

Perceived Health Mediates Effects of Physical Activity on Quality of Life in Patients With a Fontan Circulation



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Patients with a Fontan circulation are at risk of a sedentary lifestyle. Given the direct relationship between physical activity and health, promotion of physical activity has the potential to improve outcomes, including quality of life (QOL). This study aimed to describe self-reported physical activity levels in adult Fontan patients and examine associations between physical activity, perceived health status and QOL. The sample consisted of 177 Fontan patients ($M_{age} = 27.5 \pm 7.6$ years, 52% male) who reported their physical activity, perceived health status, and QOL as part of the cross-sectional Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease – International Study. Descriptive statistics and univariate analyses of variance with planned contrasts were computed to describe physical activity characteristics. Mediation analyses tested whether perceived health status variables mediated the association between physical activity and QOL. Forty-six percent of patients were sedentary while only 40% met international physical activity guidelines. Higher physical activity was associated with younger age, lower NYHA class, higher perceived general health, and greater QOL. Patients who commuted by walking and engaged in sports reported better perceived

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health and QOL. Mediation analyses revealed that perceived general health but not NYHA functional class mediated the association between physical activity and QOL ($\alpha\beta = 0.22$, 95% confidence interval = 0.04 to 0.49). In conclusion, Fontan patients likely benefit from regular physical activity, having both higher perceived general health and functional capacity; greater perceived health status may contribute to enhanced QOL. In conclusion, these data support the pivotal role of regular physical activity for Fontan patients. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;124:144–150)

An active lifestyle has the potential to improve clinical status in adults with a Fontan circulation. Nevertheless, physical activity in this population requires unique hemodynamic adjustments that have been suggested to contribute to end-organ damage.¹ This notion, along with other views about the potential dangers of physical activity, has prompted many providers to advise restrictive exercise recommendations for Fontan patients.^{2,3} Such physician advice likely has contributed to both youth and adults with Fontan circulations having lower rates of achieving ideal physical activity targets^{4,5} and a baseline disinclination to engage in physical activity.⁶ Nevertheless, patients with a Fontan circulation are susceptible to the liabilities of a sedentary lifestyle^{4,5} including the potential for muscle loss, poor endothelial function,⁷ and risks to both physiologic and psychosocial health.⁸ To better understand the relationship between physical activity and psychosocial health domains in this population, we conducted the present analyses of a large multinational cohort of Fontan patients. We aimed to describe self-reported physical activity in adult Fontan patients and to examine the relations between physical activity, perceived health status, and quality of life (QOL).

METHODS

The Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease—International Study (APPROACH-IS)⁹ is a cross-sectional study that includes 24 centers across 15 countries (Argentina, Australia, Belgium, Canada, France, India, Italy, Japan, Malta, Norway, Taiwan, The Netherlands, Sweden, Switzerland, and USA). The goal of APPROACH-IS is to examine patient-reported outcomes in a multinational sample of adult congenital heart disease (ACHD). APPROACH-IS was approved by the Institutional Review Board of the University Hospitals Leuven/KU Leuven as well as the Institutional Review Board of each participating center or country, as appropriate and required. Only patients living with a Fontan circulation were included in this study's analyses. Data collection procedures have been described in detail elsewhere.⁹ The study protocol is recorded at ClinicalTrials.gov: [NCT02150603](https://clinicaltrials.gov/ct2/show/study/NCT02150603).

All study data were acquired via participant self-report on a set of questionnaires. *Physical activity* was assessed by items (e.g., walking commute to work, sport participation, weekly hours in minimal, moderate, and vigorous physical activity) from the Health Behaviors Scale – Congenital Heart Disease (CHD).¹⁰ A physical activity score was calculated by summing weekly physical activity and walking commute hours weighted by intensity level. Patients' responses were also used to create a binary

variable assessing whether they met World Health Organization (WHO) guidelines for physical activity (i.e., 150 minutes of moderate aerobics, 75 minutes of vigorous aerobics, or equivalent combination each week).¹¹ *Perceived health* was assessed by patient report of their functional limitations (i.e., NYHA class) and an item on the SF-12v2¹² assessing perceived general health. Lower scores on both items indicate better perceived health. *QOL* was measured by mean scores on the 5-item Satisfaction with Life Scale.¹³ Expanded definitions of the variables measured in APPROACH-IS as well as the interpretation of scores have been provided previously.⁹

