed for these 2 largest groups an additional comparison. Baseline characteristics for both groups are reported in Supplementary Table 1. Comparison on functional parameters showed that the PPEC was significantly lower in the PVR group compared to the AVR group ($P = 0.001$). PVR patients showed worse left and right ventricular function, as well on echocardiography as on CMR data (Supplementary Table 2). The PVR group scored better on all subscales of the QOL questionnaire compared to the AVR group, but significance was reached only on physical functioning, physical role functioning, bodily pain, vitality, and social functioning. For the general health, emotional functioning, and mental health domains, no significant differences were observed. Compared with the general population, both groups reported a significantly lower general health. Additionally, the AVR group reported significantly lower scores on physical role performance, vitality, and social functioning. The PVR group reported significantly higher QOL on physical functioning and bodily pain compared with the general population (Supplementary Table 3).

DISCUSSION

The lifespan of patients with CHD has increased drastically over the last decades, putting more emphasis on QOL of this group. The results of this study show that adult CHD patients with a prosthetic valve experienced the same QOL in the domains physical functioning, physical role performance and mental health domains, and significantly worse QOL in the domains general health, vitality, and social functioning scale, as compared to the Dutch reference population (Fig. 3). The most important but not surprising association with QOL measures was NYHA class, and exercise capacity and employment status, of which the first 2 reflect the importance of functional capacity. Variables that are somewhat unexpected related to

Table 1. Baseline Characteristics

Variable	
N	324
AVR	127 (39.2%)
PVR	112 (34.6%)
AVR, PVR	46 (14.2%)
MVR, AVR	9 (2.8%)
MVR	16 (4.9%)
TVR	11 (3.4%)
TVR, PVR	2 (0.6%)
MVR, AVR, PVR	1 (0.3%)
Age at inclusion (y)	40.6 ± 11.9
Female	116 (35.8%)
BSA (m^2)	1.9 ± 0.2
*Number of prior median sternotomies**	
0	88 (27.2%)
1	139 (42.9%)
2	63 (19.4%)
3	27 (8.3%)
4	4 (1.2%)
5	3 (0.9%)
Age at last implantation (y)	29.3 ± 12.03
Follow-up since last implantation (y)	10.4 ± 7.2
Valve type (% mechanical valves)	173 (53.6%)
Cardiac diagnosis n (%)	
Aortic valvar stenosis	138 (42.6%)
Tetralogy of Fallot	74 (22.8%)
Marfan syndrome	27 (8.3%)
Pulmonary atresia	16 (4.9%)
Pulmonary stenosis	14 (4.3%)
Aortic subvalvar stenosis	5 (1.5%)
Transposition of the great arteries	5 (1.5%)
CC transposition of the great arteries	5 (1.5%)
Truncus arteriosus	5 (1.5%)
Ebstein	5 (1.5%)
Mitral stenosis	4 (1.2%)
AVSD	8 (2.5%)
Other	20 (3.7%)
Unknown	1 (0.9%)
Questionnaire	Missing (N = 89)
Education n (%)	
University	92 (39.1%)
Secondary school	95 (40.4%)
Primary school	48 (20.4%)
Sport (%)	180 (76.6%)
Employed, studying, or retired	179 (76.8%)

AVSD, atrial ventricular septum defect, BSA, body surface area.
Sport, 1 hour a week of physical activity.
*Number of median sternotomies before last valve implantation.

Table 2. Functional Parameters

Echo		N (324)
LVEF (%)	54.6 ± 8.6	262
TAPSE (mm)	17.5 ± 4.1	277
Valve insufficiency (*N* (%))	32 (9.9%)	274
Valve stenosis (*N* (%))	72 (28%)	257
MRI		
LV stroke volume (mL)	97.74 ± 25.79	141
LVEF (%)	55.30 ± 7.9	141
RV stroke volume (mL)	95.51 ± 24.62	141
RVEF (%)	48.12 ± 9.2	141
Cardiopulmonary exercise testing		
PPEC (%)	82.75 ± 22.49	265
NYHA-class		234
NYHA-class I	157 (67.4%)	
NYHA-class II	61 (26.2%)	
NYHA-class III	14 (6.0%)	
NYHA-class IV	1 (0.4%)	

RVEF, right ventricular ejection fraction; LVEF, left ventricular ejection fraction; TPASE, tricuspid annulus plane systolic excursion; PPEC, predicted percentage exercise capacity.

