Cardiology in the Young

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Despite reductions in muscle mass and muscle strength in adults with CHD, the muscle strength per muscle mass relationship does not differ from controls

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Abstract

Background: Patients with CHD exhibit reduced isometric muscle strength and muscle mass; however, little is known how these parameters relate. Therefore, the aim was to investigate the relation between isometric limb muscle strength and muscle mass for patients in comparison to age- and sex-matched control subjects. *Methods:* Seventy-four patients (35.6 ± 14.3 years, women n = 22) and 74 matched controls were included. Isometric muscle strength in elbow flexion, knee extension, and hand grip was assessed using dynamometers. Lean mass, reflecting skeletal muscle mass, in the arms and legs was assessed with dual-energy x-ray absorptiometry. *Results:* Compared to controls, patients had lower muscle strength in elbow flexion, knee extension, and hand grip, and lower muscle mass in the arms (6.6 ± 1.8 kg versus 5.8 ± 1.7 kg, $p < 0.001$) and legs (18.4 ± 3.5 kg versus 15.9 ± 3.2 kg, $p < 0.001$). There was no difference in achieved muscle force per unit muscle mass in patients compared to controls (elbow flexion 0.03 ± 0.004 versus 0.03 ± 0.005 N/g, $p = 0.5$; grip strength 0.008 ± 0.001 versus 0.008 ± 0.001 N/g, $p = 0.7$; knee extension 0.027 ± 0.06 versus 0.028 ± 0.06 N/g, $p = 0.5$). For both groups, muscle mass in the arms correlated strongly with muscle strength in elbow flexion (patients $r = 0.86$, controls, $r = 0.89$), hand grip (patients, $r = 0.84$, controls, $r = 0.81$), and muscle mass in the leg to knee extension (patients $r = 0.64$, controls $r = 0.68$). *Conclusion:* The relationship between isometric muscle strength and limb muscle mass in adults with CHD indicates that the skeletal muscles have the same efficiency as in healthy controls.

Aerobic capacity is commonly reduced in patients with CHD, and skeletal muscle function (e.g., muscle strength, muscle endurance) is suggested to contribute to this reduction.[1–4] Accordingly, in adults with CHD, lower isometric muscle strength has been reported in some studies in comparison to control subjects.[4–6] However, one study found no difference in isometric muscle strength in patients when compared to a reference population.[7] We recently showed a high prevalence of sarcopenia, i.e., loss of skeletal muscle mass, due to ageing or to secondary causes in patients with CHD.[6] It is generally acknowledged that muscle strength and muscle size are strongly related; however, this may not be constant across all settings. For example, some studies show that trained individuals (increased muscle size) had a larger strength to size ratio than untrained individuals and elderly individuals (decreased muscle size) had a lower strength to size ratio than young adults.[8] Currently, it is unknown if patients with CHD have the same efficiency (i.e., produce the same force in relation to muscle mass) as healthy controls, or how well muscle strength correlates with muscle size within the patient group. These types of data are important to help in abetting future designs of exercise programmes.

The aim of the present study was to investigate the limb isometric muscle strength and the limb muscle mass, and to determine the relation between these parameters in adults with complex CHD in comparison to age- and gender-matched control subjects. Our hypothesis was that the isometric muscle strength and muscle mass would be lower in adults with complex CHD, but that the muscle strength to size ratio would be similar in patients and controls.

Materials and methods

Study population

In this cross-sectional study, 74 adults (mean age 35.6 ± 14.3 years, females n = 22) with complex CHD were included. The inclusion criteria were adult age (≥18 years old), clinically stable

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condition the past 3 months and complex CHD. The exclusion criteria were cognitive impairment affecting independent decision capacity, comorbidity (e.g., rheumatoid arthritis), or other circumstances (e.g., pregnancy) affecting the ability to participate.

