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ORIGINAL ARTICLE

Clinical and Sociodemographic Factors Associated With Health-Related Quality of Life in Patients With Adult Congenital Heart Disease

— A Nationwide Cross-Sectional Multicenter Study —

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Background: Little is known about clinical or sociodemographic factors that influence health-related quality of life (HRQoL) in patients with adult congenital heart disease (ACHD).

Methods and Results: We conducted a nationwide prospective cross-sectional multicenter study at 4 large ACHD centers in Japan. From November 2016 to June 2018, we enrolled 1,223 ACHD patients; 1,025 patients had an HRQoL score. Patients completed a questionnaire survey, including sociodemographic characteristics, and the 36-Item Short-Form Health Survey (SF-36). To determine factors associated with HRQoL, correlations between 2 SF-36 summary scores (i.e., physical component score [PCS] and mental component score [MCS]) and other clinical or sociodemographic variables were examined using linear regression analysis. In multivariable analysis, poorer PCS was significantly associated with 11 variables, including older age, higher New York Heart Association class, previous cerebral infarction, being unemployed, and limited participation in physical education classes and sports clubs. Poorer MCS was associated with congenital heart disease of great complexity, being part of a non-sports club, current smoking, and social drinking. Student status and a higher number of family members were positively correlated with MCS.

Conclusions: This study demonstrates that HRQoL in ACHD patients is associated with various clinical and sociodemographic factors. Further studies are needed to clarify whether some of these factors could be targets for future intervention programs to improve HRQoL outcomes.

Key Words: Adult congenital heart disease; Health-related quality of life; 36-Item Short-Form Health Survey (SF-36); Physical activity; Sociodemographic factor

The World Health Organization defined health as a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.[1] This indicates that, in addition to morbidity and mortality, health-related quality of life (HRQoL) is important when measuring a patient's health status. It was previously reported that patient-reported outcomes, including HRQoL, should be considered in cardiovascular clinical research to improve the quality of care for patients.[2]

Along with improvements in the treatment of congenital heart disease (CHD) during childhood, the number of patients with adult CHD (ACHD) continues to increase worldwide.[3] The HRQoL of ACHD patients also has gained considerable interest because chronic medical con-

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Table 1. Baseline Characteristics of All 1,025 Japanese Adult CHD Patients

Age (years)	33.8±14.9
Age group	
<35 years	635/1,025 (62)
≥35 years	390/1,025 (38)
Male sex	468/1,025 (46)
CHD complexity[A]	
Simple	400/1,005 (40)
Moderate	342/1,005 (34)
Great	263/1,005 (26)
NYHA functional class	
I	684/1,018 (67)
II	309/1,018 (30)
III	24/1,018 (2.4)
IV	1/1,018 (0.1)
After intervention for CHD[B]	810/1,025 (79)
Pulmonary hypertension	
Diagnosed by RHC	36/1,001 (3.6)
Diagnosed by echocardiography	56/1,002 (5.6)
Fontan circulation	77/1,025 (7.5)
Eisenmenger syndrome	11/1,025 (1.1)
Past medical history	
Hypertension	68/1,021 (6.7)
Dyslipidemia	32/1,021 (3.1)
Diabetes	24/1,021 (2.4)
Hyperuricemia	16/1,021 (1.6)
Myocardial infarction	14/1,021 (1.4)
Syncope	33/1,021 (3.2)
Cerebral infarction	24/1,021 (2.4)
Infective endocarditis	23/1,020 (2.3)
Cancer	26/1,021 (2.5)
Viral hepatitis	21/1,021 (2.1)
Employment status	
Part-time or full-time work	615/1,020 (60)
Unemployed	120/1,020 (12)
Full-time student	182/1,020 (18)
Retired or homemaker	103/1,020 (10)
Education level	
University degree	290/1,006 (29)
Junior college or vocational school	217/1,006 (22)
High school	432/1,006 (43)
Less than high school	67/1,006 (6.7)
Participation in PE classes	
Rare	183/1,000 (18)
Occasional	237/1,000 (24)
Frequent	580/1,000 (58)
Participation in ECAs	
No club	178/989 (18)
Non-sports club	477/989 (48)
Sports club	334/989 (34)
No. family members	3.4±1.6
Living alone	121/993 (12)
Marital status	
Never married	589/1,012 (58)
Married or living with a partner	385/1,012 (38)
Divorced or widowed	38/1,012 (3.8)
Religious	63/1,003 (6.3)
Smoking status	
Never smoker	761/1,011 (75)
Past smoker	162/1,011 (16)
Current smoker	88/1,011 (8.7)
Alcohol consumption	
Non-drinker	449/1,016 (44)
Social drinker	449/1,016 (44)
Regular drinker	118/1,016 (12)

Continuous variables are presented as the mean±SD. Categorical variables are presented as n/N (%), where N is the number of patients for whom data are available. [A]Congenital heart disease (CHD) complexity was assigned according to the Bethesda classification.[14] [B]Number of patients who underwent surgical repair or a palliative surgical procedure for CHD. ECAs, extracurricular activities; NYHA, New York Heart Association; PE, physical education; RHC, right heart catheterization.