al did describe the QOL (SF36/SF10) in a series of bio prosthetic pulmonary valve replacements; however, the number of participants was very limited as they only had 34 adults and 17 children returning the questionnaire.[23] In our study concerning the physical QOL domains (general health, bodily pain, physical functioning, physical role performance), patients did not experience a reduction in the bodily pain, physical functioning, and physical role performance but did experience a reduced general health score. The QOL of the general CHD population has been studied before as described in a systematic review by Fteropoulli et al.[4] The majority of studies described by Fteropulli report a reduction in QOL in the physical function domain, whereas we found no difference. Furthermore, Fteropoulli described that only a small minority of studies reported a better QOL for bodily pain when compared to a reference population. A finding that was, replicated in our study. An explanation for this could lie in the fact that maximum age in our population was only 70 years. Bodily pain is likely to increase with increasing age. Where the majority of studies on the general CHD population, as well as the study by Chen et al report no difference on the psychosocial domains, our population has reported a reduced score on 2 (vitality and social functioning) of the psychosocial domains (mental health, vitality, emotional functioning, and social functioning). Most prominent is the reduced QOL on the social function domain, while from the CHD studies only 2 other studies described by Fteropoulli also reported a poorer QOL on this domain.[4] However, when comparing studies concerning CHD caution is warranted, the CHD population is an exceedingly heterogeneous population.

Associations With QOL

In accordance with previous literature, we found NYHA class to be associated with all domains of QOL.[24] In addition,

aspects of QOL were age and gender. Valve position was also of influence on some aspects of QOL, which somewhat of a surprise.

Comparison With the General Population

To our knowledge, there is a very limited amount of studies on the QOL of CHD patients with a prosthetic heart valve. Chen et
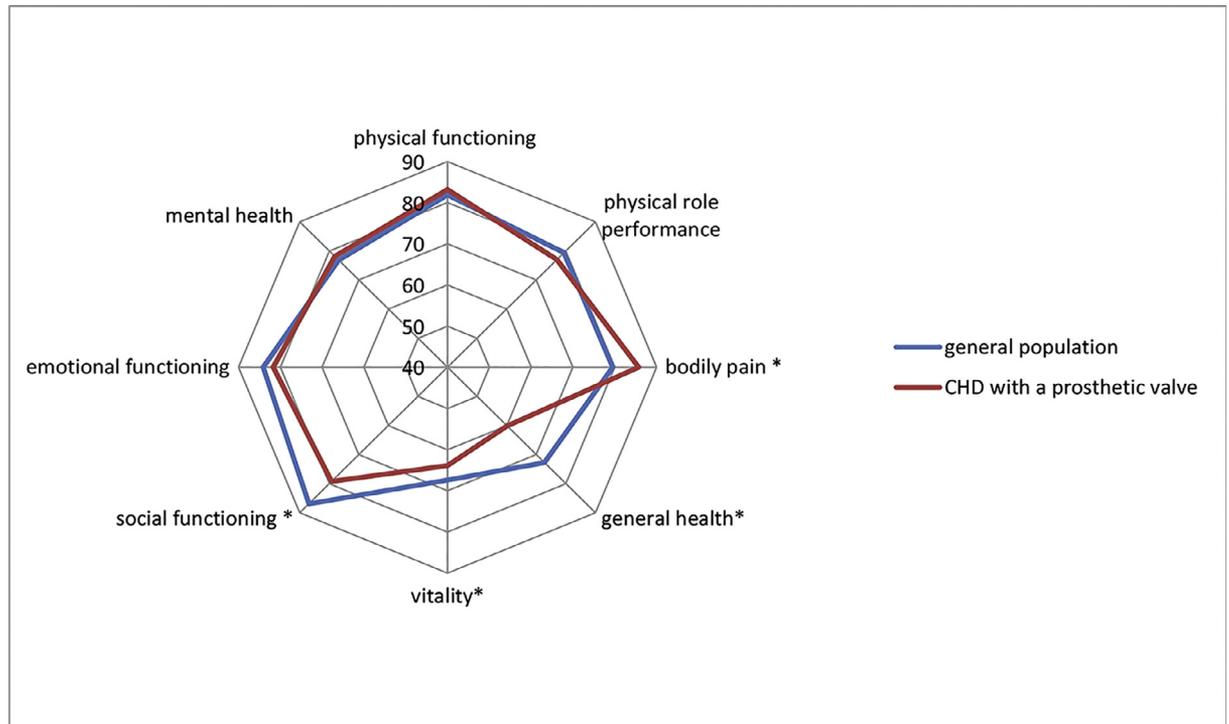
Figure 2. Quality of life evaluated by the RAND-36 questionnaire. A comparison between congenital heart disease (CHD) patients with a prosthetic heart valve and a reference sample of the Dutch population, $n = 324$, *$P < 0.05$.

the effect of age, employment status, and functional performance on the physical functioning domain has also been reported before.[4,24,25] The effect of employment was possibly underestimated in our questionnaire, as both volunteer work and a regularly payed job were considered as employment. Although we describe a much younger population, our finding that valve type (mechanical vs biological) has no effect on all of the QOL domains is in line with previous research.[26] We do have to recognize that valve type was very unequally distributed between valve positions.

