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Original Article

Exercise capacity and muscle strength in patients who have undergone the Fontan procedure: a retrospective follow-up study

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ABSTRACT

Background. Due to their relationship with clinical progression, follow-up of exercise capacity and muscle strength is important for optimal disease management in patients who have undergone the Fontan procedure. We aimed to retrospectively analyze exercise capacity and muscle strength trajectory over approximately 2 years.

Methods. Exercise capacity was assessed using an exercise stress test with the modified Bruce protocol on a treadmill, hand grip and knee extensor strength using a hand dynamometer, and body composition using a bioelectrical impedance device. Exercise capacity, muscle strength, and body composition follow-up data recorded between 2020 and 2022 were compared.

Results. Fifteen patients [median age from 17 (first assessment) to 18 years (last assessment), 5 females)] with a 20-month median follow-up time were analyzed retrospectively. There was an increase in weight, height, body mass index, and body fat weight ($p<0.05$). There was a tendency for increased handgrip strength (%) ($p=0.069$), but no significant difference was observed in the knee extensor strength of patients during the follow-up period ($p>0.05$). The changes in heart rate (HR) and oxygen saturation were higher in the last test than in the first test ($p<0.05$). Maximum HR (HRmax), % predicted HRmax and HR reserve recorded during the test and HR 1 minute after the test were similar between the first and last tests ($p>0.05$).

Conclusions. After 20 months of follow-up, exercise capacity and muscle strength did not decline; instead, the body mass index and fat weight increased. Patients who have undergone the Fontan procedure may not be experiencing a decline in exercise capacity and muscle strength over relatively short time periods during childhood, adolescence, and early adulthood.

Key words: Fontan procedure, Fontan circulation, exercise capacity, muscle strength, follow-up, exercise testing.

The importance of rehabilitative management in patients who have undergone the Fontan procedure (hereafter referred to as "Fontan patients" for brevity) has increased due to their longer life expectancy thanks to medical advancements. Exercise is crucial for providing better disease management as a diagnostic and therapeutic tool in the Fontan population.[1] Decreased exercise capacity is common in Fontan patients due to a variety of potential factors such as primary diagnosis, Fontan physiology, and pre-and postoperative clinical characteristics. The four main factors implicated in decreased exercise capacity in the Fontan circulation are preload failure, chronotropic incompetency, restrictive lung problems, and underlying and residual lesions

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such as no subpulmonary ventricle, valve disease, and systemic ventricular dysfunction. These are usually caused by the absence of a subpulmonary pump and high systemic venous pressure, which are specific to the physiology of the Fontan circulation.[2]

In addition, peripheral muscle strength is an extracardiac factor that can affect exercise capacity in Fontan patients.[1-3] It is accepted that the pump effect created by peripheral muscles is important in increasing preload and therefore stroke volume during exercise in Fontan patients without a subpulmonary ventricle.[4] Fontan-associated myopenia and increased adiposity are common in Fontan patients. Furthermore, increased adiposity is linked to an increased risk of Fontan failure or moderate-to-severe ventricular dysfunction.[5] Secondary sarcopenia is an adjunctive predictor of hospitalization and so may lead to a negative prognosis in this population.[6] Turquetto et al.[7] reported that reduced skeletal muscle strength is associated with suboptimal peripheral blood supply and diminished exercise capacity in Fontan patients.

The relationship between exercise capacity and clinical status has previously been reported in Fontan patients. The positive exercise capacity trajectory during childhood was linked to improved clinical status in adulthood and a significant decrease in exercise performance was associated with worse functional status in these patients.[8,9] Therefore, follow-up data obtained via periodic assessments may be of prognostic importance for clinical status and medical and rehabilitative treatment in Fontan patients. The present study aimed to retrospectively analyze the exercise capacity and muscle strength follow-up data of Fontan patients obtained between 2020 and 2022.

Materıals and Methods

Study design

This observational follow-up study was carried out retrospectively using the data of Fontan patients who were followed up in Hacettepe University's Faculty of Medicine, Department of Pediatric Cardiology and who were referred to Hacettepe University's Faculty of Physical Therapy and Rehabilitation, Cardiopulmonary Rehabilitation Unit in 2020-2022. The Hacettepe University Non-interventional Clinical Research Ethics Board approved the study (06.09.2022, GO22/786). The parental written informed consent form and the child informed assent form for patients aged 8-17 years as well as the written informed consent form for patients aged 18 years and older were waived.

