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Body Composition and Exercise Performance in Youth With a Fontan Circulation: A Bio-Impedance Based Study

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BACKGROUND: Adults with a Fontan circulation tend to have myopenia and elevated adiposity when measured by dual energy x-ray absorptiometry. Bioelectrical impedance analysis is an alternative validated approach to assess body composition. We used bioelectrical impedance analysis to compare body composition between pediatric patients with a Fontan circulation and control individuals without heart disease.

METHODS AND RESULTS: A retrospective chart review identified all patients aged <22 years with a Fontan circulation who presented for cardiopulmonary exercise testing and bioelectrical impedance analysis from April 2019 to January 2020. Data were compared with control subjects tested during the same period. We studied 47 patients with a Fontan circulation (53% boys; 15±3.1 years) and 165 controls (48% boys; 14.4±2.5 years). Fontan status was associated with shorter height, but similar age, sex, and overall body mass. Patients with Fontan had lower lean body mass (−12.0±22%, Z-score −0.5±1, P=0.005), skeletal muscle mass (−13.6±1.4%; Z-score, −0.5±1; P=0.004), skeletal muscle indexed to height (−10.3±13.3%; Z-score, −0.5±1; P=0.005), and higher percent body fat (+13.8±18.6%; Z-score, 0.4±1.2; P=0.03). Greater skeletal muscle mass was associated with higher peak oxygen consumption (r^2=0.52, P<0.0001) and oxygen pulse (r^2=0.68, P<0.0001). Patients who had suffered a late complication (ie, heart transplant referral or evidence of extracardiac organ dysfunction) of the Fontan operation (13 of 47, 27.7%) had lower skeletal muscle mass (P=0.048) and higher body fat percentage (P=0.003).

CONCLUSIONS: The Fontan circulation is associated with marked myopenia and increased adiposity. Higher muscle mass was associated with better exercise capacity. Fontan complications are associated with lower muscle mass and increased adiposity.

Key Words: adiposity ■ bioimpedance ■ body composition ■ cardiopulmonary exercise testing ■ congenital heart disease ■ Fontan circulation ■ myopenia

The Fontan operation has transformed early survival for people born with univentricular physiology.[1] Improved survival to adolescence and beyond has, however, exposed an array of long-term complications of the Fontan circulation, including near universal limitation in exercise capacity.[2,3] There are a number of potential contributors to this exercise dysfunction, such as less physical activity than their peers[4] and abnormal body composition, with increased adiposity and myopenia.[5–8] Despite these known associations in adults with a Fontan circulation, little is known about body composition and its implications in children with a Fontan.

Most research of body composition in this population has almost exclusively used dual energy x-ray absorptiometry (DXA).[6] This technology involves administering a small dose of radiation and is not readily available at all pediatric facilities; when available, DXA scanners are often distant from clinical cardiology locations. Bioelectrical impedance analysis (BIA) is an

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CLINICAL PERSPECTIVE

What Is New?

- Patients with a Fontan circulation have marked myopenia and increased adiposity when measured with bioelectrical impedance analysis.
- Higher muscle mass in patients with a Fontan circulation is associated with better exercise capacity.
- Patients who suffered a late complication following their Fontan had lower skeletal muscle mass and higher body fat percentage.

What Are the Clinical Implications?

- Bioelectrical impedance analysis provides an inexpensive and user-friendly alternative for clinical implementation, and produces similar body composition findings with previous studies using dual energy x-ray absorptiometry.
- The association between skeletal muscle index and higher peak oxygen consumption and peak oxygen pulse may also point to the central role of the skeletal pump to augment cardiac output.
- Body composition and its effects on exercise may be a measurable target for intervention in the Fontan population.

Nonstandard Abbreviations and Acronyms

BIA	bioelectrical impedance analysis
CPET	cardiopulmonary exercise test
VO₂peak	peak oxygen consumption

alternative approach to measure body composition that agrees well with DXA.[9,10] BIA does not involve ionizing radiation. Instead, it surveys body composition through applying a low-level electrical current through the body and analyzing a combination of the electrical capacitance and resistance through different tissues. Bone and fat for example is considered a non-conductor, whereas by contrast, body fluid stored in muscle displays good conduction properties. Cell membranes function as capacitors when electricity passes through it. Using these differing physico-chemical properties and various software algorithms, body composition can be estimated using BIA.[11,12] It is also painless, quick, easy to perform, and simple to interpret without specialized radiology staff.[9,10,13,14]

The aims of this study were to: (1) explore the use of bioimpedance based technology to measure body composition in young patients with a Fontan circulation; and (2) examine whether such measurements can help predict anthropometrics, particular anatomic and physiologic characteristics, cardiopulmonary exercise test (CPET) parameters, and complications related to the Fontan state.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

This study was approved by the Cincinnati Children's Hospital Medical Center Institutional Review Board, and informed consent was not required for this study.