The patients were recruited from three centres specialised in CHD in Sweden (Umeå, Uppsala, and Lund). In total, 112 patients identified via the national register on CHD (SWEDCON) were found to be eligible. These patients were then contacted by phone and asked for participation; of these, 38 declined participation or were not possible to reach by phone, i.e., did not answer or had no official phone number. In total, 74 patients (female n = 22) were included. More detailed information regarding the inclusion process has been presented previously.[9]

In parallel to the recruitment of patients, an age- and sex-matched control was recruited for each patient. One hundred thirty-one persons were identified using the national register. These subjects were contacted via phone and asked to participate. Seventy-four persons fulfilled the inclusion criteria and accepted participation, i.e. 57 subjects (44%) were excluded or declined participation.

A post hoc analysis showed that there were no differences regarding age, sex, and type of lesion between the patients included in the study and those who declined or were excluded. Also, the corresponding analysis between the participating controls and those who declined or were excluded showed no differences (data not shown).

All participants gave their written informed consent for study participation. The study was approved by the Regional Ethical Review Board, Umeå (Dnr 2016-18-31M, 2016-462-32M, 2017-203-32M).

Isometric muscle strength

Isometric muscle strength in elbow flexion and knee extension was assessed using a dynamometer (333 A 500 kg model, KTOYO co, Ltd 289-7, Uijeongbusi, South Korea) – hereafter referred to as a load cell. The tests were performed on the dominant side of the participants. For each limb, tests were repeated three times with 1 minute of rest between each repetition. One minute of rest was reported to be sufficient recovery in maximal strength assessments.[10] The investigator provided verbal guidance for when to start the contraction (three-two-one-go), encouragement during the entire contraction, and when participants should stop. The peak force was registered and used in the analysis. The isometric muscle tests are briefly described below and were described in detail in a previous publication.[6]

Elbow flexion

When assessing isometric muscle strength in elbow flexion, the participants were standing with the shoulder adducted and with 90 degrees flexion in the elbow. An inelastic strap was connected to the load cell on one end and on the other end to a handle that subjects held in their hand. The forearm was in a supine position holding the handle. The subjects were instructed to flex their forearm with maximum force and to hold the contraction for 5 seconds.

Knee extension

Peak isometric force in knee extension strength was assessed while subjects were sitting on a gurney with back support and with 90 degrees of flexion in the hip and knee. A strap was connected to the load cell on one end and on the other end to a cuff that was attached around the ankle. The subjects were instructed to extend their knee with maximum force and to hold the contraction for 5 seconds.

Hand grip

The unilateral grip strength was measured using a hand-held dynamometer (SAEHAN Digital Hand Dynamometer SH5003, Saehan Corp, Masan City, South Korea). Three repeated measurements, separated by 1 minute of rest, were performed, and the peak force was registered.

Limb muscle mass

Full and regional body composition was assessed with Dual-energy X-ray Absorptiometry (Lunar iDXA, ME-200149, 210492, 210494, 212003; General Electrics Healthcare, Madison, Wisconsin, United States of America). Lean body mass refers to the total body weight minus bone and fat, thus representing the skeletal muscle mass. In the present report, only data on the total lean mass of the legs and arms are presented and will be referred to as limb muscle mass.

Self-reported physical activity

Self-reported physical activity level was assessed using the short version of the International Physical Activity Questionnaire. International Physical Activity Questionnaire includes four generic items with reference to time spent at different intensity levels of physical activity (vigorous, moderate, walking). The physical activity was categorised into three levels of physical activity expressed as metabolic equivalents minutes/week – low (≤600 metabolic equivalents min/week), moderate (601–2999 metabolic equivalents min/week), and high (≥3000 metabolic equivalents min/week).[11]

Background data

Data containing diagnosis, cardiovascular medication, and NYHA class were collected via patient records (Tables 1 and 2).

Statistics

Statistical analyses were performed using the Statistical Package for Social Sciences version 23–25 (SPSS, IBM corp., Armonk, New York, United States of America). Variables were tested for normality. The data are presented as means with standard deviations and ratios with percentages. Comparisons between patients and controls were analysed using Students t-test (means), Mann-Whitney U-test (ranks), and chi^2 test (ratios). There is a known association between body height and muscle mass and muscle strength. Additionally, a shorter stature is common in adults with complex congenital heart lesions.[12] Therefore, a one-way analysis of variance was conducted to determine differences between patients and controls subject regarding lean mass and isometric strength variables correcting for height. Correlation analyses between muscle mass of arms/legs and isometric muscle strength were performed with Pearson correlation analysis. The null hypothesis was rejected on p-values <0.05.