Procedure and participants

The medical information of each patient was obtained from clinical records. Echocardiographic measurements were performed by a pediatric cardiologist and the exercise stress test, peripheral muscle strength test, and body composition test by a pediatric cardiologist and specialist physiotherapist during routine controls in the Department of Pediatric Cardiology and Cardiopulmonary Rehabilitation Unit. All assessments were performed by the same pediatric cardiologist and specialist physiotherapist during the follow-up.

After a detailed clinical examination of each patient, consisting of a physical examination and imaging and laboratory tests, a pediatric cardiologist confirmed their eligibility to participate in the tests. The patients meeting the following criteria were included: those between the ages of 8 and 50 years, who had undergone the Fontan operation, who were clinically stable, and had no change in ongoing medication therapy adversely affecting clinical stability in the last one year, and had at least one year follow-up after the operation. Patients unable to cooperate in the assessments and/or who had a neurological, musculoskeletal, or cognitive disorder that would affect the tests were excluded.

Assessments

Clinical characteristics

The medical and clinical information including age, sex, weight, height, age at Fontan operation, initial diagnosis, technique of Fontan surgery, functional ventricle, and fenestration was obtained from a physical examination and clinical records. The hemoglobin (Hb) and brain natriuretic peptide (BNP) values of the patients at the last outpatient visits were also recorded. Echocardiographic measurements were performed using a GE Vivid E9 with XDclear (GE Healthcare, Horten, Norway) or EPIQ CVx (Philips Medical Systems, Andover, MA, USA) according to the standards of the American Society of Echocardiography.[10] The main diagnoses of the Fontan patients and other echocardiographic findings (functional ventricular structure, Fontan pulsatility, and presence of fenestration) were noted from the echocardiography reports.

Exercise capacity

Exercise capacity was assessed with an exercise stress test using the modified Bruce protocol on a treadmill ergometer (GE T2100-ST2, GE HealthCare, WI, USA).[11-13] Heart rate (HR) and electrocardiography (ECG) changes were monitored closely during the rest, test, and recovery periods. Every 3 min during the test and in the recovery period, perceived dyspnea, leg fatigue, and fatigue were assessed using the modified Borg scale; systolic (SBP) and diastolic blood pressure (DBP) and oxygen saturation (SpO_2) were measured with a sphygmomanometer and pulse oximeter, respectively. Additionally, maximum HR (HRmax), heart rate reserve (HRR), and HR 1 min immediately after cessation of exercise (HRR_1_min) were recorded. The exercise stress test was terminated with the exhaustion of the participant, indicated by symptoms such as dyspnea, leg fatigue, fatigue, chest pain, or HR reaching 90% of predicted HRmax.[11]

Peripheral muscle strength

Knee extensor muscle strength was measured using a hand dynamometer (Lafayette Instrument Inc., Lafayette, IN, USA). The physiotherapist held the dynamometer while the patient applied maximum force to it for 5 s and the muscle force was gradually overcome; the test ended at the moment the extremity gave way. The highest value of the dominant leg achieved in three trials was used as the strength measure and recorded in kilograms.[14] Predicted percentages of normal values for children and adults were calculated by age and sex and were used in the interpretation of the measurements.[15,16]

Hand grip strength was measured using a hand dynamometer (Jamar, Sammons Preston, Rolyon, Bolingbrook, IL, USA). Measurements were obtained using standard procedures on the right and left sides, with the arms at the side of the trunk, the elbow in a 90-degree flexion position, and the forearm and wrist in a neutral position.[17] The highest value of three measurements of the dominant hand was accepted as hand grip strength and recorded in kilograms.[18] Predicted percentages of normal values for children and adults were calculated by age and sex and were used in the interpretation of the measurements.[19,20]

Body composition

Body composition was evaluated by bioelectrical impedance analysis. A Tanita Body Fat Analyzer (model TBF 300, Tokyo, Japan) was used to analyze body mass index (BMI), body fat, and lean body weight.[21] The fat-free mass index (FFMI) was recorded. It was calculated by dividing the lean body mass by the height in meters squared (kg/m^2).[22]

Statistical analysis

The statistical analyses were performed using SPSS v. 26.0 (IBM, Chicago, IL, USA). Descriptive data were presented as median (interquartile range) or number (percent) as appropriate.

Wilcoxon's test or Fisher's exact test was used to compare the follow-up data between the first and last assessment. A p-value of less than 0.05 was considered statistically significant.

