Am J Cardiovasc Dis 2021;11(1):53-64
www.AJCD.us /ISSN:2160-200X/AJCD0122134

Original Article

The effect of physical activity on quality of life and serum glucose and cholesterol levels in patients with congenital heart disease

Efrén Martínez-Quintana[1,2], Hiurma Estupiñán-León[2], Liuva Déniz-Déniz[2], Ana Beatriz Rojas-Brito[2], Alejandro Barreto-Martín[2], Jesús María González-Martín[3], Guillermo Miranda-Calderín[4], Fayna Rodríguez-González[5], Antonio Tugores[3]

[1]Cardiology Service Complejo Hospitalario Universitario Insular-Materno Infantil, Las Palmas de Gran Canaria 35016, Spain; [2]Department of Medical and Surgical Sciences, Faculty of Health Sciences, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria 35016, Spain; [3]Research Unit. Complejo Hospitalario Universitario Insular-Materno Infantil, Las Palmas de Gran Canaria 35016, Spain; [4]Rehabilitation Service, Complejo Hospitalario Universitario Insular-Materno Infantil, Las Palmas de Gran Canaria 35016, Spain; [5]Ophthalmology Service. Hospital Universitario de Gran Canaria Dr. Negrín. Las Palmas de Gran Canaria 35019, Spain

Received September 10, 2020; Accepted January 18, 2021; Epub February 15, 2021; Published February 28, 2021

Abstract: As physical activity contributes to quality of life and health, we evaluated its association, as measured by the Global physical activity (GPAQ) questionnaire, on the quality of life (QoL) and serum glucose and cholesterol levels of patients with congenital heart disease (CHD). This cross-sectional study was carried out in 200 adult patients with CHD (17 to 58 years old), of whom 45 had simple defects, 122 moderate defects and 33 great anatomical complexity defects. Physiological complexity was defined as stage A in 74 patients, stage B in 29, stage C in 86 and stage D in 11. The energy expenditure was below 600 Metabolic Equivalent of Task (MET)-minutes per week in 56 (28%) patients, while 144 (72%) were above 600 MET-minutes per week. Physically inactive patients with CHD were significantly more dyslipidemic than active ones, but no significant differences in serum glucose and cholesterol levels were observed. Logistic regression analysis showed that physical activity was associated with a better QoL rating [0.28 (0.10-0.17), P=0.014] and health satisfaction [0.24 (0.09-0.62), P=0.003]. Physically active patients with CHD scored 7.7 and 8.9 points higher, on a 100-point scale, in the physical and social relationships domains respectively, than physically inactive ones. No significant differences were seen in the psychological and the environment domains associated with physical activity. Additionally, a worse New York Heart Association (NYHA) functional class (≥ 2) was identified as a risk factor for dissatisfaction with health [OR 7.48, 95% CI (1.55-47.14), P=0.020], having a significantly negative impact of 8.5 and 7.6, on a 100-point scale, in the physical and psychological domains respectively. In conclusion, physically active patients with CHD had a better QoL assessment, were more satisfied with their health and scored higher in the physical and social relationships domains.

Keywords: Congenital heart disease, physical activity, quality of life, psychological, social relationship, environment

Introduction

Physical activity (PA) is a substantial contributor to global health and has a significant impact on the burden of chronic non-communicable diseases [1]. As more children and adults with congenital heart disease (CHD) increase their life expectancy [2], it has become a topic of interest to know whether PA could influence and, to what extent, the disease burden of adult CHD patients. To date, it is known that CHD patients are less physically active [3-5], even though physical fitness has been heavily associated with future health outcomes in this population [6-9]. In fact, research on patients with CHD show that, even in complex disease scenarios, routine moderate exercise is safe and can be beneficial. Likewise, PA has shown to have a positive impact on the quality of life (QoL), independently of age, PA, and health status [10], and on serum lipid [11] and glucose [12] levels. Because most of these studies have focused on the anatomical classification, and not according to their physiological stage, the latest American guidelines for the management of adults with CHD have proposed a new classification scheme, combining the patient's both anatomic complexity and physiological stage in order to shed light on the subject.

Therefore, the objective of this study was to determine (a) how PA assessment varied according to this new anatomic and physiological classification system proposed for CHD patients, (b) how physical activity level influenced their QoL and (c) evaluate the effect of physical activity on their lipid and serum glucose levels.

Material and methods

Subjects

Two hundred consecutive patients were recruited from a single outpatient CHD unit between October 2018 and April 2019. Inclusion criteria were being, at least, 16 years old, with structural CHD verified by cardiac imaging. Excluded from the study were patients unable to answer the survey, those who did not want to participate or with a life expectancy of less than one year. The researchers conducted the physical activity and QoL questionnaires in a face-to-face interview after ensuring their ability to understand them. Either patients or their legal representatives gave written informed consent to participate in the study, which was approved by the Hospital's Ethics Committee (CEIc/CEIm 890) and was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Clinical data

Patients with CHD were classified into diagnostic groups, according to the newly elaborated AHA/ACC guidelines, that aim to capture the complexity of CHD anatomy and physiology. Cardiac defects were categorized as simple, moderate, or those of great complexity, from an anatomical point of view, and the physiological stage was graded as A, B, C and D from lower to greater severity. Physiological variables included, among others, cyanosis, arrhythmias, hemodynamic sequelae, Eisenmenger syndrome or functional class according to the New York Heart Association (NYHA) [13]. Other clinical variables were systemic arterial hypertension, diabetes mellitus, dyslipidaemia and smoking habit, as previously reported [14]. Body weight and height were measured when the patients were wearing light clothes and barefoot and the body mass index (BMI) was calculated by the formula weight (kg)/[height (m) x height (m)]. The education level (none, primary, middle or university) and marital status (single, divorced, separated, cohabit, married or widower) were also recorded.