(**Table 1** continued the next column.)

ditions cause psychosocial difficulties. It was previously reported that the physical component of HRQoL was significantly worse in ACHD patients than in the general population, although the mental component of HRQoL was comparable.[4,5] Clinical and sociodemographic factors associated with HRQoL have been investigated in ACHD patients.[6–9] However, few studies regarding HRQoL in ACHD patients have used multivariable analysis by which independent predictors of HRQoL can be identified.

A previous study revealed that HRQoL scores in ACHD patients differed among 15 countries.[6] Among these 15 countries, Japanese patients reported the worst quality of life (QoL).[10] In the present study, we conducted a nationwide cross-sectional multicenter study at 4 ACHD centers in Japan, namely Tohoku University Hospital, Chiba Cardiovascular Center, Iwate Medical University, and Chiba Children's Hospital, to identify potentially modifiable factors associated with HRQoL in ACHD patients and to generate a hypothesis that may lead to future intervention studies for improving HRQoL in ACHD patients.

Methods

Study Population

From November 2016 to June 2018, we prospectively enrolled 1,223 ACHD patients aged 15 to 87 years at the 4 large ACHD centers in Japan. The number of patients enrolled at each institution is listed in **Supplementary Table 1**. A self-report questionnaire, including HRQoL, was provided to the patients at outpatient clinics. Of the 1,223 patients, 1,025 were able to report by themselves, with the remaining 198 supported by their family. Thus, the final sample size available for statistical analysis was 1,025 (**Supplementary Table 1**).

Written informed consent was obtained from each participant. The study was performed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the ethics committees of the Tohoku University Graduate School of Medicine and all participating centers.

Data Collection

HRQoL was measured using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36).[11] The SF-36 is a generic HRQoL assessment tool and has been used most frequently in the past decade in the field of HRQoL

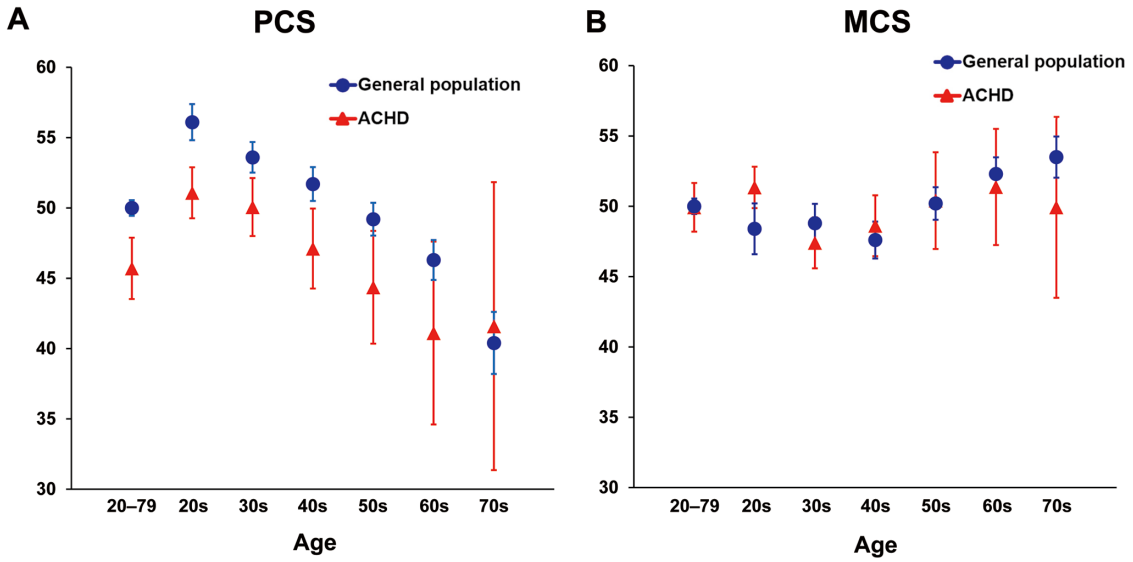

Figure. Mean (**A**) physical component summary (PCS) and (**B**) mental component summary (MCS) scored on the 36-Item Short-Form Health Survey among Japanese adult congenital heart disease (ACHD) patients and the general Japanese population by age group. Error bars indicate 95% confidence intervals after applying Bonferroni correction to account for multiple comparisons.