Results

Follow-up data on exercise capacity, muscle strength, and body composition recorded between 2020 (first assessment) and 2022 (last assessment) from 15 Fontan patients (5 women) with a median follow-up period of 20 months were retrospectively analyzed. The clinical characteristics are presented in Table I. Although there was a difference in the age of the patients at the first and last assessment (p<0.001), there was no change in the age groups (<12 years, 12-17 years, ≥18 years) (p=0.805).

There was an increase in the weight, height, BMI, and body fat weight of the patients during the follow-up (p<0.05, Table II). Although it was not statistically significant, there was an increase in other body composition parameters as well (p>0.05, Table II). Furthermore, the median BMI z-score for pediatric Fontan patients (<18 years) was -0.59 (1.26) at the first assessment and -0.52 (1.50) at the last assessment (p=0.499). The BMI z-scores of pediatric Fontan patients ranged between -2SD and 2SD. Only one patient had a

Table I. Clinical characteristics (n=15).

Characteristics			
Age at Fontan operation (years)	7.00 (7.00)		NA
Follow-up time (months)	20 (7)		NA
Sex (female/male)	5 (34) / 10 (66)		NA
Main diagnosis			
Tricuspid atresia	6 (40)		NA
Double inlet right ventricle	2 (14)		NA
Double outlet right ventricle	2 (14)		NA
Ventricular septal defect	4 (26)		NA
Hypoplastic left heart syndrome	1 (6)		NA
Functional ventricular structure			
Left ventricle	9 (60)		NA
Right ventricle	5 (33)		NA
Undetermined	1 (7)		NA
Technique of Fontan surgery			
Lateral tunnel	1 (7)		NA
Extracardiac conduit	5 (33)		NA
Intra-/extracardiac conduit	9 (60)		NA
Pulsatility (yes/no)	5 (33) / 10 (67)		NA
Fenestrated Fontan	9 (60)		NA
	First assessment	Last assessment	p*
Age (years)	17.00 (9)	18.00 (9)	<0.001*[a]
<12 years	4 (26.70)	3 (20)	
12-17 years	5 (33.30)	4 (26.70)	<0.001*[b]
≥18 years	6 (40.00)	8 (53.30)	
Hemoglobin (g/dl)	14.75 (2.72)	14.95 (2.05)	0.551[a]
BNP (ng/L)	10.50 (12.75)	10.50 (7.15)	0.859[a]

BNP: brain natriuretic peptide, Data are presented as n (%) or median (interquartile range).
[a]Wilcoxon's test was performed. [b]Fisher's exact test was performed.
*Statistical significance is set at p<0.05.

Table II. Body composition and peripheral skeletal muscle strength (n=15).

Characteristics	First assessment (<18 years, n=9)	Last assessment (<18 years, n=7)	p*,a
Body composition			
Weight (kg)	51.30 (32.30)	53.40 (35.00)	0.001*
	(24.00 - 78.50)	(28.00 - 86.00)	
<18 years	38.70 (26.13)	46.00 (29.00)	0.018*
	(24.00 - 57.50)	(28.00 - 64.00)	
z-score	-0.63 (1.40)	-.56 (1.62)	0.091
	(-1.42 - 0.37)	(-1.57 - 0.44)	
Height (cm)	159.00 (31.00)	165.00 (22.00)	0.005*
	(122.00 - 181.00)	(130.00 - 182.00)	
<18 years	150.00 (24.50)	153.00 (28.00)	0.027*
	(122.00 - 165.00)	(130.00 - 170.00)	
z-score	-0.38 (1.47)	-0.56 (1.94)	0.499
	(-2.07 - 0.51)	(-2.15 - 0.61)	
Body mass index (kg/m^2)	19.70 (5.60)	19.85 (7.41)	0.008*
	(13.50 - 26.00)	(15.48 - 26.40)	
<18 years	17.40 (4.76)	19.11 (5.58)	0.066
	(13.50 - 20.30)	(15.48 - 22.77)	
z-score	-0.59 (1.26)	-0.52 (1.50)	0.499
	(-1.62 - 0.18)	(-1.50 - 0.46)	
Body fat weight (kg)	8.02 (8.09)	9.85 (16.39)	0.008*
	(1.20 - 18.80)	(1.40 - 21.58)	
Lean body weight (kg)	41.10 (28.18)	46.02 (21.56)	0.112
	(22.32 - 65.40)	(26.60 - 64.42)	
Fat free mass index (kg/m^2)	15.57 (5.36)	16.80 (3.74)	0.733
	(7.07 - 19.96)	(13.79 - 19.75)	
Peripheral skeletal muscle strength			
Handgrip strength (kg)	30.00 (22.00)	32.00 (18.00)	0.003*
	(12.00 - 50.00)	(16.00 - 52.00)	
Handgrip strength (% predicted)	83.91 (28.88)	96.47 (10.30)	0.069
	(60.04 - 146.34)	(71.29 - 145.45)	
Knee extensors strength (kg)	27.60 (11.60)	27.15 (11.45)	0.256
	(12.00 - 39.30)	(16.00 - 41.20)	
Knee extensors strength (% predicted)	65.49 (34.89)	58.78 (40.91)	0.372
	(45.43 - 136.44)	(47.64 - 115.31)	