Global physical activity questionnaire (GPAQ)

The GPAQ was used to measure subjective PA [15]. It has a total of 16 questions that assess sedentary behavior and three domains where PA was evaluated: work, transport, and leisure-time PA. Calculation of the overall PA was done according to the guidelines on the GPAQ [16]. The participants were asked about the intensity, frequency, and duration of the three domains of PA: 1) at work; 2) during travel or transport and 3) during recreational or leisure time. According to the GPAQ, a metabolic equivalent of task (MET) value of 4 was assigned for moderately intense PA and a value of 8 was assigned for vigorously intense PA. The assigned value MET was then multiplied by the number of days per week of PA and duration on a typical day for each domain to create a PA score as the metabolic equivalent of task-minutes per week (MET-minutes/week). According to WHO guidelines, insufficient PA scores below 600 MET-minutes/week of total energy expenditure, so patients with CHD were classified into two groups: individuals who achieved the recommended PA levels (≥ 600 MET-minutes/week) and those considered as physically inactive (< 600 MET-minutes/week) [16].

World Health Organization (WHO) QoL-BREF questionnaire

QoL was defined as an individual's satisfaction with his or her perceived life comparing with his or her ideal life. The WHO QoL-BREF instrument comprises 26 items, which measure the following broad domains: physical health, psychological health, social relationships, and environment [17]. In addition, the WHO QoL-BREF questionnaire includes two stand-alone questions, one pertaining to the respondents' rated QoL and one related to their satisfaction with their health status. Domain scores of the WHO QoL-BREF instrument scale in a positive direction: 1 point meant nothing, 2 points very little, 3 points more or less, 4 points very much and 5 points extremely. Scores were transformed to a 0-100 scale as recommended [17]. The first two stand-alone questions including five-point response categories were dichotomized to 0: very poor/poor/neither poor nor good overall and 1: good/very good overall. The same applies to satisfaction with health status (0: very dissatisfied/dissatisfied/neither satisfied nor dissatisfied and 1: satisfied/very satisfied).

Blood testing

Blood tests were carried out on the following days after completing the survey. After an overnight fast of at least 10 hours blood samples were drawn for the measurements by spectrophotometric methods of plasma glucose, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) (in milligrams per deciliter) using an Olympus AU 2700 chemistry analyzer (Olympus Diagnostic, Hamburg, Germany).

Statistical analysis

Quantitative variables were expressed as mean and standard deviation or median and quartiles (5-95), depending on the normality of distribution, by using the Kolmogorov-Smirnov test. Qualitative variables were expressed as percentages. The association between categorical variables was examined by using the Pearson chi-square test (χ^2), while the Fisher exact test was used instead for small sample sizes. Continuous data were compared by Student's t-test or Mann-Whitney test for variables with or without normal distribution, respectively. Logistic regression analysis was performed to predict the two questions treated as binary outcomes in the WHO QoL-BREF questionnaire (QoL rating and satisfaction with health) and check the association between them and covariates. The technique of genetic algorithms was used to select the most optimal variables for the logistic regression model. The fitness function was used to minimize the Akaike information criterion error. To check the multicollinearity between the variables the variance inflation factor was calculated. Multiple linear regression was used to predict numerical variables (the 4 domains of the WHO QoL-BREF questionnaire) and check the associations between them and covariates. The statistical program used was the R Core Team 2019, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

CHD population

Two hundred out of 204 patients with CHD, median age 28 (17-58) years old and 102 (60%) male patients accepted their participation and were included in the study. Four patients with Down syndrome, unable to answer the questionnaire, were excluded. No patient was ruled out due to a life expectancy of less than one year. According to anatomical complexity, 45 patients had simple defects, 122 moderate defects and 33 great complexity defects. Meanwhile, according to physiological complexity, 74 patients were in stage A, 29 in stage B, 86 in stage C and 11 in stage D. **Table 1** shows the classification of the different types of CHD according to their anatomical and physiological classification.

PA according to the CHD anatomical and physiological classification

The analysis of demographic, clinical, and physical activity data in patients with CHD according to the anatomical classification showed no significant differences when age, BMI, cardiovascular risk factors, educational level or marital status were compared between patients with mild, moderate or great anatomical complexity, with the exception of vigorous physical activity at work, which was significantly lower in the group of great anatomical complexity (**Table 2**). Likewise, no significant differences were seen when cardiovascular risk factors, sex and any of the physical activity parameters were compared among patients with CHD according to their physiological stage (**Table 3**).