Table 2. Univariable and Multivariable Linear Regression Analysis of Factors Affecting the Physical Component Summary Score of the 36-Item Short-Form Health Survey

	Univariable (n=1,025)		Multivariable (n=897)	
	Coefficient (SE)	P value	Coefficient (SE)	P value
Age	−0.23 (0.03)	<0.001	−0.18 (0.03)	<0.001
Male sex	3.40 (0.80)	<0.001		
CHD complexity[A]				
Simple	Ref.			
Moderate	−2.07 (0.93)	0.026		
Great	−4.89 (1.00)	<0.001		
NYHA functional class				
I	Ref.		Ref.	
II	−6.10 (0.84)	<0.001	−2.85 (0.81)	<0.001
>II	−20.36 (2.50)	<0.001	−7.62 (2.64)	0.004
After intervention for CHD[B]	−0.75 (0.99)	0.447		
Pulmonary hypertension				
Diagnosed by RHC	−11.70 (2.13)	<0.001		
Diagnosed by echocardiography	−11.69 (1.72)	<0.001	−3.44 (1.77)	0.052
Fontan circulation	−4.40 (1.52)	0.004	−4.26 (1.35)	0.002
Eisenmenger syndrome	−20.08 (3.86)	<0.001	−9.17 (3.69)	0.013
Past medical history				
Hypertension	−4.68 (1.61)	0.004		
Dyslipidemia	−6.67 (2.65)	0.012		
Diabetes	−7.54 (2.30)	0.001		
Hyperuricemia	−2.47 (3.24)	0.446		
Myocardial infarction	−15.28 (3.43)	<0.001	−5.03 (3.22)	0.118
Syncope	−10.30 (2.25)	<0.001	−5.22 (2.05)	0.011
Cerebral infarction	−19.55 (2.59)	<0.001	−15.74 (2.29)	<0.001
Infective endocarditis	−6.04 (2.71)	0.026		
Cancer	−6.22 (2.55)	0.015		
Viral hepatitis	−7.24 (2.83)	0.011	−3.53 (2.47)	0.152

(**Table 2** continued the next page.)

	Univariable (n=1,025)		Multivariable (n=897)	
	Coefficient (SE)	P value	Coefficient (SE)	P value
Employment status				
Part-time or full-time work	Ref.		Ref.	
Unemployed	−14.25 (1.19)	<0.001	−7.90 (1.17)	<0.001
Full-time student	1.31 (1.00)	0.191	−1.83 (1.02)	0.073
Retired or homemaker	−7.03 (1.27)	<0.001	−1.89 (1.29)	0.144
Education level				
University degree	Ref.		Ref.	
Junior college or vocational school	−1.98 (1.13)	0.080	0.02 (0.98)	0.980
High school	−4.89 (0.95)	<0.001	−3.82 (0.83)	<0.001
Less than high school	−7.87 (1.70)	<0.001	−2.05 (1.54)	0.183
Participation in PE classes				
Rare	Ref.		Ref.	
Occasional	5.00 (1.18)	<0.001	1.29 (1.09)	0.240
Frequent	11.23 (1.01)	<0.001	4.27 (1.05)	<0.001
Participation in ECAs				
No club	Ref.		Ref.	
Non-sports club	3.84 (1.09)	<0.001	1.47 (0.97)	0.131
Sports club	8.84 (1.15)	<0.001	3.28 (1.06)	0.002
No. family members	0.21 (0.26)	0.430		
Living alone	2.94 (1.24)	0.018		
Marital status				
Never married	Ref.			
Married or living with partner	−0.59 (0.84)	0.483		
Divorced or widowed	−4.91 (2.15)	0.023		
Religious	1.47 (1.67)	0.379		
Smoking				
Never smoker	Ref.			
Past smoker	−0.60 (1.11)	0.587		
Current smoker	4.00 (1.44)	0.006		
Alcohol consumption				
Non-drinker	Ref.			
Social drinker	4.07 (0.84)	<0.001		
Regular drinker	5.78 (1.31)	<0.001		

Association of the physical component summary with clinical or sociodemographic variables (model P<0.001 in multivariable analysis). [A]CHD complexity was assigned according to the Bethesda classification.[14] [B]Number of patients who underwent surgical repair or a palliative surgical procedure for CHD. Abbreviations as in Table 1.

research in CHD.[12] Two summary scores, a physical component summary score (PCS) and a mental component summary score (MCS), were derived from 8 components of the SF-36,[11] and were the primary outcomes in the present study. Higher scores on the PCS and MCS mean better HRQoL. We also collected sociodemographic data from a self-report questionnaire, including education level, employment status, marital status, participation in physical education classes and school-based extracurricular activities during school days, the number of family members in the household, religious beliefs, smoking, and alcohol consumption. Medical information was obtained through a review of medical records review and included demographics, New York Heart Association (NYHA) functional class, diagnosis of CHD, cardiac repaired status, presence of Fontan circulation and Eisenmenger syndrome, and past medical history, including myocardial infarction, syncope, cerebral infarction, infective endocarditis, cancer, and viral hepatitis. Pulmonary hypertension was defined as mean pulmonary arterial pressure ≥25 mmHg on right heart catheterization[13] or estimated pulmonary artery systolic pressure ≥40 mmHg on echocardiography. The complexity of CHD was assigned according to the Bethesda classification.[14] These patient characteristics were collected as potential predictors of the primary outcomes.