Data are presented as median (interquartile range) (min-max).
[a]Wilcoxon's test was performed. *Statistical significance is set at p<0.05.

height z-score below -2SD at both the first and last assessments (Table II).

The data for follow-up peripheral muscle strength are presented in Table II. At the end of follow-up, there was an increase in handgrip strength in kilograms ($p<0.05$) and a tendency for increased handgrip strength as a percentage ($p=0.069$). However, no significant difference was observed in knee extensor muscle strength ($p>0.05$).

The changes in vital signs including HR, SpO_2, SBP/DBP, dyspnea, leg fatigue, and fatigue

Table III. Exercise stress test findings (n=15).

Characteristics	First assessment	Last assessment	p*,a
Test protocol			
Time (s)	822.00 (183.25)	806.50 (148.00)	0.570
	(586.00 - 918.00)	(636.00 - 895.00)	
Speed (km/h)	5.50 (1.50)	5.50 (0)	0.680
	(4.00 - 6.80)	(4.00 - 5.50)	
Grade (%)	14.00 (2.00)	14.00 (0)	0.655
	(12.00 - 16.00)	(12.00 - 14.00)	
Vital signs (Δ)			
HR (bpm)	33.50 (24.25)	42.00 (19.00)	0.008*
	(1.00 - 81.00)	(22.00 - 68.00)	
SpO_2 (%)	-1.00 (5.00)	-3.00 (4.00)	0.020*
	(-6.00 - 2.00)	(-7.00 - 0.00)	
SBP (mmHg)	17.50 (16.50)	26.00 (8.50)	0.065
	(-8.00 - 50.00)	(10.00 - 35.00)	
DBP (mmHg)	10.00 (15.50)	15.00 (16.50)	0.069
	(-9.00 - 30.00)	(2.00 - 30.00)	
Dyspnea (MBS)	2.00 (3.00)	3.25 (3.25)	0.345
	(0.00 - 7.00)	(-0.50 - 5.00)	
Leg fatigue (MBS)	2.00 (2.25)	3.00 (3.38)	0.138
	(0.50 - 5.00)	(0.00 - 7.00)	
Fatigue (MBS)	2.00 (3.25)	1.75 (3.75)	0.550
	(0.00 - 7.00)	(0.00 - 7.00)	
Other cardiac parameters			
HRmax (bpm)	178.50 (16.50)	181.00 (14.50)	0.432
	(141.00 - 200.00)	(123.00 - 196.00)	
HRmax (% predicted)	89.50 (8.50)	89.50 (7.00)	0.775
	(67.00 - 96.00)	(60.00 - 95.00)	
HRR (bpm)	21.00 (20.00)	23.00 (21.00)	0.198
	(7.00 - 70.00)	(15.00 - 90.00)	
HRR_1_min (bpm)	26.50 (16.25)	29.50 (13.50)	0.167
	(3.00 - 45.00)	(6.00 - 39.00)	

DBP: diastolic blood pressure, MBS: modified Borg scale, HR: heart rate, HRR: heart rate reserve, HRR_1_min: heart rate recovery 1 minute after test, SBP: systolic blood pressure, SpO_2: oxygen saturation, .
Data are presented as median (interquartile range) (min-max).
[a]Wilcoxon's test was performed. *Statistical significance is set at $p<0.05$.

recorded immediately before the test and during active recovery are presented in Table III. The changes in vital signs were similar except for HR and SpO_2 between the first and last assessments ($p>0.05$, Table III). The changes in HR and SpO_2 were higher in the last test than in the first test ($p<0.05$). Desaturation (a reduction in $SpO_2 \geq 4\%$) was recorded in four (26%) and six patients (40%) in the first test and last test, respectively ($p=0.700$). Additionally, during both tests, the patients reached a median of 89% and 90% predicted HRmax, respectively. HRmax, % predicted HRmax, HRR, and HRR_1_min were similar between the first and last tests ($p>0.05$).