PA, clinical variables, and QoL in CHD patients

When PA was considered, 56 (28%) patients with CHD exercised below 600 MET-minutes per week and 144 patients (72%) had energy

Table 1. Congenital heart disease (CHD) anatomical and physiological classification

Types of congenital heart disease, n	Anatomical	Physiological			
		A	B	C	D
Simple defects					
Native disease					
Isolated small ASD	1	0	1	0	0
Isolated small VSD	20	9	7	4	0
Mild isolated pulmonary stenosis	2	2	0	0	0
Mild repaired conditions	1	1	0	0	0
Previously ligated or occluded ductus arteriosus	2	2	0	0	0
Repaired secundum ASD or sinus venous defect without significant shunt	10	8	0	2	0
Repaired VSD without significant shunt	9	2	2	5	0
Total of simple CHD defects	45	24	1	11	0
Moderate defects					
Repaired or unrepaired conditions					
Aorto-left unrepaired conditions	1	0	1	0	0
Anomalous pulmonary venous connection	1	0	0	1	0
AVSD partial or complete	21	7	3	9	2
Congenital aortic stenosis	16	6	1	9	0
Congenital mitral valve disease	1	0	0	1	0
Coarctation of the aorta	22	18	2	2	0
Ebstein anomaly (spectrum from mild to severe)	2	0	0	2	0
Pulmonary valve regurgitation (moderate or greater)	21	3	5	13	0
Peripheral pulmonary stenosis	2	1	0	0	1
Subvalvular aortic stenosis	7	0	1	6	0
Repaired Tetralogy of Fallot	27	6	3	17	1
VSD with a great shunt	1	0	0	0	1
Total of moderate CHD defects	122	41	16	60	5
Great defects					
Cyanotic CHD (unrepaired or palliated, all forms)	1	0	0	0	1
Double outlet right ventricle	4	2	0	2	0
Fontan procedures	1	0	0	1	0
Single ventricle	2	0	0	0	2
Pulmonary atresia	6	3	0	1	2
Dextro and Levo transposition of the great arteries	18	4	2	11	1
Truncus arteriosus	1	0	1	0	0
Total of great CHD defects	33	9	3	15	6
Total of CHD patients	200	74	29	86	11

n: number of patients, CHD: congenital heart disease, ASD: Atrial septal defect, VSD: Ventricular septal defect, AVSD: atrioventricular septal defect.

expenditure above 600 MET-minutes per week. Physically inactive patients with CHD were significantly more dyslipidemic than active ones (**Table 4**). Also, but without reaching statistical significance, physically inactive CHD patients had higher total and LDL-cholesterol levels and were more diabetic and hypertensive than physically inactive ones. In relation to the QoL test, physically inactive patients with CHD had a significantly lower rated QoL, were less happy with their lives, needed more medical treatment, seemed less energetic and referred a lower capacity to work than physically active patients with CHD. The median values of the 4 domains and the two stand-alone questions of the WHO QoL-BREF questionnaire, in physically active and inactive patients with CHD are shown (**Table 4**).

Table 2. Demographic, clinical, and physical activity data in CHD patients according to anatomical classification

	CHD anatomical classification			P
	Mild	Moderate	Great	
Number of patients	45	122	33	
Age, years	23 (16-70)	30 (16-55)	29 (17-48)	0.185
Sex (male), n	30 (67)	69 (57)	21 (64)	0.445
BMI, kg/m^2	23 (17-34)	24 (17-35)	24 (17-38)	0.991
Arterial hypertension, n	4 (9)	11 (9)	2 (6)	0.859
Diabetes mellitus, n	2 (4)	3 (2)	2 (6)	0.562
Dyslipidaemia, n	8 (12)	16 (13)	1 (3)	0.143
Smoking, n	3 (7)	7 (5)	2 (6)	0.975
Down syndrome, n	3 (7)	10 (8)	1 (3)	0.584
Educational levels				0.064
None, n	6 (13)	10 (8)	0 (0)	
Primary, n	13 (29)	29 (24)	3 (9)	
Medium, n	20 (44)	67 (56)	26 (78)	
University, n	6 (13)	16 (13)	4 (12)	
Marital status				0.508
Single, n	35 (78)	85 (70)	24 (73)	
Divorced, n	1 (2)	1 (1)	0 (0)	
Separated, n	4 (9)	18 (15)	4 (12)	
Cohabit, n	0 (0)	3 (2)	0 (0)	
Married, n	5 (11)	15 (12)	4 (12)	
Widower, n	0 (0)	0 (0)	1 (3)	
Physical activity				
At work vigorous, min/week	0 (0-1506)	0 (0-1692)	0 (0-0)	0.023
At work moderate, min/week	0 (0-2142)	0 (0-2502)	0 (0-2688)	0.717
Transportation, min/week	100 (0-576)	70 (0-840)	140 (0-1422)	0.483
Leisure vigorous, min/week	0 (0-564)	0 (0-436)	0 (0-696)	0.750
Leisure moderate, min/week	0 (0-555)	0 (0-420)	0 (0-693)	0.541
Total of time, min/week	280 (0-3588)	400 (0-3810)	450 (0-3822)	0.894
Time spent sitting, min/week	300 (60-840)	360 (64-840)	360 (60-858)	0.780
Total METs a week	1260 (0-20736)	1680 (0-19860)	1800 (0-15288)	0.937
Physical activity (> 600 MET)[l], n	35 (78)	86 (70)	23 (70)	0.610

n: number of patients, CHD: congenital heart disease, NYHA: New York Heart Association. [l]Physical activity is measured in MET-minutes per week. The data are expressed as median and percentiles (5-95), mean and standard deviation and number and percentages.