Statistical Analysis

Continuous variables are expressed as the mean±SD and were assessed by the Student's t-test or Wilcoxon rank-sum test as appropriate. Categorical variables are expressed as proportions and were analyzed by Fisher's exact test. Missing data were not imputed for the analysis because less than 3.5% of data were missing for any of the variables. Age–gender weighted average PCS and MCS in ACHD patients were calculated and compared with those in the general Japanese population (n=2,279) reported by Suzukamo et al.[11] For calculating these average scores, we excluded those aged <20 or >79 years due to the lack of normative data for these age groups.[11] Multiple comparisons were

corrected using the Bonferroni method. If the reference value was outside the 95% confidence interval (CI) regarding the ACHD study population, the difference was considered to be statistically significant. Univariable and multivariable linear regression analyses were performed to evaluate the association of PCS and MCS with baseline variables. In the multivariable models, we selected the variables by using a forward stepwise method with variables entered if P<0.05 on univariable linear regression analysis. Because it was previously reported that larger families have positive development effects in childhood and adolescence,[15] but not in midlife,[16] in the general population, the interaction between the number of family members and age for MCS was assessed by the linear regression model with interaction terms, where P value for interaction <0.10 was considered to be statistically significant.

All statistical analyses were performed using JMP® Pro 14.3 (SAS Institute Inc., Cary, NC, USA) and R version 3.5.1 (The R Project for Statistical Computing; https://www.r-project.org/). Results were considered to be statistically significant at two-tailed P<0.05.

Results

The most common diagnosis of CHD was ventricular septal defect (22%), followed by tetralogy of Fallot (15%) and atrial septal defect (11%; **Supplementary Table 2**). The baseline characteristics of the study population are presented in **Table 1**. The prevalence of patients with complex CHD was 60%. Pulmonary hypertension was diagnosed by right heart catheterization in 36 (3.6%) patients and by echocardiography in 56 (5.6%). The prevalence of a past history of myocardial infarction, syncope, and cerebral infarction was 1.4%, 3.2%, and 2.4%, respectively. Approximately 60% of patients had a job and were not married. More than half the patients (51%) had an education level greater than high school. With regard to physical education classes and school-based extracurricular activities during school days, 580 (58%) patients mostly participated in physical education classes and 334 (34%) belonged to a sports club. The mean number of family members was 3.4. There were 88 (8.7%) current smokers in the present study.

We compared age-gender weighted average PCS and

Table 3. Univariable and Multivariable Linear Regression Analysis of Factors Affecting the Mental Component Summary Score of the 36-Item Short-Form Health Survey

	Univariable (n=1,025)		Multivariable (n=935)	
	Coefficient (SE)	P value	Coefficient (SE)	P value
Age	−0.06 (0.02)	0.004		
Male sex	−0.13 (0.65)	0.843		
CHD complexity[A]				
Simple	Ref.		Ref.	
Moderate	−1.81 (0.76)	0.018	−1.18 (0.78)	0.130
Great	−1.69 (0.82)	0.041	−1.82 (0.86)	0.036
NYHA functional class				
I	Ref.			
II	−1.35 (0.71)	0.059		
>II	0.97 (2.12)	0.648		
After intervention for CHD[B]	−0.40 (0.80)	0.616		
Pulmonary hypertension				
Diagnosed by RHC	−0.81 (1.77)	0.646		
Diagnosed by echocardiography	−0.56 (1.43)	0.694		
Fontan circulation	−0.61 (1.23)	0.620		
Eisenmenger syndrome	−3.39 (3.15)	0.283		
Past medical history				
Hypertension	−1.69 (1.30)	0.197		
Dyslipidemia	2.29 (2.15)	0.286		
Diabetes	1.10 (1.87)	0.557		
Hyperuricemia	−1.37 (2.62)	0.602		
Myocardial infarction	−3.40 (2.80)	0.224		
Syncope	−3.87 (1.84)	0.036		
Cerebral infarction	0.84 (2.15)	0.695		
Infective endocarditis	2.68 (2.19)	0.222		
Cancer	−1.66 (2.07)	0.422		
Viral hepatitis	−4.56 (2.29)	0.046	−3.86 (2.31)	0.094
Employment status				
Part-time or full-time work	Ref.		Ref.	
Unemployed	−0.06 (1.02)	0.951	−1.04 (1.09)	0.338
Full-time student	5.96 (0.86)	<0.001	4.05 (0.96)	<0.001
Retired or homemaker	1.82 (1.08)	0.094	0.54 (1.16)	0.639

(**Table 3** continued the next page.)