Descriptive statistics, independent *t* tests, chi-square tests, and univariate analyses of variance with planned contrasts were computed to describe physical activity in the study sample. Due to the positive skew of physical activity scores (i.e., many patients reported no physical activity hours from sport or commute), this variable was logarithmically transformed. Bivariate Pearson correlations were conducted to examine associations between physical activity, perceived health status variables, and QOL. The PROCESS macro,¹⁴ which utilizes ordinary least squares path analysis and listwise deletion for missing data (<6% excluded from analyses), was used to test whether perceived health status variables (i.e., NYHA class, perceived general health) mediated the association between physical activity and QOL using 1,000 bootstrap samples; demographic and medical covariates (i.e., age, gender, presence of arrhythmia, heart failure status, and past-year admission) were included in the model. PROCESS tests the indirect effect (i.e., the relation between physical activity and QOL that is accountable for by the associations between the effect of physical activity on perceived health status and, in turn, perceived health status on QOL while controlling for physical activity levels) relative to 95% confidence intervals. Statistical significance was defined as 2-tailed $p < 0.05$.

RESULTS

The present study included 177 patients with Fontan circulations from 14 countries. The sample was 52% male with a mean age of 27.5 ($SD = 7.6$) years. Approximately 40% were employed full time, 21% were employed part time, 18% were unemployed or job-seeking, 11% were receiving disability or government financial assistance, and 28% were full-time students. Additional patient demographic and medical characteristics are included in [Table 1](#).

Of all patients, 17.5% reported regularly walking to and from their workplace or school (i.e., walking commuters), 16.9% participated in sports, 19.2% both walked and participated in sports, and 46.3% were sedentary (i.e., no walking

Table 1
Demographic and geographic information for Fontan patients

	Patients (n = 177)
Mean (SD) age (years)	27.5 (7.6)
Male (n = 92)	52.0%
Race/Ethnicity	
White	118 (67.8%)
Asian	41 (23.6%)
Hispanic	8 (4.6%)
Black	4 (2.3%)
Middle-eastern/Arabic	3 (1.7%)
Country	
Argentina	8 (4.5%)
Australia	5 (2.8%)
Belgium	2 (1.1%)
Canada	18 (10.2%)
France	16 (9.0%)
India	21 (11.9%)
Italy	1 (0.6%)
Japan	13 (7.3%)
Malta	4 (2.3%)
The Netherlands	1 (0.6%)
Norway	16 (9.0%)
Sweden	22 (12.4%)
Switzerland	2 (1.1%)
USA	48 (27.1%)
Arrhythmia (present)	80 (45.5%)
Heart failure	
Past, not current	25 (14.6%)
Current	13 (7.6%)
Cardiac admissions in past year (% present)	52 (29.4%)
NYHA functional class	
I	46 (26.7%)
II	81 (47.1%)
III	31 (18.0%)
IV	14 (8.1%)
Perceived general health	
Excellent	15 (8.7%)
Very good	53 (30.6%)
Good	68 (39.3%)
Fair	34 (19.7%)
Poor	3 (1.7%)

Note: NYHA = New York Heart Association.

commute or sports). See Table 2 for univariate analysis of variance results demonstrating differences between subsamples on study variables and Figure 1 for descriptive results on outcomes for the full sample.