Valve Position

Our multivariate analyses showed that AVR was negatively associated with bodily pain and physical role performance, whereas PVR was positively associated with higher social

functioning scores. When comparing these 2 groups, PVR patients score equally or better on QOL compared to the AVR on most domains, while paradoxically PVR patients have a reduced ventricular function and exercise capacity. This could conceivably be explained by their more complex medical history. PVR patients usually have been receiving medical and surgical treatment all of their lives. Therefore, PVR patients likely require more frequent monitoring in the context of the expectation of repeated surgeries. For 47.2% of the AVR patients, this was their first procedure, in contrast only 1.8% of the PVR patients did not have a prior thoracotomy. It has also previously been reported that for AVR patients, the first surgery is usually at a later stage in life.[27] Probably, patients with a PVR have had more time to adapt to their CHD by means of their coping skills, where for AVR patients the burden of the CHD

Table 3. QOL Scores Compared Between Groups and the General Population

	General Population (GP) ($n = 1063$)	CHD With Prosthetic Valve ($n = 309$)	GP-CHD *P* Value
Physical functioning	81.9 ± 23.3	83.2 ± 20.6	0.2
Physical role performance	79.4 ± 35.5	77.0 ± 36.7	0.25
Bodily pain	79.5 ± 25.6	85.7 ± 20.4	<0.0001
General health	72.7 ± 22.7	60.14 ± 23.1	<0.0001
Vitality	67.4 ± 19.9	63.9 ± 20.5	0.002
Social functioning	86.9 ± 20.5	79.2 ± 24.3	<0.0001
Emotional functioning	84.1 ± 32.2	81.7 ± 34.0	0.2
Mental health	76.8 ± 18.4	78.1 ± 16.9	0.2

CHD, congenital heart disease.