	Univariable (n=1,025)		Multivariable (n=935)	
	Coefficient (SE)	P value	Coefficient (SE)	P value
Education level				
University degree	Ref.		Ref.	
Junior college or vocational school	−0.65 (0.93)	0.483	−0.65 (0.93)	0.483
High school	1.84 (0.78)	0.019	1.84 (0.78)	0.019
Less than high school	−0.92 (1.40)	0.512	−0.92 (1.40)	0.512
Participation in PE classes				
Rare	Ref.		Ref.	
Occasional	−0.90 (1.02)	0.379	−0.90 (1.02)	0.379
Frequent	1.04 (0.88)	0.236	1.04 (0.88)	0.236
Participation in ECAs				
No club	Ref.		Ref.	
Non-sports club	−1.81 (0.91)	0.046	−2.14 (0.93)	0.022
Sports club	0.25 (0.96)	0.799	−0.26 (0.99)	0.796
No. family members	0.73 (0.21)	0.001	0.49 (0.22)	0.024
Living alone	−1.16 (1.01)	0.251		
Marital status				
Never married	Ref.			
Married or living with partner	−1.24 (0.68)	0.069		
Divorced or widowed	−1.67 (1.74)	0.337		
Religious	1.13 (1.36)	0.406		
Smoking				
Never smoker	Ref.		Ref.	
Past smoker	−1.99 (0.89)	0.026	−1.03 (0.97)	0.289
Current smoker	−4.38 (1.16)	<0.001	−3.74 (1.23)	0.002
Alcohol consumption				
Non-drinker	Ref.		Ref.	
Social drinker	−2.97 (0.69)	<0.001	−1.67 (0.77)	0.030
Regular drinker	−2.98 (1.06)	0.005	−1.53 (1.19)	0.199

Association of the mental component summary with clinical or sociodemographic variables (model P<0.001 in multivariable analysis). [A]CHD complexity was assigned according to the Bethesda classification.[14] [B]Number of patients who underwent surgical repair or a palliative surgical procedure for CHD. Abbreviations as in Table 1.

MCS between ACHD patients and the general Japanese population (**Figure**). In the group aged 20–79 years, PCS was significantly lower in the ACHD group than in the general population (48.8±13.0 vs. 50.0±9.8, respectively), whereas MCS was comparable between the 2 groups (49.9±10.3 vs. 50.0±9.8, respectively). Broken down by age group, PCS was significantly lower in the ACHD patients aged 20–29, 30–39, and 40–49 years (**Figure A**). MCS for those aged 20–29 years tended to be higher for the ACHD patients (95% CI with Bonferroni correction: 49.9–52.8) than in the general population (95% CI with Bonferroni correction: 46.6–50.2; **Figure B**).

Univariable linear regression analysis showed that all the factors, except for status after intervention for CHD, hyperuricemia, the number of family members, and religious beliefs, were significantly associated with PCS (**Table 2**). In contrast, 13 variables were significantly associated with MCS, including age, complexity of CHD, history of syncope and hepatitis, student status, high school degree, being part of a non-sports club, the number of family members, smoking status, and alcohol consumption (**Table 3**). PCS was affected by more factors than MCS. Factors associated with both summary scores were age, complexity of CHD, history of syncope and hepatitis, high school degree, being part of a non-sports club, smoking status, and alcohol consumption.

In multivariable linear regression analysis, 11 variables remained significant predictors for PCS (**Table 2**). Notably, both participation in physical education classes and a sports club during school days were independently associated with better PCS, even after adjusting for clinical and sociodemographic factors, such as NYHA functional class, pulmonary hypertension, past medical history, employment status, and education level. Conversely, MCS was significantly associated with 7 variables on multivariable analysis (**Table 3**). Student status and a higher number of family members were positively correlated with MCS. There was a significant interaction between age and the number of family members on MCS (P for interaction=0.014). When patients were divided into 2 groups by the mean age (35 years) of the overall population, the effect of the number of family members on MCS was significantly different between the 2 groups (P for interaction=0.068; **Supplementary Figure**). A greater complexity of CHD, being part of a non-sports club, being a current smoker, and being a social drinker were associated with poor MCS (**Table 3**).

Discussion

We conducted a large-scale prospective cross-sectional study of HRQoL in ACHD patients. By using a questionnaire survey, including the SF-36, we demonstrated that

PCS was significantly worse in ACHD patients than in the general population in most age groups, whereas MCS was comparable between the 2 groups. We also characterized factors influencing HRQoL in ACHD patients and, more importantly, identified some modifiable factors, such as less exercise during school days and smoking.

Strengths of the Present Study

One of the strengths of this study was that we enrolled a large number of AHCD patients (n=1,025). This enabled us to compare the results of HRQoL in ACHD patients with those in the general population, including the elderly group. Furthermore, medical information was obtained from medical records in addition to self-reported patient information. Thus, we were able to identify independent clinical or sociodemographic contributors related to HRQoL among a wide range of variables in ACHD patients by using multivariable analysis. Although the exact reason why Japanese patients reported the worst QoL among the 15 countries remains unknown,[6,10] our study enrolled patients only from Japanese centers and excluded the possibility of intercountry variation.