Table 2
Univariate ANOVA analyses examining subsample differences in study variables

Univariate results	n	Age		QOL		NYHA Class		Perceived General Health	
		F	p Value	F	p Value	F	p Value	F	p Value
		2.82	0.040	2.32	0.077	2.84	0.039	3.00	0.032
		M (SD)	Contrast p-value	M (SD)	Contrast p-value	M (SD)	Contrast p-value	M (SD)	Contrast p-value
Sedentary	82	28.98 (8.42)	—	4.49 (1.51)	—	2.20 (0.87)	—	2.11 (0.93)	—
Walking commuters	31	25.35 (5.78)	0.024	4.76 (1.23)	0.36	2.23 (0.97)	0.85	2.16 (0.86)	0.80
Sport participants	30	27.93 (7.59)	0.517	4.65 (1.37)	0.58	1.97 (0.91)	0.22	2.24 (0.95)	0.52
Walking and sports	34	25.38 (6.47)	0.020	5.24 (1.24)	0.010	1.72 (0.68)	0.009	2.67 (0.89)	0.004
Total sample	177	27.47 (7.64)	—	4.71 (1.41)	—	2.08 (0.88)	—	2.25 (0.93)	—

Bold values indicate statistically significant results ($p < .05$).

Note: Simple planned contrasts were conducted with the sedentary subsample as the reference group.

NYHA = New York Heart Association; QOL = Quality of life.

Average weekly minutes spent in vigorous or moderate physical activity for the entire sample were 32.4 and 51, respectively, while corresponding times in those who participated in sports were higher (i.e., 88.8 and 141.6, respectively). Further, the 39.5% of patients who met WHO guidelines for physical activity were younger, $M_{\text{age}} = 25.87$ versus 28.52, $t = 2.29$, $p = 0.024$, and reported better NYHA class, 37% Class I, 43% Class II, and 19% Class III/IV versus 20% Class I, 50% Class II, and 30% Class III/IV, $\chi^2 = 7.64$, $p = 0.022$, than those who did not meet guidelines. Of the 65 walking commuters, 83.9% had a commute time of less than 30 minutes. See Table 3 for additional physical activity statistics.

Physical activity scores were inversely related to NYHA class, $r = -0.15$, $p = 0.046$, and age, $r = -0.17$, $p = 0.023$, and were positively related to perceived general health status, $r = 0.21$, $p = 0.006$, and QOL, $r = 0.16$, $p = 0.039$. Further, NYHA class and perceived general health were significantly associated with QOL, $r = -0.33$, $p < 0.001$, and $r = 0.41$, $p < 0.001$, respectively. Correlations between all study variables are presented in Table 4.

Both NYHA class and perceived general health were included simultaneously as parallel mediators of the association between physical activity and QOL in a bootstrapping model with the following covariates: age, gender, presence of arrhythmia, heart failure status, and past-year admission. Physical activity was negatively related to NYHA class and positively related to perceived general health, although only the latter was significantly related to QOL. Furthermore, perceived general health alone mediated the relation between physical activity and QOL (95% confidence interval = 0.04, 0.49). Total variance explained by the model was 22.0%. See Figure 2 for the mediation model.

DISCUSSION

Cardiorespiratory fitness and physical activity are known to improve overall cardiovascular health.^{8,15,16} However, very little is known about typical physical activity levels and health benefits in the most complex forms of congenital heart disease. Our study, the largest to assess physical activity in patients with Fontan circulations, demonstrates that approximately half of Fontan patients are sedentary and only 40% meet WHO recommendations for weekly physical activity. Moreover, we found that physical activity is