Patients

We identified all patients with a Fontan operation aged <22 years who underwent a routine CPET at Cincinnati Children's Hospital between April 2019 and January 2020. Exclusion criteria included a submaximal test (details below) and missing CPET data. Control subjects were formed by age-matched subjects without congenital or other structural heart disease who were referred for CPET for other clinical reasons. All of these control patients were tested during the same period as the Fontan cohort and had body composition analysis with BIA before their CPET per local standard of care. Reasons for CPET referral in the control group included: symptoms suggestive of autonomic dysfunction or postural orthostatic tachycardia syndrome (39%), ventricular pre-excitation (11%), prolonged QT interval (9.5%), chest pain (9%), normal pediatric patients tested as controls for research (8.5%), ectopy on ECG (8%), palpitations (6%), mild left ventricular trabeculations (4%), family history of heart disease (3%), dyspnea on exertion (1%), and prior pericarditis (1%).

Study Measures

Baseline Data

We extracted demographic and other baseline data from the electronic medical record including: age, sex, height, weight, medications, age at Fontan, other operative Fontan surgical details, self-reported physical activity, and New York Heart Association functional classification. Self reported physical activity was graded as: (1) physically active (participation in organized sports, regular attendance at fitness classes, or other moderate-to-vigorous exercise ≥4 days a week for 30 minutes) or (2) physically inactive when not engaged in such activity.[4] The presence of ventricular systolic dysfunction and atrioventricular valve insufficiency severity were denoted from the echocardiogram within 6 months of the

CPET. Annual screening laboratory results were recorded including the following: hemoglobin concentration, platelet count, aspartate aminotransferase, alanine aminotransferase, total protein, albumin, and gamma-glutamyl transferase.

Late Fontan Complications

Late Fontan complications were defined as any of the following occurring before the time of index CPET: heart transplant referral, evidence of extracardiac organ dysfunction (plastic bronchitis, protein-losing enteropathy, and cirrhosis), or evidence of advanced Fontan-associated liver disease, which was defined as a combination of irregular/nodular surface contour, heterogeneous parenchyma, or imaging evidence of portal hypertension (splenomegaly, ascites, varices) by either liver ultrasound or liver magnetic resonance imaging.

Bioimpedance Assessment

Anthropometric data were measured by BIA (InBody370; InBody, Cerritos, CA, USA) (Figure 1) immediately before the CPET. All patients stood on the InBody scale unsupported with their bare hands and feet making contact with the 8 total electrodes (2 palm, 2 thumb, 2 toe, and 2 heel); the measurement takes on average about 30 seconds. BIA output variables included total lean body mass, appendicular lean body mass (sum of appendicular lean mass of both upper extremities and lower extremities), lean body mass of trunk, skeletal muscle mass, skeletal muscle index (appendicular lean mass/ height^2), and body fat percentage. Skeletal muscle mass was estimated from appendicular lean mass using the commonly accepted assumption that $\approx$75% of total skeletal muscle mass is carried in the extremities. Percent predicted by limb or trunk is based on comparing ideal body type based on age and size and is calculated automatically by InBody.

Cardiopulmonary Exercise Test

Exercise testing was performed on a stationary cycle ergometer (Corival; Lode; Groningen, The Netherlands) with an individualized incremental ramp protocol. The rate of increase was chosen by experienced clinical exercise physiologists based on the patient's body size and expected fitness, targeting an exercise duration of $\approx$10 minutes. Cardiopulmonary responses to exercise were assessed breath-by-breath (Ultima CardiO2; MGC Diagnostics; Saint Paul, MN, USA). Criteria for a maximal effort exercise test was that 2 of the following 3 criteria were met: respiratory exchange ratio (RER) >1.10; maximal heart

Figure 1. Pictures showing the InBody 370 (A) and demonstration of its use (B) in the Cardiopulmonary Exercise Laboratory at Cincinnati Children's Hospital.

rate ≥85% of the age-predicted maximum (220-age in years); or maximal rating of perceived exertion >18 on a 6 to 20 scale.[15] Predicted peak oxygen consumption (VO$_2$peak) was calculated per Wasserman et al and Cooper et al.[16,17] In adult patients with a body mass index <18 and >25, the underweight and overweight regression equations were used.[16]

Statistical Analysis

Descriptive normally distributed data are presented as mean±SD with the Z scores calculated from the normal control data. Differences between young patients with a Fontan and normal controls were assessed using an unpaired *t*-test for normally distributed data and the Wilcoxon rank-sum test for non-normally distributed data where appropriate. Univariate associations were estimated using linear regressions models. All presented *P* values are 2-tailed (where applicable) and differences and associations were considered significant when *P*<0.05. Statistical analyses were performed using JMP, Version 14 from SAS Institute Inc. (Cary, NC).