Comparison of HRQoL Between ACHD Patients and the General Population

In the present study, PCS was worse in ACHD patients aged 20–79 years compared with the general population, although MCS was comparable. These results are similar to the previous report by Enomoto et al.[5] The authors of that study reported that physical functioning was worse in ACHD patients aged 18–39 years compared with the controls, although MCS was comparable between the 2 groups. We confirmed their results in a large number of ACHD patients across a wide range of age groups. Interestingly, PCS was similar between the 2 groups for those aged 50–59, 60–69, and 70–79 years. This result may contribute to the reduced influence of CHD on health status in ACHD patients who can survive into old age. Unexpectedly, ACHD patients aged 20–29 years tended to have a better MCS than the general population of the same age. Multivariable analysis showed that both being a full-time student and a higher number of family members were associated with a better MCS. In the present study, all patients with a student status were aged 20–29 years, and the number of family members was significantly associated with MCS in young ACHD patients. In addition, the proportion of young ACHD patients living with their parents was higher than in the general population.[17] These 2 factors (i.e., better family support and student status) may contribute to relatively less stressful situations for ACHD patients in this age category, resulting in a better mental component of the HRQoL. However, the high proportion of patients living with their parents indicates that ACHD patients establish their independence later in life than the general population.

Past Medical Conditions Associated With HRQoL

In univariable analysis, PCS and MCS were significantly associated with 32 and 13 variables, respectively. As in the present study, previous studies reported that PCS was affected by more factors than MCS.[6–9] PCS was associated with more clinical factors than MCS (e.g., NYHA functional class, Fontan circulation, Eisenmenger syndrome, history of stroke). Comorbidities, such as heart failure and post-stroke sequelae that result in limitations in physical function, may have contributed to this finding.

Some of the clinical and sociodemographic factors, such as age, NYHA class, cyanosis, being unemployed, and education level, were identified as determinant factors of HRQoL in the present study, as in previous reports.[6–8,18,19] However, little is known about the association of the physical component of HRQoL with a past medical history in ACHD patients. We found that previous cerebral infarction and syncope were significantly associated with PCS.

Factors Associated With the Physical Component of HRQoL

In the present study, both participation in physical education classes and being a member of a sports club were significantly associated with a better PCS, even after adjusting for age, comorbid conditions, and NYHA class. It was previously reported that sports participation was associated with better HRQoL in adolescents and young adults with CHD.[20] Aerobic exercise improved HRQoL in patients with CHD aged 10–15 years.[21] Furthermore, nearly one-third of parents tended to excessively limit the physical activity of their children with CHD.[22] This indicates that in order to make the physical component of HRQoL better in ACHD patients, healthcare providers should assess the risk of physical activity and provide exercise advice to children, their parents, and their schools about the appropriate intensity of sports.[23,24] The present results are consistent with this evidence and further demonstrate that reduced exercise habits in childhood and adolescence are associated with long-term HRQoL in ACHD patients. This association may derive from not only increased exercise capacity and muscle strength, but also other benefits of sports, such as self-efficacy and confidence in physical activity.[25] We also consider that exercise habits during school days is one of the important targets for future intervention programs.

Factors Associated With the Mental Component of HRQoL

Student status was associated with a better mental component of HRQoL in multivariable analysis. It was previously reported that psychological distress was related to a poor mental component of HRQoL in ACHD patients.[9] As CHD patients grow from childhood to adulthood, they need to become independent adults and take responsibility for their own lives. Non-student adults are likely to make choices by themselves about their treatment, work, and life more often than students. ACHD patients may not become aware of various stresses until they are employed. This may cause psychological distress, which results in a worse mental component of HRQoL in ACHD patients. Thus, healthcare providers and patients' parents should pay attention to the decline in the mental component of HRQoL in CHD patients after graduation, including after employment, and support the transition to adulthood.

Family support was one of the factors influencing the mental component of HRQoL in ACHD patients.[9] In the general population, a larger family size was correlated with better mental health in children[26] and employed heads of households in Japan.[27] In contrast, family size was not related to mental distress in the general population in Colombia.[28] In a birth cohort in Scotland, family size was associated with psychiatric admissions but not with suicide.[29] Thus, the effect of family size on mental health seems to be influenced by environmental, cultural, and social factors. In the present study, we demonstrated a positive correlation between the number of family mem-

bers and MCS in young ACHD patients. More detailed studies are needed that focus on the relationship between the mental component of HRQoL in ACHD patients and their families.

Regarding lifestyle factors, current smokers had a worse mental component of HRQoL than never or past smokers in the general population.[30] We observed the same result in our study. The mental component of HRQoL may also be improved by quitting smoking in this population, as reported in the general population.[31]

Participating in a non-sports club was significantly associated with a worse mental component of HRQoL in multivariable analysis. This may reflect introversion or restriction of participation in sports activities in patients who belonged to a non-sports club during school days. Pearsonality traits were also reported to be a significant predictor of HRQoL in ACHD patients.[9]

It was previously reported that poor HRQoL and QoL were associated with depression and anxiety in adolescents and adults with CHD.[32–34] Introversion and smoking were associated with anxiety and depression, respectively, in previous reports.[35,36] The effects of factors associated with MCS may be mediated by psychiatric disorders, such as anxiety and depression. Further studies are needed to clarify this point.