Results

A total of 74 patients and 74 age- and sex-matched controls were included in the analysis. There were no differences regarding weight, BMI or physical activity between patients and controls.

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Table 1. Descriptive data of patients with complex CHD and sex- and age-matched controls

	Patients (n = 74)	Controls (n = 74)	p-Value
Age, years	35.6 ± 14.3	35.6 ± 14.3	0.97
Sex, men	52 (70.3)	52 (70.3)	1.0
Height, cm	173.3 ± 9.6	176.8 ± 9.2	**0.024**
Weight, kg	73.4 ± 12.0	76.6 ± 13.8	1.00
BMI, kg/m^2	24.6 ± 3.4 (n = 73)	24.5 ± 3.5	0.75
Cardiovascular medication*, yes	45 (60.8)	6 (8.1)	<**0.001**
Physical activity level (IPAQ)			
Low	11 (6.8)	5 (6.8)	0.50
Moderate	40 (54.1)	47 (63.5)	
High	23 (31.1)	22 (29.7)	

Data are presented as the mean ± SD and n (%).
BMI = body mass index; IPAQ = international physical activity questionnaire – Low, <600 MET (metabolic equivalents) min per week; Moderate, 600–2999 MET min per week; High>3000 MET min per week; Comparisons between patients and controls were performed using Students t-test and chi^2 test. Bold values denotes p-values <0.05.
*The most common cardiovascular medications were angiotensin renin blockers, angiotensin conversion enzyme inhibitors, beta-blockers, diuretics, warfarin, and aspirin. More details regarding medications have been reported previously.[6]

The patients, however, were shorter and more often had prescribed cardiovascular medication (Table 1).

Isometric muscle strength

The adults with CHD had lower isometric knee extension strength, elbow flexion strength, and grip strength in comparison to the control subjects (Fig 1a, b and c). When adjusted for height, the isometric knee extension strength and grip strength in patients remained lower, while the elbow flexion strength was borderline lower (knee extension strength; adjusted means ± SEM; 443 ± 15 N versus 494 ± 15 N, F[1, 145]5.7, p = 0.018, grip strength; adjusted means ± SEM; 46 ± 1 N versus 49 ± 1 N, F[1, 145]5.1, p = 0.026, elbow flexion strength; adjusted means ± SEM; 190 ± 6 N versus 206 ± 6 N F[1, 145] 3.8, p = 0.054).

Limb muscle mass

The patients had lower muscle mass in both the arms and legs in comparison to the controls (Fig 2a and b). When adjusted for height, the muscle mass in legs remained lower in patients, while the muscle mass in arms was borderline lower (muscle mass in legs; adjusted means ± SEM, 16,417 ± 248 g versus 17,877 ± 247 g, F[1, 144] 17.1, p < 0.001, muscle mass in arms; adjusted means ± SEM, 6019 ± 144 g versus 6389 ± 143 g, F[1, 144] 3.3, p = 0.072).

Muscle force to mass ratio

There was no difference in the achieved muscle force per muscle mass in patients compared to controls (Fig 3a, b and c).