Logistic and linear regression analysis

Logistic regression analysis revealed PA as a protective factor associated with a better QoL rating [0.28 (0.10-0.17), P=0.014] and health satisfaction [0.24 (0.09-0.62), P=0.003] (**Table 5**). Similarly, physically active patients with CHD scored 7.7 and 8.9 points higher, on a 100-point scale, in the physical and social relationships domains respectively than physically inactive ones. However, physical activity scores did not obtain statistical significance in the psychological and environment domains after applying the genetic algorithms technique to select those optimal variables for the predictive model. A worse NYHA functional class (≥ 2) was a risk factor for dissatisfaction with health [7.48 (1.55-47.14), P=0.020] having a significantly negative impact of 8.5 and 7.6, on a 100-point scale, in the physical and psychological domains, respectively. Finally, having a physiological stage C or D did not influence the

Table 3. Demographic, clinical, and physical activity according to physiological classification

	CHD physiological classification				P
	Stage A	Stage B	Stage C	Stage D	
Number of patients	74	29	86	11	
Age, years	25 (16-53)	24 (16-52)	32 (17-60)	35 (17-57)	0.005
Sex (male), n	45 (61)	19 (65)	49 (57)	7 (63)	0.885
BMI, kg/m^2	24 (18-38)	22 (17-34)	24 (17-38)	24 (18-28)	0.496
Arterial hypertension, n	5 (7)	3 (10)	9 (10)	0 (0)	0.601
Diabetes mellitus, n	2 (3)	0 (0)	5 (6)	0 (0)	0.399
Dyslipidaemia, n	4 (5)	1 (3)	6 (7)	(0)	0.744
Smoking, n	1 (1)	1 (3)	9 (10)	1 (9)	0.094
Educational levels					0.811
None, n	6 (8)	2 (7)	5 (6)	1 (9)	
Primary, n	14 (19)	9 (31)	20 (23)	2 (18)	
Medium, n	42 (57)	16 (55)	49 (57)	8 (73)	
University, n	12 (16)	2 (7)	12 (14)	0 (0)	
Marital status					0.448
Single, n	61 (82)	23 (80)	51 (60)	9 (82)	
Divorced, n	0 (0)	0 (0)	2 (2)	0 (0)	
Separated, n	5 (7)	3 (10)	18 (21)	0 (0)	
Cohabit, n	0 (0)	0 (0)	1 (1)	0 (0)	
Married, n	8 (11)	2 (7)	12 (14)	2 (18)	
Widower, n	0 (0)	1 (3)	2 (2)	0 (0)	
Physical activity					
At work vigorous, min/week	0 (0-1980)	0 (0-780)	0 (0-1548)	0 (0-0)	0.670
At work moderate, min/week	0 (0.2182)	0 (0-3060)	0 (0-2628)	0 (0-2520)	0.639
Transportation, min/week	100 (0-693)	150 (0-945)	70 (0-840)	0 (0-840)	0.946
Leisure vigorous, min/week	0 (0-450)	0 (0-660)	0 (0-450)	0 (0-480)	0.444
Leisure moderate, min/week	0 (0-630)	0 (0-435)	10 (0-630)	0 (0-225)	0.190
Total of time, min/week	420 (0-3252)	420 (55-3795)	322 (0-4126)	600 (0-2520)	0.735
Time spent sitting, min/week	300 (60-840)	360 (60-900)	300 (60-720)	480 (90-960)	0.576
Total METs a week	1680 (0-22032)	2840 (220-15740)	1500 (0-19710)	2520 (0-10080)	0.716
Physical activity (> 600 MET)[l], n	56 (76)	23 (79)	59 (69)	6 (55)	0.331

n: number of patients, CHD: congenital heart disease, NYHA: New York Heart Association. [l]Physical activity is measured in MET-minutes per week. The data are expressed as median and percentiles (5-95), mean and standard deviation and number and percentages.

rated QoL, the satisfaction with health and any of the four domains of the QoL test.

Discussion

The increase in life expectancy of individuals with CHD has created the need to analyze their QoL in order to evaluate treatments, to increase self-efficacy, social and psychological support and to provide health education. As PA has well-documented benefits for fitness, psychological well-being, and social interaction, as well as a positive effect preventing the risk of acquired heart disease, we wished to analyze its effects on the QoL of patients with CHD according to their most recent classification.

Physical activity (PA) is defined as bodily movement, produced by the contraction of skeletal muscle, that increases energy expenditure above the basal level, a concept that incorporates all types of physical movement and not solely those designated as exercise. Questionnaires are effective tools to assess PA and have been widely used in population-based samples due to its low cost and its capacity to collect detailed information [18]. One of the most widely used is the GPAQ questionnaire [19-21], developed by the WHO for physical activity surveillance, as it has high levels of agreement with objective measurements [22].