Study Limitations

Several limitations of this study should be mentioned. First, because this is a cross-sectional study, causality cannot be confirmed. There may be different interpretations of the correlation results. For example, smoking may be the result of mental stress. It remains possible that CHD patients with higher physical HRQoL were more likely to have participated in sports clubs. Second, although this is a multicenter study with a large number of ACHD patients, all participants were enrolled only from Japanese institutions. Our results may have limited generalizability. However, some of the factors associated with HRQoL in ACHD in the present study were consistent with previous overseas studies.[6–9] Third, the possibility of selection bias cannot be ruled out because we enrolled only patients who were managed at centers that specialize in ACHD and could complete the SF-36 by themselves. Fourth, there were missing data in the questionnaire because of omission or reluctance to answer personal questions. However, the proportion of missing data was small. The variable with the highest percentage of missing data was participation in school-based extracurricular activities during school days (3.5%), followed by the number of family members (3.1%). Fifth, factors influencing the physical component of HRQoL are complex and influenced by clinical practice as well as the sociodemographic environment. It is conceivable that unmeasured or unknown factors are involved in the study outcomes. Finally, the hemodynamic definition of pulmonary hypertension was modified in the 2022 European Society of Cardiology guidelines.[37] Thus, the results of this study can be interpreted according to the previous criteria.

Conclusions

The physical component of HRQoL was significantly worse in ACHD patients than in the general population, although the mental component of HRQoL was comparable. Participation in physical education classes and a sports club during school days remained significant predictors of a better physical component of HRQoL, even after adjusting for clinical and sociodemographic factors. In contrast, student status, the number of family members, and smoking were significantly associated with a poor mental component of HRQoL. Some of these factors could be targets for future intervention programs to improve HRQoL outcomes in this population.

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Disclosures

S.Y., Y. Sakata, K. Satoh, Y. Saiki, and H.S. are members of *Circulation Journal*'s Editorial Team. The remaining authors have no conflicts of interest to disclose.

IRB Information

This study was approved by the ethics committees of the Tohoku University Graduate School of Medicine (No. 2019-1-492), Iwate Medical University (No. H28-125), Chiba Cardiovascular Center (No. 610), and Chiba Children's Hospital (No. 2016-10-31).

Data Availability

The deidentified participant data will not be shared.

References

1. Constitution of the World Health Organization. *Am J Public Health Nations Health* 1946; **36:** 1315–1323.
2. Anker SD, Agewall S, Borggrefe M, Calvert M, Caro JJ, Cowie MR, et al. The importance of patient-reported outcomes: A call for their comprehensive integration in cardiovascular clinical trials. *Eur Heart J* 2014; **35:** 2001–2009.
3. Mulder BJ. Epidemiology of adult congenital heart disease: Demographic variations worldwide. *Neth Heart J* 2012; **20:** 505–508.
4. Fteropoulli T, Stygall J, Cullen S, Deanfield J, Newman SP. Quality of life of adult congenital heart disease patients: A systematic review of the literature. *Cardiol Young* 2013; **23:** 473–485.
5. Enomoto J, Nakazawa J, Mizuno Y, Shirai T, Ogawa J, Niwa K. Psychosocial factors influencing mental health in adults with congenital heart disease. *Circ J* 2013; **77:** 749–755.
6. Moons P, Kovacs AH, Luyckx K, Thomet C, Budts W, Enomoto J, et al. Patient-reported outcomes in adults with congenital heart disease: Inter-country variation, standard of living and health-care system factors. *Int J Cardiol* 2018; **251:** 34–41.
7. Jackson JL, Hassen L, Gerardo GM, Vannatta K, Daniels CJ. Medical factors that predict quality of life for young adults with congenital heart disease: What matters most? *Int J Cardiol* 2016; **202:** 804–809.
8. Vigl M, Niggemeyer E, Hager A, Schwedler G, Kropf S, Bauer U. The importance of socio-demographic factors for the quality of life of adults with congenital heart disease. *Qual Life Res* 2011; **20:** 169–177.
9. Chen CA, Liao SC, Wang JK, Chang CI, Chiu IS, Chen YS, et al. Quality of life in adults with congenital heart disease: Biopsychosocial determinants and sex-related differences. *Heart* 2011; **97:** 38–43.
10. Apers S, Kovacs AH, Luyckx K, Thomet C, Budts W, Enomoto J, et al. Quality of life of adults with congenital heart disease in 15 countries: Evaluating country-specific characteristics. *J Am Coll Cardiol* 2016; **67:** 2237–2245.
11. Suzukamo Y, Fukuhara S, Green J, Kosinski M, Gandek B, Ware JE. Validation testing of a three-component model of Short Form-36 scores. *J Clin Epidemiol* 2011; **64:** 301–308.