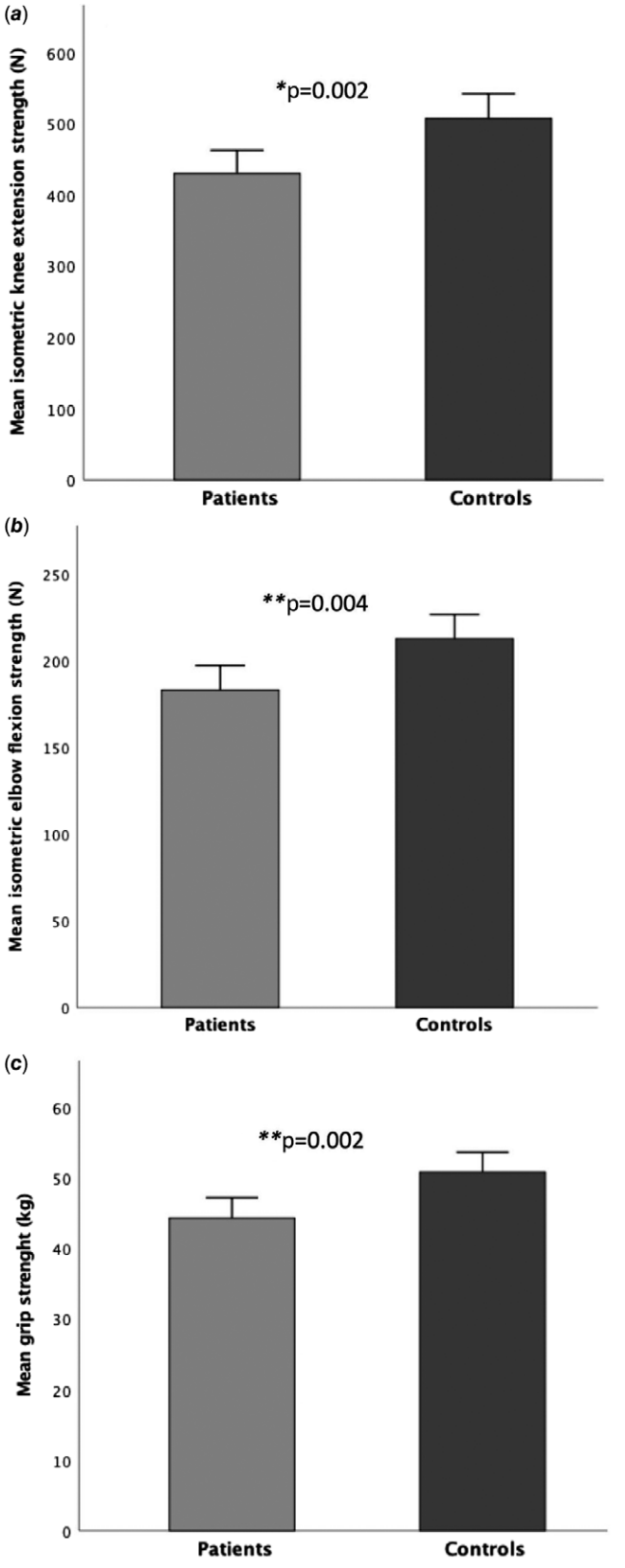

Figure 1. (*a–c*) Comparison of isometric muscle strength between patients with complex CHD and age- and sex-matched control subjects. Data are presented as the mean and 95% CI. N, Newton. *p < 0.05, **p > 0.01.

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Table 2. Distribution of diagnoses, NYHA class, and ejection fraction

Diagnose	n (%)
ToF	20 (27.0)
ccTGA	4 (5.4)
dTGA atrial switch	15 (20.3)
dTGA arterial switch	6 (8.1)
Fontan/TCPC	22 (29.7)
Pulmonary atresia	3 (4.1)
Complete AV-septal defect	1 (1.4)
Miscellaneous	2 (2.7)
Truncus arteriosus	1 (1.4)
NYHA class	
I	49 (66.2)
II	19 (25.7)
III	3 (4.1)
Extra cardiac limitation*	3 (4.1)
EF > 40%	61 (82.4)

ccTGA = congenital corrected transposition of the great arteries; dTGA = dextro transposition of the great arteries; EF = ejection fraction; NYHA class = New York Heart Association classification; TCPC = total cavopulmonary connection; ToF = tetralogy of Fallot.
*Limited by joint-related problem while walking/running (n = 2), impaired balance post stroke (n = 1).

Correlation

For both groups, there were strong correlations between muscle mass in the arms and peak isometric elbow flexion strength (patients $r = 0.86$, $p < 0.001$, controls $r = 0.89$, $p < 0.001$) and hand grip strength (patients $r = 0.84$, $p < 0.001$, controls $r = 0.81$, $p < 0.001$). Also, there were strong correlations between muscle mass in the legs and peak isometric knee extension strength for both groups (patients $r = 0.64$, $p < 0.001$, controls $r = 0.68$, $p < 0.001$) (Fig 4a, b and c).