RESULTS

A total of 53 patients aged <22 years with a Fontan circulation underwent CPET between April 2019 and January 2020 (Figure 2). There were 6 (11%) patients excluded from the analysis because of a submaximal exercise test. Cycle ergometry was used for 45 tests, while a treadmill was used for 2 tests. Baseline characteristics of the Fontan cohort are shown in Table 1. All 45 patients with known Fontan type had a total cavopulmonary anastomosis, either extracardiac conduit (n=31, 66%) or lateral tunnel (n=14, 30%), (Table 1). Fontan surgical records and detailed discharge summaries from hospitalization for Fontan completion were available for 25 patients (53%).

Laboratory findings are reported in Table 1. Six (13%) patients with a Fontan circulation had clinically diagnosed advanced Fontan-associated liver disease. There were 6 other patients with long-term complications from their Fontan, including recent cardiac transplant listing (n=3), plastic bronchitis (n=2), and protein-losing enteropathy (n=1). None of the patients with long-term complications were prescribed oral steroids during the study period.
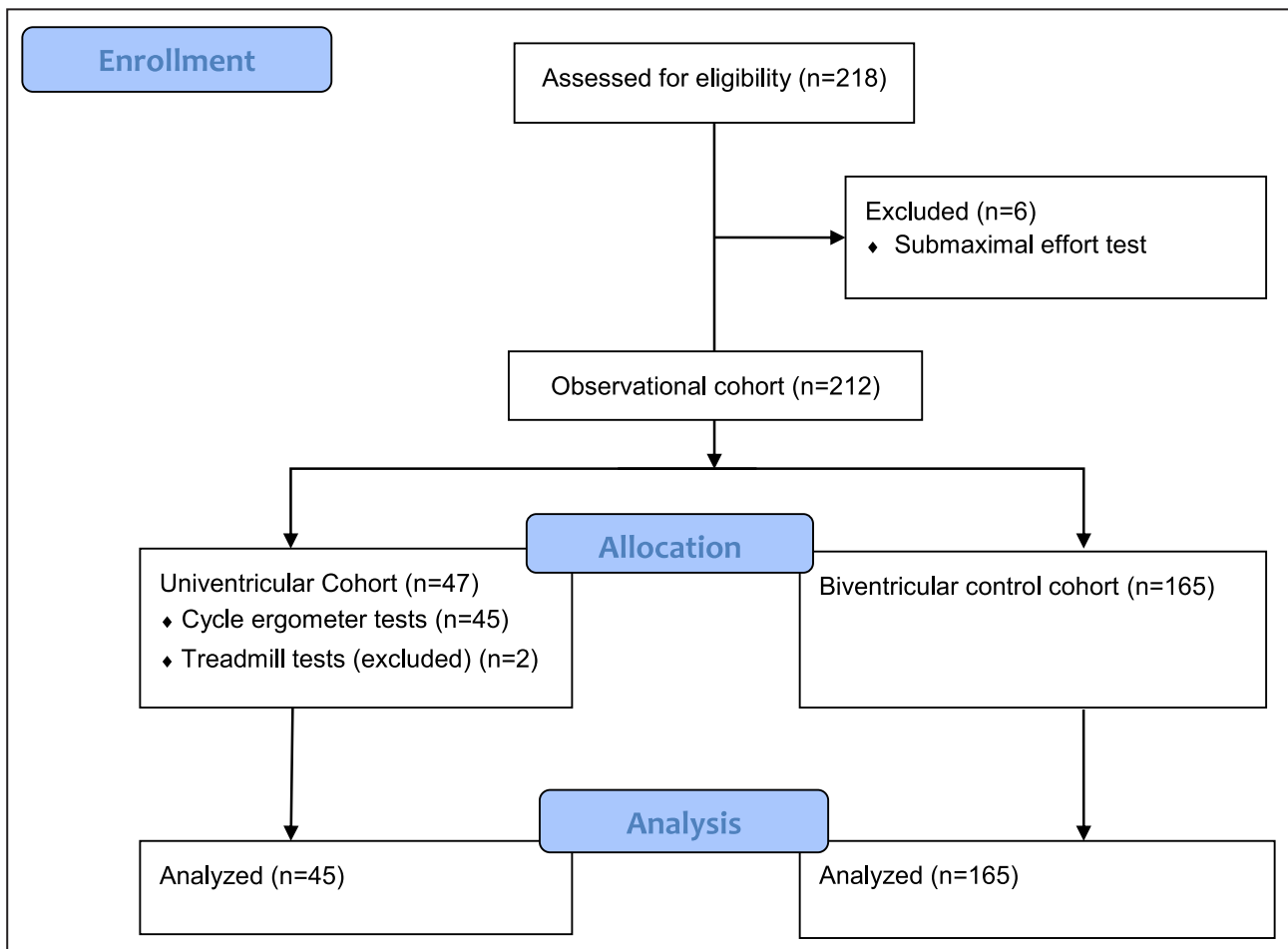
Figure 2. Flow diagram demonstrating selection of patients for the study.