All patients performed and completed the first and last exercise stress test with no adverse events in median times of 13 min 52 s and 13 min 29 s, respectively ($p>0.05$, Table III). The median peak speed was 5.50 km per hour and the grade was 14% in both exercise stress tests ($p>0.05$, Table III).

Discussion

After 20 months of follow-up, exercise capacity was similar, but HR increase and oxygen desaturation were higher compared to a similar exercise test workload in the last assessment in Fontan patients. In addition to the increase in body composition parameters including height, body weight, body fat weight, and BMI, there was also a tendency for higher handgrip strength in the Fontan patients. Exercise capacity and muscle strength may not decline in these patients over relatively short time periods during childhood, adolescence, and early adulthood.

A serial evaluation of exercise capacity may be important and predictive in terms of determining the current clinical status, prognosis, and adverse cardiovascular events in Fontan patients. In follow-up studies, decreased exercise capacity over time was generally reported in Fontan patients. In a previous study, the 5-year risk of adverse cardiovascular events was 30%, and a decrease of ≥3% in predicted peak oxygen consumption (VO_2) points/year was associated with an increase in this risk.[23] Ohuchi et al.[8] reported that a positive exercise capacity trajectory in childhood can lead to better exercise capacity, hemodynamics, pulmonary function, hepatorenal function, and body composition in adulthood in Fontan patients. In their well-designed 12-year follow-up study, Atz et al.[9] reported that a significant decrease in exercise performance was associated with worse functional status.

In contrast to the studies mentioned, there was no decrease in the exercise capacity of the patients during the follow-up period in our study. In general, exercise capacity increases during physical growth and reaches its peak in early adulthood.[24,25] Therefore, this growth may lead to confusion in the interpretation of exercise capacity. In previous studies, a cardiopulmonary exercise test (CPET) was used in the assessment of exercise capacity and longer-term follow-up was performed.[8,9,23] In our study, a CPET could not be conducted and follow-up was shorter than that in other studies. In addition, due to the heterogeneity in the test protocol and ergometer, the exercise test workloads achieved during the follow-up tests could not be compared with our results.[8,9,23] However, changes in HR increase and oxygen saturation were higher at the same workload compared to the first test. Desaturation is considered present when the SpO_2 ≥4% decreases from baseline to peak exercise.[26] In the current study, four patients had desaturation in the first assessment and six patients in the last assessment. These results show that the cardiorespiratory responses demanded by the test workload should also be greater in the last assessment. This may indicate a regression in terms of cardiorespiratory fitness in Fontan patients.

According to some studies, serum BNP levels may affect exercise capacity in patients with congenital heart disease. In their study, which excluded Fontan patients, Gavotto et al.[27] reported that BNP levels were related to impaired exercise capacity in patients with systemic right ventricles. In another study that included Fontan patients, serum BNP concentrations did not correlate with CPET parameters in adult patients with single or systemic right ventricles.[28] However, the baseline age and serum BNP concentration of the patients in these studies were higher than those in our study. As previously reported, BNP concentrations were higher in patients in more advanced New York Heart Association (NYHA) functional classes[29]; however, data on the patients' NYHA classes were not collected in our study. During the follow-up, the patients' serum BNP concentration and exercise test parameters were mostly similar, but correlation analysis between these parameters was not performed. For this reason, the relationship between BNP concentration and exercise capacity could not be interpreted based on our results.

In the literature, peripheral muscle strength follow-up data are rarely collected in Fontan patients. Despite a tendency for higher hand grip strength in patients during follow-up, there was no significant change in lower extremity peripheral muscle strength in our study. This result may cause a positive impression, although, considering the age of the patients at the first and last assessments, it is highly likely that preserved hang grip strength was due to physical growth. In a previous study, significant myopenia, especially in the lower extremities, and increased adiposity were reported in young Fontan patients.[30] Therefore, myopenia, especially in the legs, may be associated with the absence of any increase in knee extensor muscle strength, while hand grip strength tends to increase during the physical growth process in our Fontan population. Sandberg et al.[31] reported that isometric knee extension muscle strength was impaired in adolescents (13-18 years) but not in younger children (6-12 years) who had undergone the Fontan procedure compared to the controls. In another study involving 6- to 12-year-old Fontan patients, it was reported that hand grip strength was similar to that in healthy individuals.[32]