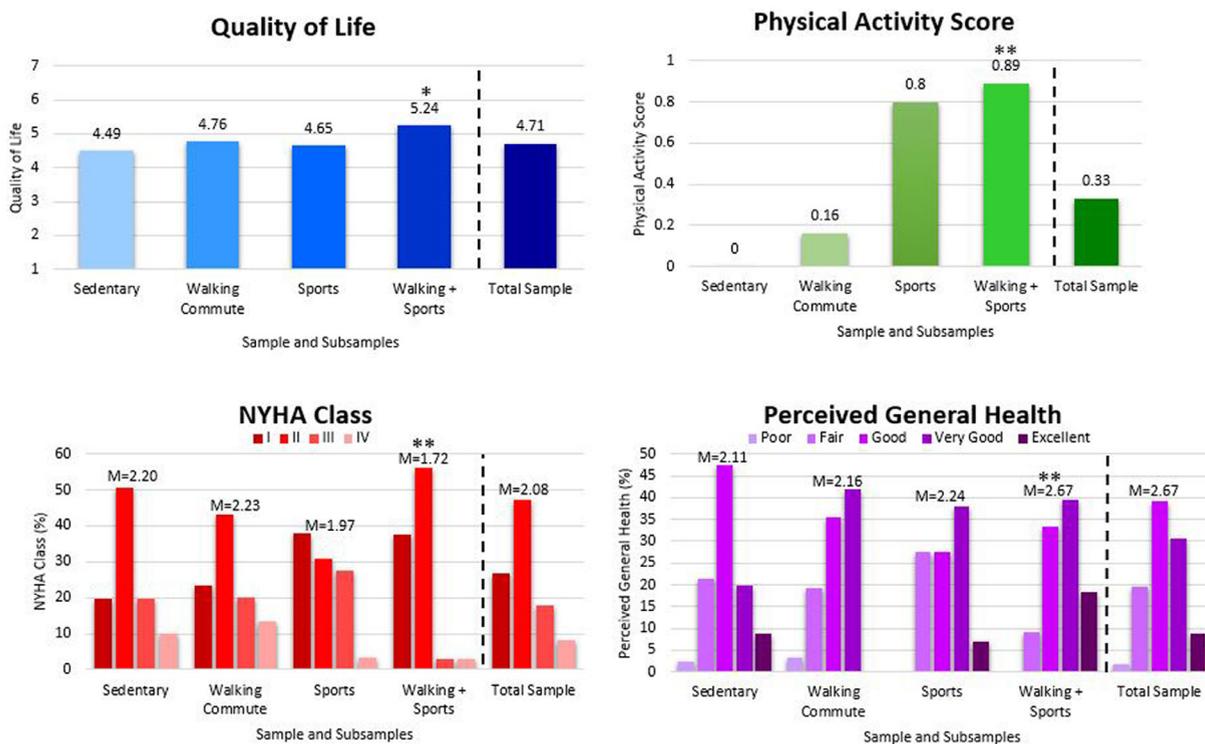


Figure 1. Descriptive data for patients with Fontan circulations and subsamples.

Note: * indicates $p < 0.05$ and ** indicates $p < 0.01$ for subsample comparisons with the sedentary subsample as the reference group. NYHA = New York Heart Association.

associated with younger age, better functional class, improved perceived general health, and superior QOL. We uniquely show that the relation between physical activity and greater QOL is mediated specifically by perceived general health status.

Physical activity has been demonstrated to improve cardiovascular outcomes in the general population;^{4,7,9,17} however, exercise benefits in patients with a Fontan circulation

are more complex. Peak aerobic performance is severely reduced compared with healthy patients¹⁸ due to a combination of relatively fixed pulmonary vascular resistance during exercise, poor myocardial relaxation at higher heart rates, poor skeletal muscle development and strength,¹⁹ and a greater dependence on respiratory pump function.⁷ These factors synergistically decrease preload to the single ventricle, leading to inadequate cardiac output augmentation and

Table 3
Physical activity in patients with Fontan circulations

Characteristic	Full sample (n = 177)		Sport participants only (n = 64)	
	M ± SD	Range	M ± SD	Range
Walk to work/school				
Commute time (minutes)				
<15			26 (41.9%)	
15-30			26 (41.9%)	
30-45			6 (9.7%)	
>45			4 (6.5%)	
Participate in sports				
Yes			64 (36.4%)	
No walking or sports			82 (46.3%)	
Met WHO guidelines			70 (39.5%)	
Weekly physical activity at school (minutes)	8.4 ± 34.8	0-240	22.8 ± 54.6	0-240
Weekly vigorous activity (minutes)	32.4 ± 97.2	0-840	88.8 ± 145.8	0-840
Weekly moderate activity (minutes)	51 ± 117.6	0-720	141.6 ± 160.2	0-720
Weekly minimal activity (minutes)	32.4 ± 116.4	0-1200	89.4 ± 180.6	0-1200
Physical exercise score ^a	0.33 ± 0.42	0-1.49	0.84 ± 0.27	0.21-1.49

Note: WHO = World Health Organization.

^a Variable underwent logarithmic transformation due to skewness.