Table 1. Summary of Clinical Characteristics and Laboratory Findings in the Fontan Group

	Fontan Group (n=47)
Age at Fontan, y (n=45)	3.9±1.9
Fontan surgery length of stay, d (n=31)	11.1±8.6
Fontan type (n=45)	Extracardiac, 31; lateral tunnel, 14
Ventricular dysfunction (n=43)	None, 34; mild, 4; moderate, 4; severe, 1
Atrioventricular valve regurgitation (n=43)	None or trivial, 18; mild, 15; moderate, 10; severe, 0
NYHA Functional Class (n=42)	I, 31; II, 10; III, 1
Self-reported physical activity (n=41)	Active, 13; sedentary, 28
Hemoglobin, g/dL	15.3±1.2
Platelets, K/µL	199.3±70.9
Albumin, g/dL	4.4±0.5
AST, µL	32.8±14.2
ALT, µ/L	31.3±12.7
Total protein, mg/dL	7.1±1.2
GGT, µ/L	51.9±21.3

Data are presented as mean±SD or number of patients. For variables with missing data, the number of patients with available data is provided. ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; and NYHA, New York Heart Association.

There were 5 patients who suffered from heart failure and other cardiac complications in the 12 months before testing (1 patient with severe systolic dysfunction leading to heart transplant evaluation, 3 patients with unplanned stent placements in their Fontan conduits, 1 patient with admission for atrial tachycardia). Three of these patients also had significant liver disease.

An echocardiogram was available in 43 of 47 patients (91%) within 6 months of the CPET and these data are denoted in Table 1. Only 5 of 43 (12%) had moderate or severe ventricular systolic dysfunction. Likewise, a minority, 10 of 43 (23%), had moderate or severe atrioventricular valve regurgitation.

There were 17 of 47 patients (36%) who self-reported physical activity level as active, while 7 of 47 (15%) patients did not have their activity level recorded in the electronic medical record.

BIA measurements for the 47 patients with a Fontan circulation were compared withthe 165 controls (Table 2). Those with a Fontan circulation were shorter, but there were no significant differences in age, sex, weight, or body mass index. Based on body mass index, 62% (29 of 47) patients with a Fontan were normal weight, 23% (11 of 47) of patients were overweight, and 15% (7 of 47) were underweight. While patients with a Fontan circulation tended to have similar body mass index compared with the normal controls, they had higher body fat percentage (26.0±11.8% versus 22.4±9.6%, P=0.03) and lower lean muscle mass (40.9±12.1 versus 46.5±12 kg,

P=0.005) and skeletal muscle index (6.1±1.5 kg/m^2 versus 6.8±1.3 kg/m^2, P=0.005). On segmental analysis, there was approximately a 15% difference in muscle mass between patients with a Fontan and controls in both upper and lower extremity muscle mass, although the absolute differences were greater in the legs compared with the arms (Table 2; Figure 3). There were 7 patients with a skeletal muscle index Z-score <−2 with 3 of these patients having significant complications following their Fontan (1 patient with clinically impactful liver disease, 1 patient with plastic bronchitis, 1 patient with severe systolic dysfunction).