12. Bratt EL, Moons P. Forty years of quality-of-life research in congenital heart disease: Temporal trends in conceptual and methodological rigor. *Int J Cardiol* 2015; **195:** 1–6.
13. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2016; **37:** 67–119.
14. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: The changing profile of congenital heart disease in adult life. *J Am Coll Cardiol* 2001; **37:** 1170–1175.
15. Levitt MJ. Social relations in childhood and adolescence: The convoy model perspective. *Hum Dev* 2005; **48:** 28–47.
16. Ward RA, Spitze G, Deane G. The more the merrier?: Multiple parent-adult child relations. *J Marriage Fam* 2009; **71:** 161–173.
17. Utens EM, Verhulst FC, Erdman RA, Meijboom FJ, Duivenvoorden HJ, Bos E, et al. Psychosocial functioning of young adults after surgical correction for congenital heart disease in childhood: A follow-up study. *J Psychosom Res* 1994; **38:** 745–758.
18. Muller J, Berner A, Ewert P, Hager A. Reduced health-related quality of life in older patients with congenital heart disease: A cross sectional study in 2360 patients. *Int J Cardiol* 2014; **175:** 358–362.
19. Lane DA, Lip GY, Millane TA. Quality of life in adults with congenital heart disease. *Heart* 2002; **88:** 71–75.
20. Dean PN, Gillespie CW, Greene EA, Pearson GD, Robb AS, Berul CI, et al. Sports participation and quality of life in adolescents and young adults with congenital heart disease. *Congenit Heart Dis* 2015; **10:** 169–179.
21. Dulfer K, Duppen N, Kuipers IM, Schokking M, van Domburg RT, Verhulst FC, et al. Aerobic exercise influences quality of life of children and youngsters with congenital heart disease: A randomized controlled trial. *J Adolesc Health* 2014; **55:** 65–72.
22. Cheuk DK, Wong SM, Choi YP, Chau AK, Cheung YF. Parents' understanding of their child's congenital heart disease. *Heart* 2004; **90:** 435–439.
23. Budts W, Borjesson M, Chessa M, van Buuren F, Trigo Trindade P, Corrado D, et al. Physical activity in adolescents and adults with congenital heart defects: Individualized exercise prescription. *Eur Heart J* 2013; **34:** 3669–3674.
24. Longmuir PE, Brothers JA, de Ferranti SD, Hayman LL, Van Hare GF, Matherne GP, et al. Promotion of physical activity for children and adults with congenital heart disease: A scientific statement from the American Heart Association. *Circulation* 2013; **127:** 2147–2159.
25. Ko JM, White KS, Kovacs AH, Tecson KM, Apers S, Luyckx K, et al. Physical activity-related drivers of perceived health status in adults with congenital heart disease. *Am J Cardiol* 2018; **122:** 1437–1442.
26. Grinde B, Tambs K. Effect of household size on mental problems in children: Results from the Norwegian Mother and Child Cohort study. *BMC Psychol* 2016; **4:** 31.
27. Eguchi H, Wada K. Mental health of working-age populations in Japan who provide nursing care for a person at home: A cross-sectional analysis. *J Occup Health* 2018; **60:** 458–466.
28. Martinez LM, Estrada D, Prada SI. Mental health, interpersonal trust and subjective well-being in a high violence context. *SSM Popul Health* 2019; **8:** 100423.
29. Riordan DV, Morris C, Hattie J, Stark C. Family size and perinatal circumstances, as mental health risk factors in a Scottish birth cohort. *Soc Psychiatry Psychiatr Epidemiol* 2012; **47:** 975–983.
30. Mulder I, Tijhuis M, Smit HA, Kromhout D. Smoking cessation and quality of life: The effect of amount of smoking and time since quitting. *Prev Med* 2001; **33:** 653–660.
31. Mino Y, Shigemi J, Otsu T, Tsuda T, Babazono A. Does smoking cessation improve mental health? *Psychiatry Clin Neurosci* 2000; **54:** 169–172.
32. Westhoff-Bleck M, Briest J, Fraccarollo D, Hilfiker-Kleiner D, Winter L, Maske U, et al. Mental disorders in adults with congenital heart disease: Unmet needs and impact on quality of life. *J Affect Disord* 2016; **204:** 180–186.
33. Wang Q, Hay M, Clarke D, Menahem S. Associations between knowledge of disease, depression and anxiety, social support, sense of coherence and optimism with health-related quality of life in an ambulatory sample of adolescents with heart disease. *Cardiol Young* 2014; **24:** 126–133.
34. Drakouli M, Petsios K, Giannakopoulou M, Patiraki E, Voutoufianaki I, Matziou V. Determinants of quality of life in children and adolescents with CHD: A systematic review. *Cardiol Young* 2015; **25:** 1027–1036.
35. Gershuny BS, Sher KJ. The relation between personality and anxiety: Findings from a 3-year prospective study. *J Abnorm Psychol* 1998; **107:** 252–262.
36. Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. Major depression and stages of smoking. A longitudinal investigation. *Arch Gen Psychiatry* 1998; **55:** 161–166.
37. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J* 2022; **43:** 3618–3731.

Supplementary Files

Please find supplementary file(s);
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