Table 4
Bivariate correlations between study variables

Variable	Physical activity	NYHA Class	Perceived general health	Quality of life	Age
Physical activity	—				
NYHA Class	-0.15 p = 0.046 n = 172	—			
Perceived general health	-0.22 p = 0.006 n = 173	0.55 p < 0.001 n = 169	—		
Quality of Life	0.16 p = 0.039 n = 173	-0.33 p < 0.001 n = 169	-0.41 p < 0.001 n = 169	—	
Age	-0.17 p = 0.023 n = 177	-0.06 p = 0.410 n = 172	0.14 p = 0.066 n = 173	0.03 p = 0.698 n = 173	—
Sex	-0.07 p = 0.330 n = 177	0.09 p = 0.238 n = 172	0.10 p = 0.198 n = 173	0.09 p = 0.258 n = 173	-0.00 p = 0.979 n = 177
Heart failure	-0.04 p = 0.583 n = 171	0.23 p = 0.003 n = 166	0.14 p = 0.081 n = 167	-0.06 p = 0.417 n = 167	0.15 p = 0.045 n = 171
Arrhythmia	0.04 p = 0.508 n = 176	0.12 p = 0.110 n = 171	0.17 p = 0.027 n = 172	-0.05 p = 0.535 n = 172	0.41 p < 0.001 n = 176
Hospital admission – 1 year	-0.11 p = 0.144 n = 177	0.28 p < 0.001 n = 172	0.22 p = 0.005 n = 173	-0.13 p = 0.100 n = 173	0.14 p = 0.072 n = 177

Note: Coefficients related to sex, arrhythmia, and hospital admissions represent point-biserial correlations; all other coefficients represent bivariate Pearson correlations. Gender was coded such that the higher value indicated females. Lower values of NYHA class and perceived general health indicate better perceived health.

NYHA = New York Heart Association.

profound rises in venous pressure during exercise.^{7,20} Encouragingly, new evidence suggests that exercise training may positively impact aerobic capacity and pulmonary function in Fontan patients.²¹ Beneficial effects are particularly notable at submaximal exercise²¹ and appear to be mediated by greater respiratory muscle strength, better ventilatory efficiency, and a greater resting cardiac output.²⁰ These functional benefits have the potential to improve physical and psychosocial outcomes, including increasing exercise capacity,²² in this at-risk population.^{4,21}

This study provides further evidence for an association between physical activity levels, better patient-perceived health status, and superior QOL in this cohort with complex ACHD. This observation has been previously noted in non-CHD cohorts²³ and in Fontan patients in whom routine physical activity is associated with a better QOL regardless of exercise capacity,⁴ which encouragement of regular endurance training may further improve.²¹ Our results uniquely suggest that the mechanism by which physical activity relates to improved QOL is through greater