The contribution of physical activity to QoL has been known for centuries, appearing to be a graded linear relationship between the volume of physical activity and physical health [23, 24], as also seen in our series. In this context, there

Table 4. Demographic and clinical data according to physical activity and inactivity

	Physical Activity (Mets-minute/week)		P
	< 600 Mets	≥ 600 Mets	
Number of patients	56	144	
Age, years	26 (19-58)	29 (16-53)	0.900
Sex (male), n	31 (55)	89 (62)	0.403
BMI, kg/m^2	24 (17-36)	24 (17-35)	0.834
Arterial hypertension, n	8 (14)	9 (6)	0.067
Diabetes mellitus, n	4 (7)	3 (2)	0.080
Dyslipidaemia, n	12 (21)	13 (9)	0.017
Smoking, n	5 (9)	7 (5)	0.277
Down syndrome, n	5 (9)	9 (6)	0.505
NYHA functional class (≥ 2), n	12 (21)	15 (10)	0.038
Educational levels			0.604
None, n	4 (7)	12 (8)	
Primary, n	15 (27)	30 (21)	
Medium, n	28 (50)	85 (59)	
University, n	9 (16)	17 (12)	
Marital status			0.494
Single, n	45 (80)	99 (69)	
Divorced, n	1 (2)	1 (1)	
Separated, n	5 (9)	21 (14)	
Cohabit, n	0 (0)	3 (2)	
Married, n	5 (9)	19 (13)	
Widower, n	0 (0)	1 (1)	
CHD anatomical classification			0.616
Mild, n	10 (18)	35 (24)	
Moderate, n	36 (64)	86 (60)	
Great, n	10 (18)	23 (16)	
CHD physiological classification			0.331
Stage A, n	18 (32)	56 (39)	
Stage B, n	6 (11)	23 (16)	
Stage C, n	27 (48)	59 (41)	
Stage D, n	5 (9)	6 (4)	
WHO QoL-BREF questionnaire			
Good QoL rating, n	42 (75)	126 (87)	0.014
Satisfied with own health, n	38 (68)	123 (85)	0.002
Physical health domain, 0-100 scale	63 ± 22	72 ± 17	0.007
Psychological domain, 0-100 scale	67 ± 18	71 ± 17	0.129
Social relationships domain, 0-100 scale	64 ± 23	73 ± 20	0.010
Environment domain, 0-100 scale	65 ± 18	68 ± 15	0.438
Blood test data			
Serum glucose, mg/dL	95 (75-130)	94 (81-116)	0.692
Total cholesterol, mg/dL	166 (92-240)	153 (106-230)	0.835
LDL cholesterol, mg/dL	94 (36-158)	84 (47-144)	0.490
HDL cholesterol, mg/dL	49 ± 10	50 ± 11	0.678
Triglycerides, mg/dL	83 (35-334)	86 (43-214)	0.632

n: number of patients, CHD: congenital heart disease, BMI: body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, QoL: quality of life. The data are expressed as median and percentiles (5-95), mean and standard deviation and number and percentages.

Table 5. Logistic and linear genetic algorithms analysis of quality of life in CHD patients

Logistic regression	Genetic algorithms analysis*				
	b	SE	OR	CI (95%)	P
QoL rating					
METs (≥ 600 METs-minute/week)	-1.26	0.51	0.28	0.10-0.17	0.014
Sex (female)	0.75	0.50	2.11	0.79-5.82	0.137
BMI (kg/m^2)	0.10	0.05	1.10	1.01-1.21	0.030
Educational level (Medium & University)	-0.78	0.52	0.46	0.17-1.29	0.130
Marital status (Cohabit & Married)	1.66	0.59	5.25	1.60-17.05	0.005
Satisfaction with health					
METs (≥ 600 METs-minute/week)	-1.42	0.48	0.24	0.09-0.62	0.003
Age (years)	0.03	0.02	1.03	1.0-1.07	0.060
BMI (kg/m^2)	0.11	0.04	1.11	1.02-1.22	0.010
Cardiovascular risk factors† (yes)	-1.13	0.70	0.32	0.07-1.15	0.110
NYHA functional class (≥ 2)	2.01	0.85	7.48	1.55-47.14	0.020
CHD complexity (great)	-2.60	0.97	0.07	0.01-0.42	0.007
CHD physiological stage (C & D)	0.85	0.55	2.34	0.78-6.90	0.120
Linear regression	b	SE		CI (95%)	p
Physical health domain					
METs (≥ 600 METs-minute/week)	7.74	2.70		2.41-13.06	0.005
Sex (female)	-4.03	2.45		-8.86-0.80	0.101
Age (years)	-0.32	0.10		-0.51--0.12	0.001
BMI (kg/m^2)	-0.73	0.24		-1.21--0.26	0.003
NYHA functional class (≥ 2)	-8.54	3.49		-15.42--1.66	0.015
Educational level (Medium & University)	4.39	2.84		-1.21-9.98	0.120
Psychological domain					
Sex (female)	-3.52	2.45		-8.35-1.31	0.150
BMI (kg/m^2)	0.69	0.23		-1.15--0.23	0.003
NYHA functional class (≥ 2)	-7.64	3.43		-14.10--0.57	0.034
Educational level (Medium & University)	3.91	2.78		-1.57-9.39	0.160
Social relationships domain					
METs (≥ 600 METs-minute/week)	8.93	3.47		2.08-15.78	0.010
Age (years)	-0.27	0.12		-0.5--0.03	0.030
Environment domain					
BMI (kg/m^2)	-0.39	0.22		-0.83-0.04	0.080
Cardiovascular risk factors† (yes)	-5.21	3.11		-11.35-0.94	0.100