Table 4. Variables Associated With QOL Domains

	Univariable		Multivariable			
	B (95% CI)	P Value	R^2	Adjusted R^2	B (95% CI)	P Value
Physical functioning			0.58	0.57		
Current age	−0.54 (−0.73 to −0.36)	<0.001			−0.49 (−0.68 to −0.30)	<0.001
Sport (Y/N)	12.3 (5.88 to 18.73)	<0.001			3.25 (−1.5 to 8.01)	0.2
Mech valve	−5.6 (−10.1 to −1.1)	0.02				
Employment (Y/N)	21.17 (15.15 to 27.2)	<0.001			11.40 (6.45 to16.44)	<0.001
NYHA ≥2	−19.69 (−23.36 to −16.02)	<0.001			−14.1 (−18.72 to −9.47)	<0.001
PPEC	0.36 (0.26 to 0.46)	<0.001			0.32 (0.23 to 0.42)	<0.001
PVR	6.32 (1.6 to 11.0)	0.016				
Physical role performance			0.30	0.28		
Current age	−0.62 (−0.95 to −0.28)	<0.001				
AVR	−10.16 (−18.33 to −2.0)	0.015			−9.3 (−18.5 to −0.1)	0.05
PVR	12.73 (4.37 to 21.10)	0.003				
Employment* (Y/N)	27.27 (16.3 to 38.23)	<0.001			18.7 (7.59 to 29.81)	0.001
NYHA ≥2	−23.04 (−30.09 to −15.99)	<0.001			−29.5 (−39.36 to −17.44)	<0.001
PPEC	0.37 (0.19 to 0.56)	<0.001			0.23 (−0.027 to 0.43)	0.03
Bodily pain			0.30	0.27		
Current age	−0.32 (−0.50 to −0.13)	0.001				
Mech valve	−4.3 (−8.80 to 0.14)	0.058			5.33 (−0.59 to 11.25)	0.08
NYHA ≥2	−12.63 (−16.77 to −8.49)	<0.001			−20.17 (−25.52 to −14.82)	<0.001
Employment (j/n)	12.36 (5.9 to 18.82)	<0.001				
Sport (j/N)	5.96 (−0.58 to 12.5)	0.07			−4.15 (−10.12 to 1.80)	0.2
PPEC	0.18 (0.075 to 0.28)	0.001			0.17 (0.046 to 0.28	0.007
AVR	−6.8 (−11.32 to −2.28)	0.003			−11.72 (−17.83 to −5.61)	<0.001
PVR	6.95 (2.32 to 11.59)	0.003				
General health			0.24	0.22		
Current age	−0.31 (−0.52 to −0.10)	0.004			−0.24 (−0.52 to 0.05)	0.1
Employment (j/n)	18.18 (11.28 to 25.08)	<0.001			10.99 (3.46 to18.52)	0.004
NYHA ≥2	−17.49 (−23.62 to −11.35)	<0.001			−10.24 (−17.19 to −3.29)	0.004
PPEC	0.30 (0.18 to 0.42)	<0.001			0.26 (0.12 to 0.40)	<0.001
AVR and PVR	6.99 (−0.21 to 14.20)	0.057			4.38 (−3.71 to 12.48)	0.3
Vitality			0.20	0.18		
Current age	−0.232 (−0.41 to −0.034)	0.02				
Gender (f = reference)	4.84 (0.17 to 9.51)	0.04				
Employment (j/n)	11.53 (5.19 to 17.86)	<0.001			6.83 (−0.056 to 13.61)	0.05
Sport (j/N)	6.33 (−0.085 to 12.75)	0.05				
NYHA ≥2	−16.33 (−21.77 to −10.89)	<0.001			−13.41 (−19.42 to −7.39)	<0.001
PPEC	0.21 (0.10 to 0.31)	<0.001			0.16 (0.035 to 0.28)	0.01
AVR	−4.08 (−8.67 to −0.50)	0.08			−3.83 (−9.44 to 1.78)	0.2
PVR	6.54 (1.86 to 11.2)	0.006				
Social functioning			0.30	0.28		
Current age	−0.31 (−0.53 to −0.08)	0.007				
Gender (f = reference)	6.8 (1.2 to −12.24)	0.02			6.97 (0.81 to −13.10)	0.03
Employment (j/n)	10.78 (3.13 to −18.44)	0.006				
NYHA ≥2	−22.14 (−28.52 to −15.76)	<0.001			−18.01 (−24.65 to −11.38)	<0.001
PPEC	0.26 (0.014 to −0.38)	<0.001			0.26 (0.12 to 0.39)	<0.001
Mech valve	−8.76 (−14.03 to −3.49)	0.001				
PVR	13.19 (7.78 to −18.60)	<0.001			12.08 (5.54 to 18.62)	<0.001

(*continued*)

Table 4. (*continued*)

	Univariable		Multivariable			
	B (95% CI)	*P* Value	R^2	Adjusted R^2	B (95% CI)	*P* Value
Emotional functioning			0.063	0.053		
Employment (*j/n*)	14.03 (3.18 to 24.88)	0.01			9.69 (−2.57 to 21.95)	0.1
NYHA ≥2	−15.38 (−25.00 to −5.76)	0.002			−14.67 (−25.31 to −4.03)	0.07
PPEC	0.17 (−0.012 to 0.35)	0.07				
Mental health			0.059	0.0438		
Gender (*f* = reference)	3.73 (−0.13 to 7.59)	0.06			2.85 (−1.80 to 7.50)	0.2
Employment	5.17 (−0.13 to 10.47)	0.06			2.70 (−2.78 to 8.17)	0.3
NYHA ≥2	−7.44 (−12.12 to −2.76)	0.002			−6.84 (−11.69 to −1.98)	0.006
AVR	−3.13 (−6.92 to 0.66)	0.1			−2.51 (−7.02 to −1.20)	0.3