Data for the 45 patients who completed a maximal effort test on the cycle ergometer are reported in Table 3. Of note, 4% (2 of 45) of patients had a VO$_2$peak >80% predicted. There was a significant association between skeletal muscle index and absolute VO$_2$peak (r^2=0.52, P<0.0001); there was also a significant association between skeletal muscle index and oxygen pulse (r^2=0.68, P<0.0001) (Table 4). There was a similar association between skeletal muscle mass and absolute VO$_2$peak (r^2=0.55, P<0.0001) and oxygen pulse (r^2=0.76, P<0.0001) in the control patients. There was a weak correlation between percent body fat and absolute VO$_2$peak (r^2=0.1, P<0.0001). Additionally, there was a significant association with lean body mass of the left leg and absolute VO$_2$peak (r^2=0.69, P<0.0001) and oxygen pulse (r^2=0.73, P<0.0001), as well as lean body mass of the right leg and absolute VO$_2$peak (r^2=0.69, P<0.0001) and oxygen pulse (r^2=0.74, P<0.0001).

Patients who had suffered a late extracardiac Fontan complication had lower skeletal muscle index (r^2=0.08, P=0.048) and higher body fat percentage (r^2=0.2, P=0.003). Longer length of stay at initial Fontan surgery was associated with higher adiposity (r^2=0.2, P=0.02) (Table 4). There was no association between either systolic dysfunction or atrioventricular valve regurgitation and either skeletal mass index or body fat percentage. Self-reported physical activity and New York Heart Association class were not significantly associated with either body fat percentage or skeletal muscle index. Neither body fat percentage nor skeletal muscle index significantly correlated with hemoglobin, platelets, aspartate aminotransferase, alanine aminotransferase, total protein, or gamma-glutamyl transferase.

Despite physically active patients having higher percent predicted VO$_2$peak (75.7±10.7% versus 59.6±10.7%, P=0.0001), there was no significant differences in lean body mass, skeletal muscle mass, body fat percentage, or percentage of lean body mass of the legs as compared with those who were not active. There were also no significant differences in body composition between those with a systemic left versus right ventricle or between those patients with or without notable exertional hypoxemia (oxygen saturation

Table 2. Comparison of Demographics and Bioelectric Impedance Analysis Among All Patients With a Fontan Circulation and Controls

	Fontan Group (n=47)	Fontan Group, Z-Score	Normal Group (n=165)	P Value
Age at testing, y	15.0±3.1	…	14.4±2.5	0.2
Sex	Boys, 25; Girls, 22	…	Boys, 79; Girls, 86	0.5
Height, cm	159.0±14.1	−0.5±1.1	165.5±12.7	0.003*
Weight, kg	56.9±20.3	−0.2±1.3	60.5±16.0	0.2
Body mass index, kg/m^2	22.1±5.7	0.05±1.4	21.8±4.1	0.8
Body fat (%) (all)	26.0±11.8	0.4±1.2	22.4±9.6	0.03*
Body fat (%) (girl)	31.9±11.8	0.6±1.4	26.9±8.2	0.02*
Body fat (%) (boy)	20.8±9.3	0.4±1.1	17.4±8.6	0.04*
Lean muscle mass, kg	40.9±12.1	−0.5±1	46.5±12.0	0.005*
Skeletal muscle mass, kg	22.2±7.2	−0.5±1	25.7±7.3	0.004*
Skeletal muscle index, kg/m^2 (all)	6.1±1.5	−0.5±1	6.8±1.3	0.005*
Skeletal muscle index, kg/m^2 (girl)	5.8±1.2	−0.4±1.4	6.1±0.9	0.06
Skeletal muscle index, kg/m^2 (boy)	6.4±1.3	−0.8±1.1	7.4±1.2	0.001*
Lean body mass right arm, kg	2.0±0.8	−0.4±0.9	2.4±0.9	0.02*
Lean body mass right arm, %	98.7±13.8	−0.3±1.1	102.3±12.8	0.1
Lean body mass left arm, kg	2.0±0.8	−0.4±1.0	2.3±0.8	0.02*
Lean body mass left arm, %	97.4±14.3	−0.2±1.2	100.4±12.3	0.2
Lean body mass trunk, kg	18.3±5.4	−0.4±1.0	20.5±5.3	0.01*
Lean body mass trunk, %	101.5±7.1	−0.2±1.0	102.5±6.6	0.3
Lean body mass right leg, kg	6.0±2.1	−0.5±1.0	7.1±2.1	0.002*
Lean body mass right leg, %	95.6±8.6	−0.8±1.1	102.0±7.6	<0.0001*
Lean body mass left leg, kg	6.0±2.1	−0.5±1.0	7.1±2.1	0.002*
Lean body mass left leg, %	95.6±8.7	−0.9±1.2	101.9±7.4	<0.0001*

Data are presented as mean±SD or number of patients. Z-score represents the difference between Fontan and control groups in multiples of 1 SD within the control group. % indicates percent of predicted.