n: number of patients, CHD: congenital heart disease, BMI: body mass index, NYHA: New York Heart Association. b: beta coefficient, SE: standard error, OR: Odds ratio, CI: confidence interval. *A multivariable analysis was carried out by introducing the variables: MET, sex, age, BMI, †cardiovascular risk factors (if the patient had arterial hypertension, diabetes mellitus, dyslipidaemia or he/she was a smoker), NYHA functional class, CHD anatomical and physiological classification, study level and marital status. Subsequently, the genetic algorithms technique was applied to select only those optimal variables for the predictive model. Bootstrapping technique confirmed the results. Variables that were not significant do not appear in the table.

is compelling evidence that regular physical activity improves physical fitness and contributes to the primary and secondary prevention of several chronic diseases not only in the general population [24] but also in patients with CHD [25].

Regarding psychological health, the second of the four domains assessed, previous cross-sectional and longitudinal studies have indicated that aerobic exercise training may have anti-depressant and anxiolytic effects protecting against the harmful consequences of stress [26]. In fact, physical activity appears to be protective against anxiety disorders in clinical and nonclinical populations and the mechanisms through which exercise produces these effects are likely to involve a combination of biological and psychological factors [27]. Participating in moderate-to-vigorous physical activity over longer durations (weeks or months of regular physical activity) reduces symptoms of anxiety in adults and the risk of developing depression [28]. Likewise, current evidence suggests that sport practice has positive effects on child's and adolescent's wellbeing when maturity status and training load are managed appropriately [29]. This is particularly relevant in patients with CHD, as they continue to face psychosocial and environmental challenges due to impaired peer relationships, family overprotection or physical activity restriction [30]. In our series, no significant differences were seen in the psychological domain between our physically active and inactive patients with CHD, probably because carrying out physical activity ≥ 600 MET-minutes per week does not necessarily mean performing regular and constant physical activity, which is the one that has been mainly associated with an improvement in psychological parameters. On the other hand, an inverse relationship between leisure-time physical activity and mental health has been reported [31], some authors proposing that the social relationships that accompany sports may explain some of its more positive effects [26], which could explain why our physically active patients with CHD scored significantly higher in the social relationships domain than inactive ones.

Finally, being physically active or inactive was not associated with either having a worse anatomic class or a more advanced physiological stage, according to the latest American guidelines [32]. On the contrary, patients with a worse NYHA functional class (≥2) scored significantly lower in the physical and psychological health domains than patients in class I. This is probably due to the fact that functional status, as determined by the NYHA classification, is the most important physiological variable and that others, such as the existence of moderate valvular heart disease, residual shunt or dilation of the aorta, do not provide relevant information in terms of clinical situation or prognosis in the short to medium term. Therefore, the NYHA functional class may have a higher impact on physical activity than the severity itself, as it has been previously reported [30, 33, 34].

Serum cholesterol and glucose levels were not significantly different between physically active and inactive patients with CHD. On one hand, other authors have found no relation between moderate-to-vigorous physical activity and LDL cholesterol levels in adolescents [35] and adult [36]. Interventions targeting sedentary behavior reductions alone or combined with increased physical activity, have found evidence of effectiveness in the improvement, to a small degree, of some cardio metabolic risk biomarkers, such as weight loss, systolic blood pressure or high-density lipoprotein cholesterol [37]. However, unlike HDL cholesterol, the effect of exercise on LDL cholesterol is inconsistent [38]. On the other hand, although numerous studies have shown that decreased physical is associated with altered glucose metabolism [39] we found no significant differences between our physically active and inactive patients with CHD, maybe because of their young age and the lack of significance in their BMI.

We acknowledge some limitations of our study. First, although PA questionnaires have been demonstrated as a feasible, cost-effective, and useful tool for detecting physically inactive adult patients with CHD, self-reported instruments may overestimate physical activity levels in comparison with accelerometers or pedometers [40]. In addition, the face-to-face interview may reduce self-consciousness and lead to variation in responses. Secondly, we measured physical activity depending on whether it was vigorous or moderate, irrespective of the sport type or job. Thirdly, a cross-sectional design does not allow making causal inferences, so, it remains unclear whether physical activity leads to a better QoL or whether patients who have a better QoL just exercise more. Finally, patients with CHD represent a heterogeneous population and the number of patients with great anatomical complexity and high physiological stage was relatively low so it may be difficult to draw final conclusions. Nonetheless, considering that patients with CHD involved in a greater physical activity show a better QoL and that routine moderate exercise is safe [41], even in cases of great complexity [8], physical activity of moderate intensity may be recommended unless a medical restriction is imposed [42]. In fact, only those patients with severe structural, hemodynamic or electrophysiological, sequelae or symptomatic limitation should be restricted from competitive sport participation [43]. Tailored exercise prescription and the promotion of sport activities, without unnecessary limitations, will engage patients with CHD in leisure time and sports practice.

In conclusion, physically active patients with CHD had a better assessment of their rated QoL, were more satisfied with their health and scored higher in the physical and social relationships than physically inactive ones. The NYHA class by itself provides, together with the physical activity, more information about how patients with CHD evaluate their QoL than the physiological classification.