PPEC, predicted percentage exercise capacity.
Variables in the multivariate analyses (with *P* < 0.1 in univariable analyses).
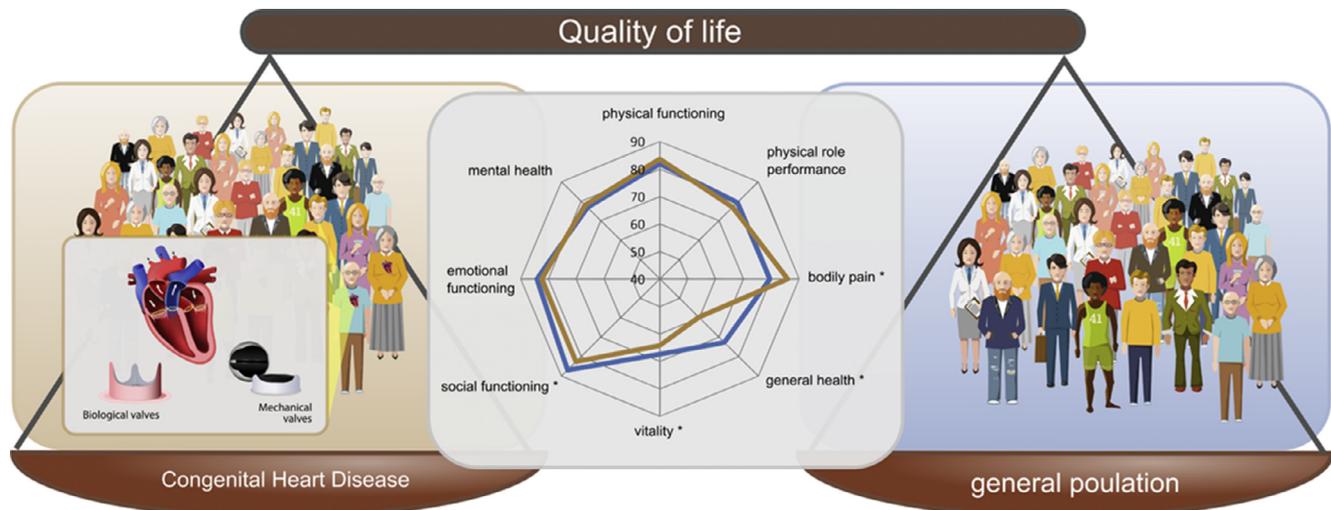*Employed, studying, or retired.

Figure 3. Comparison of quality of life between patients with congenital heart disease and a prosthetic heart valve and a reference group from the general population. Quality of life was evaluated using 8 domains of the RAND-36 questionnaire of. *P < 0.05.

often strikes suddenly at a more mature stage of life. Müller et al have previously reported that a "sense of coherence" was a strong predictor for QOL in adults with CHD, where "sense of coherence" was defined as a psychological resource of health and well-being. Patients with a strong sense of coherence perceived the world as predictable, manageable, and meaningful.[28] We speculate that patients with a PVR have a stronger sense of coherence, having had a longer time of adapting to the limitations of their CHD. It might well be that, due to their prolonged adaptation time, patients with a PVR have been able to substitute their functional limitations, as suggested by Ormel et al.[29] When, for example, considering diabetes mellitus type I, another chronic disease with frequent hospital contact at a young age, we see that also in this group QOL has not been reduced.[30] This supports our supposition that due to adaptation, QOL in a population with chronic disease is less compromised in their perception of

QOL. As suggested by Moons and Norekvål, developing a sense of coherence can improve the QOL in patients with CHD.[31] Education and supporting patients on their CHD from an early stage in life could be beneficial for the development of stronger sense of coherence. Special attention should be paid to the education and mental preparation of patients who have their first surgical treatment in their adult life.

Limitations

First, since this study was a nonrandomized observational study and, due the retrospective design, the populations were not homogeneous. Randomized studies are very unlikely to be possible in the very heterogeneous CHD population. Second, although the RAND-36 questionnaire is used worldwide to assess general QOL, the questionnaire is not a disease-specific questionnaire for patients with CHD. However, to compare with the general population, a disease-specific questionnaire is not suitable. For further

research, the addition of a disease-specific questionnaire in a longitudinal design will be the next step. Third, although this study was a multicenter study all centers were from the Netherlands. Moons et al have previously reported that Dutch patient-reported outcomes are among the best worldwide.[32] Therefore, we have to be careful when translating these results to other countries. Fourth, due to the relatively large sample size, small differences in QOL scores on the RAND-36 scale may be statistically significant but not clinically relevant. The minimal clinically important difference has been introduced as the minimal difference in scores that is clinically relevant. The minimal clinically important difference for the RAND-36 is typically in the range of 3−5 points.[33] Finally, given the fact that the QOL was measured cross sectionally, we were not able to investigate changes over time. There was no control on the time between surgery and the time of answering the QOL questionnaire. Despite these limitations, our findings contribute to the knowledge on the well-being of patients with CHD a prosthetic heart valve.

CONCLUSION

Compared to the Dutch reference population, adult patients with CHD and a prosthetic cardiac valve experienced the same QOL (physical functioning, physical role performance, and mental health domains) but significantly worse QOL in the domains general health, vitality, and social functioning. Factors associated with QOL measures were age, sex, NYHA class, exercise capacity, employment status, and the position of the prosthetic valve. Health care professionals should be aware of these patterns in counseling patients.

SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:

Video 1. Joost van Melle MD PhD, cardiologist at the University Medical Center Groningen, explaining the importance and relevance of this manuscript.

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