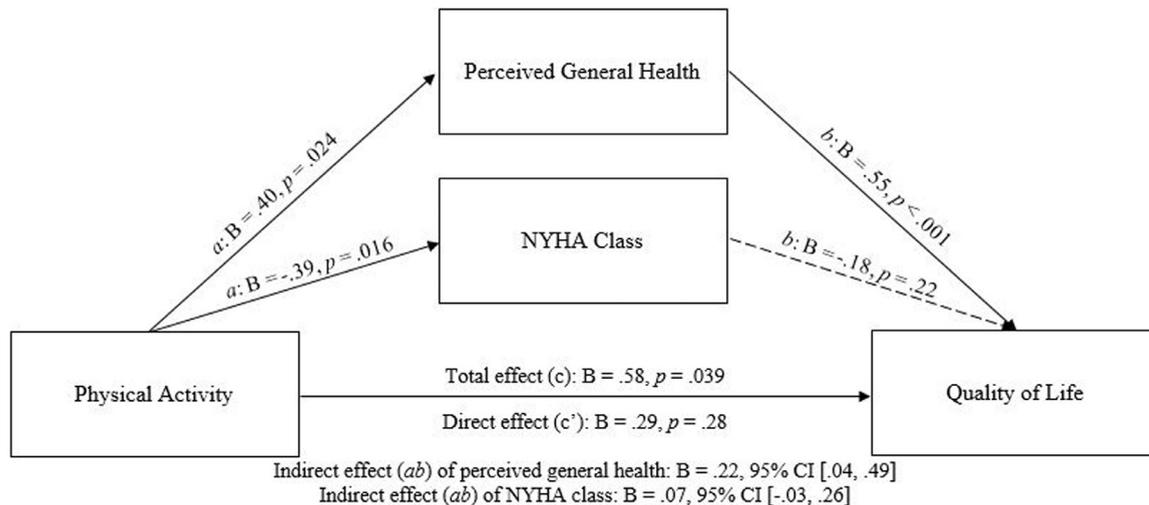


Figure 2. Mediation model utilizing data from the entire sample of patients with Fontan circulations. NYHA = New York Heart Association.

perceived health status as opposed to preventing functional decline. In other words, it was patients' beliefs about their health in general, not their reported cardiac-related physical limitations, which mediated the association between physical activity and QOL. Indeed, exercise capacity correlates rather poorly with QOL in Fontan patients,²⁴ whereas perceived health status has been shown to relate to QOL.²⁵ It must also be acknowledged that self-reported physical limitations due to symptoms associated with heart failure, obesity, hypertension, anxiety, and other co-morbidities conspire to both limit an individual's ability to be physically active and reduce perceived general health and QOL. Nonetheless, the present data suggest that physical activity may improve not only physiological parameters but also patient-perceived health status, the latter of which may in fact be more important in ameliorating QOL.

Given these findings, encouraging patients with Fontan circulations to be physically active may be particularly important. In fact, perceived health status and QOL may be 2 of the few modifiable outcomes that can effectively be targeted in this complex population.² Interestingly, in a recent study of pediatric Fontan patients, transplant-free survival correlated only with ventricular function and patient-reported functional health status,²⁶ suggesting the possibility that survival benefits may be conferred through regular physical activity via its effect on health perceptions. Despite these potential benefits and the lack of demonstrated liability,^{3,27} Fontan patients continue to be restricted in their physical activity by healthcare professionals. In one study, 61% of pediatric patients with Fontan circulations had their exercise restricted by physicians.²⁸ The present findings provide preliminary evidence that physical activity improves psychological and functional QOL which likely outweighs any risk of exercise and should encourage liberalization of recommendations in clinical practice about physical activity. As older patients in our study were less likely to engage in physical activity, ACHD providers may need to engage in regular discussions about appropriate physical activity as their patients age. ACHD providers should nevertheless individualize physical activity recommendations to reduce the likelihood that patients will engage in unsafe exercise or attribute physical limitations to poor physical fitness rather than physiological attributes of the single ventricle. A recent review of cardiac rehabilitation programs for patients with Fontan circulations concluded that such individualized interventions should become standard of care given the improvements on physiological and psychosocial outcomes.²⁷

There are multiple limitations to the present study. Recall bias is a concern for studies using patient-reported outcomes; thus, reports of regular physical activity may be inaccurate. More objective measures of physical activity may lead to different conclusions.²⁹ Caution should also be taken when generalizing results to patients who are not followed by specialized ACHD care centers. There are possible confounding variables, including geographic and cultural differences (e.g., sports participation may be less available or acceptable in some areas), which might have impacted results. Importantly, the present analysis was cross-sectional, thereby precluding the ability to derive conclusions about causation and clinical significance; future large, longitudinal studies that include both objective

and patient-reported measures of physical activity and allow for the determination of clinical significance are therefore needed. In addition, despite the statistical significance of the correlations observed between study variables, the somewhat low magnitude of the correlations precludes our ability to determine the clinical significance of these associations. The present data are thus intended to be hypothesis generating to direct future research.

Although almost half are sedentary, the present study suggests that patients with Fontan circulations experience benefits from regular physical activity in both perceived general health and in functional capacity. The beneficial effects on perceived health status may contribute to a better QOL. These data underscore the potential benefits of recommending regular individualized physical activity to Fontan patients.

Disclosures

The authors have no conflicts of interest to disclose.

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