Disclosure of conflict of interest

None.

Address correspondence to: Efrén Martínez-Quintana, Complejo Hospitalario Universitario Insular Materno Infantil, Avenida Marítima del Sur s/n, CP, Las Palmas de Gran Canaria 35016, Spain. Tel: 0034928441360; E-mail: efrencardio@gmail.com

References

[1] Jayasinghe S, Byrne NM, Patterson KAE, Ahuja KDK and Hills AP. The current global state of movement and physical activity - the health and economic costs of the inactive phenotype. Prog Cardiovasc Dis 2020: S0033-0620 (20)30178-X.
[2] Willems R, Werbrouck A, De Backer J and Annemans L. Real-world healthcare utilization in adult congenital heart disease: a systematic review of trends and ratios. Cardiol Young 2019; 29: 553-563.
[3] Brudy L, Hock J, Häcker AL, Meyer M, Oberhoffer R, Hager A, Ewert P and Müller J. Children with congenital heart disease are active but need to keep moving: a cross-sectional study using wrist-worn physical activity trackers. J Pediatr 2020; 217: 13-19.
[4] Dua JS, Cooper AR, Fox KR and Graham Stuart A. Physical activity levels in adults with congenital heart disease. Eur J Cardiovasc Prev Rehabil 2007; 14: 287-293.
[5] Sandberg C, Pomeroy J, Thilén U, Gradmark A, Wadell K and Johansson B. Habitual physical activity in adults with congenital heart disease compared with age- and sex-matched controls. Can J Cardiol 2016; 32: 547-553.
[6] Dimopoulos K, Okonko DO, Diller GP, Broberg CS, Salukhe TV, Babu-Narayan SV, Li W, Uebing A, Bayne S, Wensel R, Piepoli MF, Poole-Wilson PA, Francis DP and Gatzoulis MA. Abnormal ventilatory response to exercise in adults with congenital heart disease relates to cyanosis and predicts survival. Circulation 2006; 113: 2796-2802.
[7] Giardini A, Hager A, Lammers AE, Derrick G, Müller J, Diller GP, Dimopoulos K, Odendaal D, Gargiulo G, Picchio FM and Gatzoulis MA. Ventilatory efficiency and aerobic capacity predict event-free survival in adults with atrial repair for complete transposition of the great arteries. J Am Coll Cardiol 2009; 53: 1548-1555.
[8] Müller J, Hager A, Diller GP, Derrick G, Buys R, Dubowy KO, Takken T, Orwat S, Inuzuka R, Vanhees L, Gatzoulis M and Giardini A. Peak oxygen uptake, ventilatory efficiency and QRS-duration predict event free survival in patients late after surgical repair of tetralogy of Fallot. Int J Cardiol 2015; 196: 158-164.
[9] Udholm S, Aldweib N, Hjortdal VE and Veldtman GR. Prognostic power of cardiopulmonary exercise testing in Fontan patients: a systematic review. Open Heart 2018; 5: e000812.
[10] Anokye NK, Trueman P, Green C, Pavey TG and Taylor RS. Physical activity and health related quality of life. BMC Public Health 2012; 12: 624.
[11] Durstine J, Anderson E, Porter RR and Wang X. Physical activity, exercise, and lipids and lipoproteins. In: Kokkinos P and Narayan P, ediotrs. Cardiorespiratory Fitness in Cardiometabolic Diseases. Springer: Cham; 2019.
[12] Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, Horton ES, Castorino K and Tate DF. Physical activity/exercise and diabetes: a position statement of the american diabetes association. Diabetes Care 2016; 39: 2065-2079.
[13] Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM and Van Hare GF. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 139: e698-e800.
[14] Martínez-Quintana E, Rodríguez-Hernández JL, Rodríguez-González F, Riaño-Ruiz M, Fraguela-Medina C, Girolimetti A and Jiménez-Rodríguez S. Cardiovascular risk factors and arterial thrombotic events in congenital heart disease patients. Int J Clin Pract 2019; 73: 1-8.
[15] World Health Organization Global physical activity questionnaire (GPAQ) analysis guide. Geneva: World Health Organization; 2012.