In the current study, more than half of the population (60%) was under 18 years old; of these, 4 patients (26.70%) were below 12 years old and 5 (33.30%) were 12-17 years old. The remaining 40% of the population were 18 years old or older. As a result, in our study, both knee extension muscle strength and hand grip strength did not show a decline over approximately 2 years; in fact, there was a tendency towards increased hand grip strength. Possible explanations for this observation include the significant proportion of our patients being children and adolescents, the somatic growth process, and the promoting physical activity from the beginning of follow-up for patients. Additionally, the approximately 2-year follow-up period may be considered relatively short to observe the onset of extracardiac factors deteriorating in Fontan patients in this age group. Furthermore, in our study, subgroup analysis based on age could not be conducted due to the small sample size; if it could have been done, it could have provided more detailed clinical information about the deterioration period of muscle strength and exercise capacity in patients. Indeed, studies suggest that the decrease in muscle strength may be slower in childhood and more pronounced towards adulthood in Fontan patients.[31,32] Therefore, in future studies, longer-term analyses incorporating subgroup analyses based on age are crucial for a more comprehensive understanding of critical turnover points in terms of muscle strength and exercise capacity and determining the appropriate timing and guidance for rehabilitation in Fontan patients.

Bioelectrical impedance research reveals significant myopenia and increased adiposity in Fontan patients.[30] Greater muscle mass was correlated with better exercise capacity in this population. Lower skeletal muscle mass and a higher body fat percentage were seen in patients who experienced a late complication after their Fontan procedure.[30] Tran et al.[33] reported that Fontan patients had an unfavorable body composition profile, marked by impairments in skeletal muscle mass and a tendency for adiposity, and reduced exercise capacity and oxygen pulse (a proxy for stroke volume) were related to low skeletal muscle mass.

In the present study, the BMI of the Fontan patients were within the normal range during follow-up. Tran et al.[33] reported that BMI is a poor indicator of adiposity, and dual-energy X-ray absorptiometry often reveals excessive adiposity in Fontan patients with normal BMI. However, the Fontan patients had a significant increase in body fat weight over time in the present study. This increase was not related to any decrease in muscle strength or exercise capacity. Previously, Longmuir et al.[32] found that Fontan patients aged 6-12 years had strength and a good body composition similar to those of healthy controls. Since the same age group constituted a significant part of our sample size, body composition results may have been better preserved in Fontan patients. Therefore, the possible worsening of body composition and consequent reduced exercise capacity and muscle strength outcomes during follow-up in patients with Fontan could not be discussed in the present study.

The most important limitation of our study was the absence of a CPET in the assessment of exercise capacity. There was no change in cardiac parameters such as HR peak, HRR, or HRR at 1 min, but a CPET can provide information about changes in metabolic, ventilatory, or gas exchange parameters during follow-up, as well as cardiovascular parameters. Another significant limitation was the small sample size. With a larger sample size, subgroup analyses based on age, surgical type, or other key clinical characteristics could be performed. This would enable more detailed clinical information to be obtained regarding muscle strength and exercise capacity prognosis in the follow-up of Fontan patients. Furthermore, the presence of follow-up data from a control group would be helpful to understand the potential impacts of physical growth on the exercise capacity and muscle strength of Fontan patients in comparison with control subjects.

At the end of 20 months of follow-up, the exercise capacity and muscle strength did not regress; rather, an increase in body fat weight was observed in the Fontan patients. There may not be a decline in exercise capacity and muscle strength in these patients over relatively short periods during childhood, adolescence, and early adulthood. Long-term follow-up studies with subgroups are crucial for gaining a clearer understanding of critical turnover points for extracardiac factors. Consequently, they can aid in determining the optimal timing of cardiac rehabilitation and guiding it in Fontan patients.

Ethical approval

The Hacettepe University Non-interventional Clinical Research Ethics Board approved this study (06.09.2022, GO22/786). The parental written informed consent form and the child informed assent form for patients aged 8-17 years, as well as the written informed consent form for patients aged 18 years and older were waived.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: HT, MS, HHA, SNS; data collection: HT, SNS; analysis and interpretation of results: HT, MS, HHA, SNS; draft manuscript preparation: HT, MS, HHA, Dİİ, NVY, ECK, TK. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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