*P<0.05 was considered significant.

via pulse oximeter [SpO$_2$] < versus ≥90% at peak exercise). In comparing body composition in patients with and without extracardiac complications following their Fontan, there was a difference in body fat percentage (34.4±10.6% versus 23.1±10.9%, P=0.003) but not skeletal muscle index (6.8±1.5 kg/m^2 versus 5.9±1.2 kg/m^2; P=0.13). When patients with extracardiac and cardiac complications from their Fontan were pooled (n=15) and compared with the patients without (n=33), there was no significant difference between the groups in either skeletal muscle index (6.6±1.7 kg/m^2 versus 6±1.1 kg/m^2, P=0.18) or body fat percentage (31.6±12.1% versus 23.6±11.1%, P=0.5).

DISCUSSION

This observational study demonstrated that children with a Fontan circulation have profound differences in body composition with almost 14% higher adiposity and an almost 15% lower muscle mass as compared with a biventricular control cohort without congenital heart disease. Individuals with a Fontan also tended to be shorter, have lower skeletal muscle mass, have increased adiposity, and generally were less fit than their healthy peers (Figure 3). Further, those patients with a Fontan circulation with more severely abnormal body composition tended to have more decreased exercise capacity. Potential explanations for the differences in body composition include delayed puberty,[18] lower vitamin D levels,[19] and lower insulin-like growth factor 1,[20] though the current study did not include exploration of underlying mechanisms.

Body composition and its effects on exercise may be a measurable target for intervention in the Fontan population. Further research is needed to identify clinically actionable variables and effective approaches to improving both body composition and exercise performance.

These findings are consistent with previous research using DXA[6,18] and demonstrate further the particular clinical phenotype of children with a Fontan circulation. Although not formally tested, the similarity of findings between the present study using BIA and prior studies using DXA suggest BIA may be a useful alternative to the assessment of
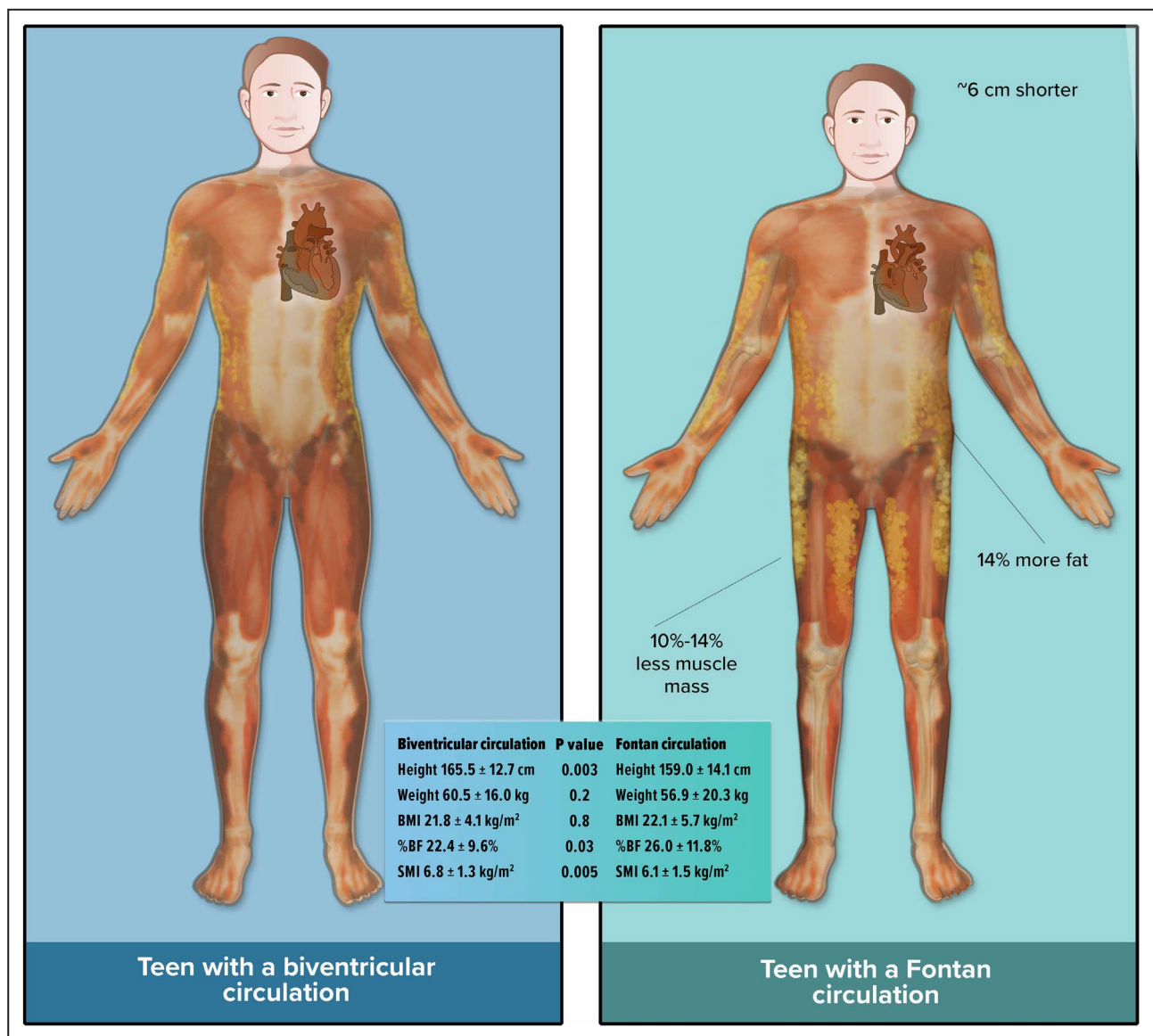
Figure 3. Schematic depicting body size and composition differences between children and adolescents with a biventricular circulation (left) vs a Fontan circulation (right).
%BF indicates body fat percentage; BMI, body mass index; and SMI, skeletal muscle index.