[16] World Health Organization. Global Physical Activity Questionnaire (GPAQ) analysis guide. Geneva: World Health Organization; 2009.
[17] World Health Organization's. Quality of Life group: WHOQOL-sBREF Introduction. Administration and scoring. Field trial version, 1996.
[18] Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, Lung B, Kluin J, Lang IM, Meijboom F, Moons P, Mulder BJM, Oechslin E, Roos-Hesselink JW, Schwerzmann M, Sondergaard L and Zeppenfeld K; ESC Scientific Document Group. ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. Eur Heart J 2020; ehaa554.
[19] Ainsworth BE, Caspersen CJ, Matthews CE, Mâsse LC, Baranowski T and Zhu W. Recommendations to improve the accuracy of estimates of physical activity derived from self report. J Phys Act Health 2012; 9 Suppl 1: 76-84.
[20] Bull FC, Maslin TS and Armstrong T. Global physical activity questionnaire (GPAQ): nine country reliability and validity study. J Phys Act Health 2009; 6: 790-804.
[21] Wanner M, Hartmann C, Pestoni G, Martin BW, Siegrist M and Martin-Diener E. Validation of the global physical activity questionnaire for self-administration in a European context. BMJ Open Sport Exerc Med 2017; 3.
[22] Cleland CL, Hunter RF, Kee F, Cupples ME, Sallis JF and Tully MA. Validity of the global physical activity questionnaire (GPAQ) in assessing levels and change in moderate-vigorous physical activity and sedentary behaviour. BMC Public Health 2014; 14: 1255.
[23] Gill DL, Hammond CC, Reifsteck EJ, Jehu CM, Williams RA, Adams MM, Lange EH, Becofsky K, Rodriguez E and Shang YT. Physical activity and quality of life. J Prev Med Public Health 2013; 46 Suppl 1: S28-34.
[24] Warburton DE, Nicol CW and Bredin SS. Health benefits of physical activity: the evidence. CMAJ 2006; 174: 801-809.
[25] Bay A, Dellborg M, Berghammer M, Sandberg C, Engström G, Moons P and Johansson B. Patient reported outcomes are associated with physical activity level in adults with congenital heart disease. Int J Cardiol 2017; 243: 174-179.
[26] Salmon P. Effects of physical exercise on anxiety, depression, and sensitivity to stress: a unifying theory. Clin Psychol Rev 2001; 21: 33-61.
[27] Kandola A and Stubbs B. Exercise and anxiety. Adv Exp Med Biol 2020; 1228: 345-352.
[28] U.S. Department of Health and Human Services. Physical Activity Guidelines for Americans, 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018.
[29] McKay CD, Cumming SP and Blake T. Youth sport: friend or foe? Best Pract Res Clin Rheumatol 2019; 33: 141-157.
[30] Kim GB. Psychosocial adjustment and quality of life of adolescents and adults with congenital heart disease. Korean J Pediatr 2014; 57: 257-263.
[31] Carek PJ, Laibstain SE and Carek SM. Exercise for the treatment of depression and anxiety. Int J Psychiatry Med 2011; 41: 15-28.
[32] Williams CA, Wadey C, Pieles G, Stuart G, Taylor RS and Long L. Physical activity interventions for people with congenital heart disease. Cochrane Database Syst Rev 2020; 10: CD013400.
[33] Lane DA, Lip GYH and Millane TA. Quality of life in adults with congenital heart disease. Heart 2002; 88: 71-75.
[34] Connor B, Osborne W, Peir G, Smith M and John A. Factors associated with increased exercise in adults with congenital heart disease. Am J Cardiol 2019; 124: 947-951.
[35] LeBlanc AG and Janssen I. Dose-response relationship between physical activity and dyslipidemia in youth. Can J Cardiol 2010; 26: 201-205.
[36] Celis-Morales CA, Perez-Bravo F, Ibañez L, Salas C, Bailey ME and Gill JM. Objective vs. self-reported physical activity and sedentary time: effects of measurement method on relationships with risk biomarkers. PLoS One 2012; 7: e36345.
[37] Hadgraft NT, Winkler E, Climie RE, Grace MS, Romero L, Owen N, Dunstan D, Healy G and Dempsey PC. Effects of sedentary behaviour interventions on biomarkers of cardiometabolic risk in adults: systematic review with meta-analyses. Br J Sports Med 2020: bjsports-2019-101154.
[38] Wang Y and Xu D. Effects of aerobic exercise on lipids and lipoproteins. Lipids Health Dis 2017; 16: 132.
[39] McLeod A, Schiffer L, Castellanos K, DeMott A, Olender S, Fitzgibbon M, Hughes S, Fantuzzi G and Tussing-Humphreys L. Impact of physical activity and weight loss on fat mass, glucose metabolism, and inflammation in older African Americans with osteoarthritis. Nutrients 2020; 12: E3299.
[40] Larsson L, Johansson B, Wadell K, Thilén U and Sandberg C. Adults with congenital heart disease overestimate their physical activity level. Int J Cardiol Heart Vasc 2018; 22: 13-17.
[41] Opić P, Utens EM, Cuypers JA, Witsenburg M, van den Bosch A, van Domburg R, Bogers AJ, Boersma E, Pelliccia A and Roos-Hesselink JW. Sports participation in adults with congenital heart disease. Int J Cardiol 2015; 187: 175-182.

[42] Reybrouck T and Mertens L. Physical performance and physical activity in grown-up congenital heart disease. Eur J Cardiovasc Prev Rehabil 2005; 12: 498-502.

[43] Budts W, Pieles GE, Roos-Hesselink JW, Sanz de la Garza M, D'Ascenzi F, Giannakoulas G, Müller J, Oberhoffer R, Ehringer-Schetitska D, Herceg-Cavrak V, Gabriel H, Corrado D, van Buuren F, Niebauer J, Börjesson M, Caselli S, Fritsch P, Pelliccia A, Heidbuchel H, Sharma S, Stuart AG and Papadakis M. Recommendations for participation in competitive sport in adolescent and adult athletes with Congenital Heart Disease (CHD): position statement of the Sports Cardiology & Exercise Section of the European Association of Preventive Cardiology (EAPC), the European Society of Cardiology (ESC) Working Group on Adult Congenital Heart Disease and the Sports Cardiology, Physical Activity and Prevention Working Group of the Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2020; 41: 4191-4199.