Discussion

Our results showed that patients with complex CHD had lower isometric muscle strength and lower muscle mass in the arms and legs in comparison to matched control subjects. Also, we found that the achieved muscle force per unit of muscle mass did not differ between patients and controls. Further, the isometric muscle strength in arms and legs strongly correlated with limb muscle mass for both patients and controls. Thus, our hypotheses were not rejected.

The finding of impaired isometric muscle strength in elbow flexion, knee extension, and hand grip in patients with complex CHD confirms previous findings.[4,5] When added together with previous research, our information provides a picture of a generalised muscle weakness in this population. However, no differences between patients with CHD and a reference group in isometric muscle strength in knee extension, hand grip, and shoulder abduction have been reported.[7] The finding in the latter study may be explained by the fact that the reference population was significantly older than the patients.[7] In addition to the lower isometric muscle strength in the patients in our study, we also found a lower limb muscle mass. This finding is in agreement with the rather high prevalence of lower muscle mass and muscle strength recently reported in patients with Fontan circulation.[13] Our results highlight that this is also the case over a much wider range of different complex congenital heart lesions. The combination of impaired isometric muscle strength and lower skeletal muscle mass in our rather young population (mean age 35.6 years) of adults with complex CHD is a matter of concern. In patients with acquired heart failure, impaired muscle strength and loss of muscle mass are markers of both more severe disease and worse prognosis.[14–16] However, in comparison to patients with CHD, patients with acquired heart failure are in general significantly older and their disease progression is relatively fast.[17] As stated previously, the present study population was relatively young; also, the majority were asymptomatic (NYHA I-II) and 61% had an ejection fraction