body composition. While DXA is considered the gold standard for body composition measurement, its limitations lead to limited clinical uptake in the care of children with heart disease. BIA provides an inexpensive and user-friendly alternative for clinical implementation.[9,10,13,14] The similarity of these findings to studies that used DXA supports BIA as a potentially useful alternative to DXA in the assessment of patients with a Fontan. Additionally, BIA has been extensively validated against DXA in pediatric patients without congenital heart disease[9,10,13,14] and in adult patients with heart failure.[21,22]

The absence of a subpulmonary ventricle requires the muscle and respiratory pumps to augment preload in patients with a Fontan circulation.[23] This study

demonstrated a significant association between VO_2peak (mL/min), peak oxygen pulse (mL/beat), skeletal muscle mass, and skeletal muscle index, with the association being stronger when examining lower extremity muscle mass. This finding is consistent with previous research.[8,24] While it may be intuitive that larger skeletal muscle is associated with higher exercise oxygen consumption, this finding in the context of already decreased muscle mass and exercise capacity supports the importance of maintaining muscle mass in these patients. Both self-reported exercise habits and formal cardiac rehabilitation are associated with higher VO_2peak.[5,25] Interestingly, children with a Fontan who perceived themselves as fit had similar muscle mass and adiposity measurements compared with more

Table 3. Summary of Cardiopulmonary Exercise Test Results in the Fontan Group for Patients Who Completed a Maximal Effort Cycle Ergometer Test

	Fontan Group
Peak heart rate, % predicted	81.1±9.8
VO$_2$peak, % predicted	64.6±13.5
O$_2$Pulse, % predicted	78.1±10.0
Resting SpO$_2$, %	96.8±1.9
Peak SpO$_2$ %	91.2±3.4
Peak systolic blood pressure, mm Hg	155.0±17.9

Data are presented as mean±SD. O$_2$Pulse indicates oxygen pulse; SpO$_2$, oxygen saturation via pulse oximeter; VO$_2$peak, peak oxygen uptake and % indicates percent of predicted.

sedentary patients with a Fontan despite having more normal percentage of predicted VO$_2$peak. Potential reasons include recall bias, poor understanding of home-based exercise training, and small sample size.

Patients who had suffered a long-term Fontan complication tended to have lower muscle mass and higher body fat percentage. Many chronic diseases are associated with greater frailty and sarcopenia. This appears to be driven by a combination of inflammation, premature cell death, and activation and a wide array of neurohormones.[26] The findings in the present study are consistent with previous research as patients with a Fontan circulation have a greater prevalence of sarcopenia.[27]

Lastly, encouraging regular exercise in children with a Fontan circulation may increase skeletal muscle mass and improve functional capacity.[25] Exercise has other benefits. This is especially notable considering that a quarter of the patients were overweight, as assessed by body mass index, and a third of the cohort self-reported a sedentary lifestyle. While there are few existing data supporting any particular approach, increasing physicial activity (or other focused exercises) and nutritional interventions are likely to have a substantive positive impact and are associated with low cost and, likely, a low probability of adverse events. For example, exercise prescription in both the hospital and home settings has been shown to improve exercise capacity and self-reported quality of life.[28] Additionally, establishing healthy, long-term exercise habits in childhood provides long-term benefits in adulthood, including improved fitness and, potentially, more favorable outcomes.[29]

Limitations

There are several potential limitations to this study. Our numbers are relatively small, and limit the statistical

Table 4. Associations Between Clinical Variables and Skeletal Muscle Mass, Skeletal Muscle Index, and Body Fat Percentage for 47 Patients With a Fontan Circulation Who Completed a Maximal Effort Cycle Ergometer Test

	Skeletal Muscle Index			Body Fat Percentage		
	Beta	R^2	P Value	Beta	R^2	P Value
Age at testing/+1 SD	0.64	0.41	<0.0001	0.047	0.0022	0.49
Height/+1 SD	0.82	0.66	<0.0001	−0.04	0.002	0.74
Weight/+1 SD	0.85	0.71	<0.0001	0.54	0.29	<0.0001
BMI/+1 SD	0.63	0.39	<0.0001	0.79	0.63	<0.0001
Age at Fontan/+1 SD	0.10	0.01	0.51	0.28	0.08	0.059
Length of stay/+1 SD	0.18	0.033	0.32	0.41	0.17	0.02
Peak heart rate/+1 SD	−0.39	0.16	0.006	−0.034	0.001	0.81
Peak heart rate (% predicted)/+1 SD	−0.39	0.15	0.006	−0.038	0.001	0.80
VO$_2$peak (mL/min)/+1 SD	0.71	0.52	<0.0001	0.0005	<0.0001	0.99
VO$_2$peak (% predicted)/+1 SD	0.11	0.053	0.12	−0.06	0.004	0.66
Peak O$_2$pulse (mL/min per bpm)/+1 SD	0.82	0.68	<0.0001	−0.01	0.0001	0.95
Peak O$_2$pulse (% predicted)/+1 SD	−0.003	<0.0001	0.98	0.47	0.12	0.46
Peak SpO$_2$/+1 SD	−0.26	0.07	0.08	0.03	0.001	0.83
Active lifestyle vs sedentary	0.17	0.028	0.29	0.22	0.049	0.17
Systolic dysfunction (0/1/2)	0.18	0.03	0.25	0.13	0.017	0.40
Atrioventricular valve regurgitation (0/1/2)	−0.27	0.07	0.08	0.07	0.005	0.64
Late Fontan complications (Y/N)	0.29	0.083	0.048	0.42	0.18	0.003
NYHA Class (I/II/III/IV)	−0.036	0.036	0.82	0.044	0.044	0.78

Analyses used univariate linear regression, with either skeletal muscle index (left) or body fat percentage (right) as the dependent variable. A P<0.05 was considered significant. The beta coefficient represents the standardized value (ie, the difference per 1 SD increase in the predictor variable). % predicted indicates percent of predicted normal; BMI, body mass index; O$_2$pulse, oxygen pulse; NYHA, New York Heart Organization; SpO$_2$, oxygen saturation via pulse oximeter; and VO$_2$, oxygen uptake.

power and inference. Second, while some BIA systems measure total body water, the available data did not include this variable; total body water could be a notable cofounder in body composition assessment, and this should be studied in the future. Third, few patients had available invasive hemodynamic data within a short period of the BIA measurement. Such data might have been helpful to determine whether limited cardiac output was an important correlate of alterations in body composition, particularly skeletal muscle index. Future research should consider invasive hemodynamic assessment in conjunction with CPET and body composition analysis. Fourth, while these data agree with other studies using DXA and while there are few methodological reasons to think BIA would systematically overestimate fat mass and underestimate skeletal muscle mass in the Fontan cohort,[30] further studies are required to confirm the accuracy of BIA measurements in the Fontan circulation. Fifth, we do not have data on pubertal status at the time of evaluation, and this may have been an important confounder. Finally, the control group represents a convenience sample of patients referred for clinical exercise testing. This may have biased us towards underestimating the difference between patients with a Fontan circulation and the general population; presumably, the controls referred for exercise testing for any reason would, on average, have less robust exercise capacity, lower muscle mass, and perhaps higher adiposity, than observed in the general population.

CONCLUSIONS

Young people with a Fontan circulation have significant myopenia, particularly in the lower extremities, and increased adiposity as measured by BIA. The association between skeletal muscle index and higher VO_2peak and peak oxygen pulse may also point to the central role of the skeletal pump to augment cardiac output. The similiarity of body composition findings using BIA with previous studies using DXA show that BIA may be a useful alternative device to measuring body composition in pediatric patients with a Fontan circulation.

ARTICLE INFORMATION

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Disclosures

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