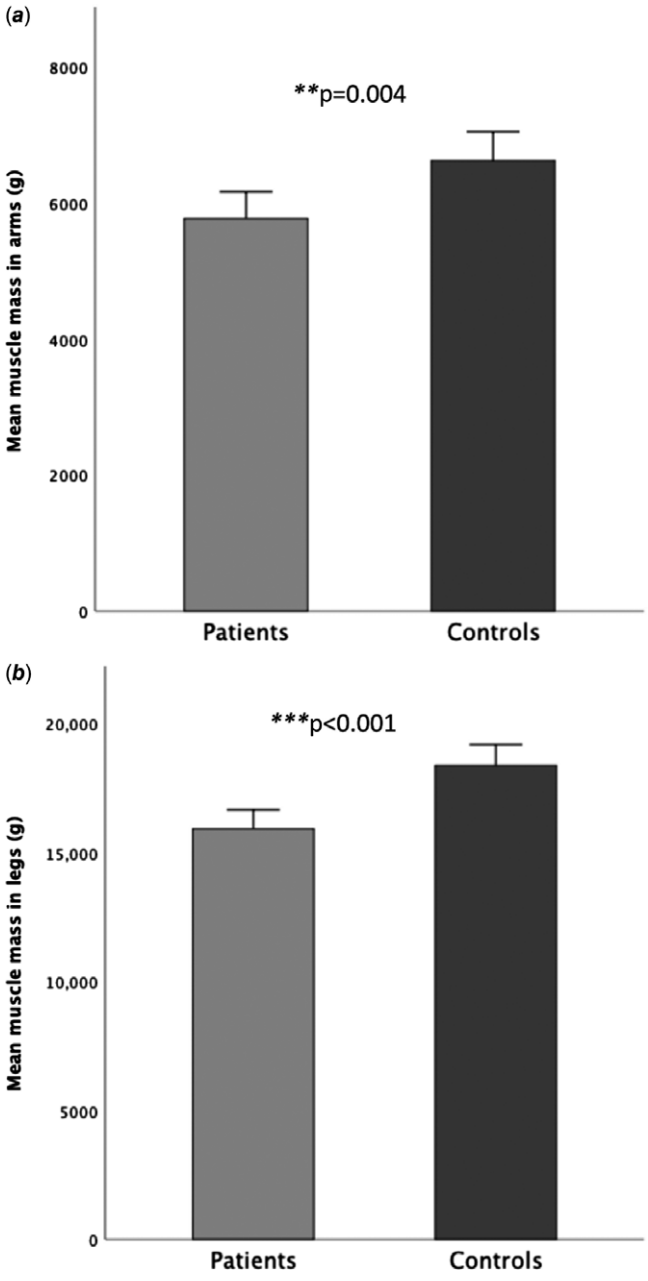

Figure 2. (*a, b*) Comparison of lean mass in arms and legs between patients with complex CHD and age- and sex-matched control subjects. Data are presented as the mean and 95% CI. **p > 0.01, ***p < 0.001.

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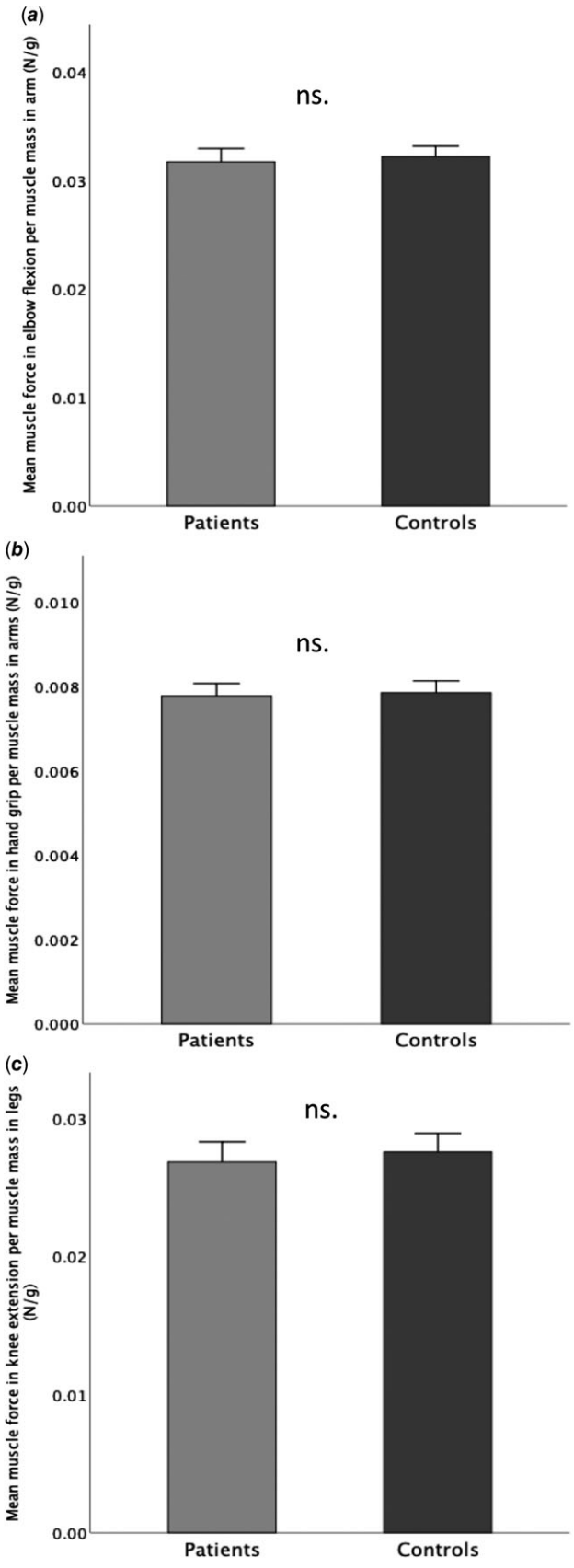

Figure 3. (***a–c***) Comparison of mean muscle force per muscle mass in elbow flexion, hand grip, and knee extension in arms and legs, respectively, between patients with complex CHD and age- and sex-matched control subjects. Data are presented as the mean and 95% CI.

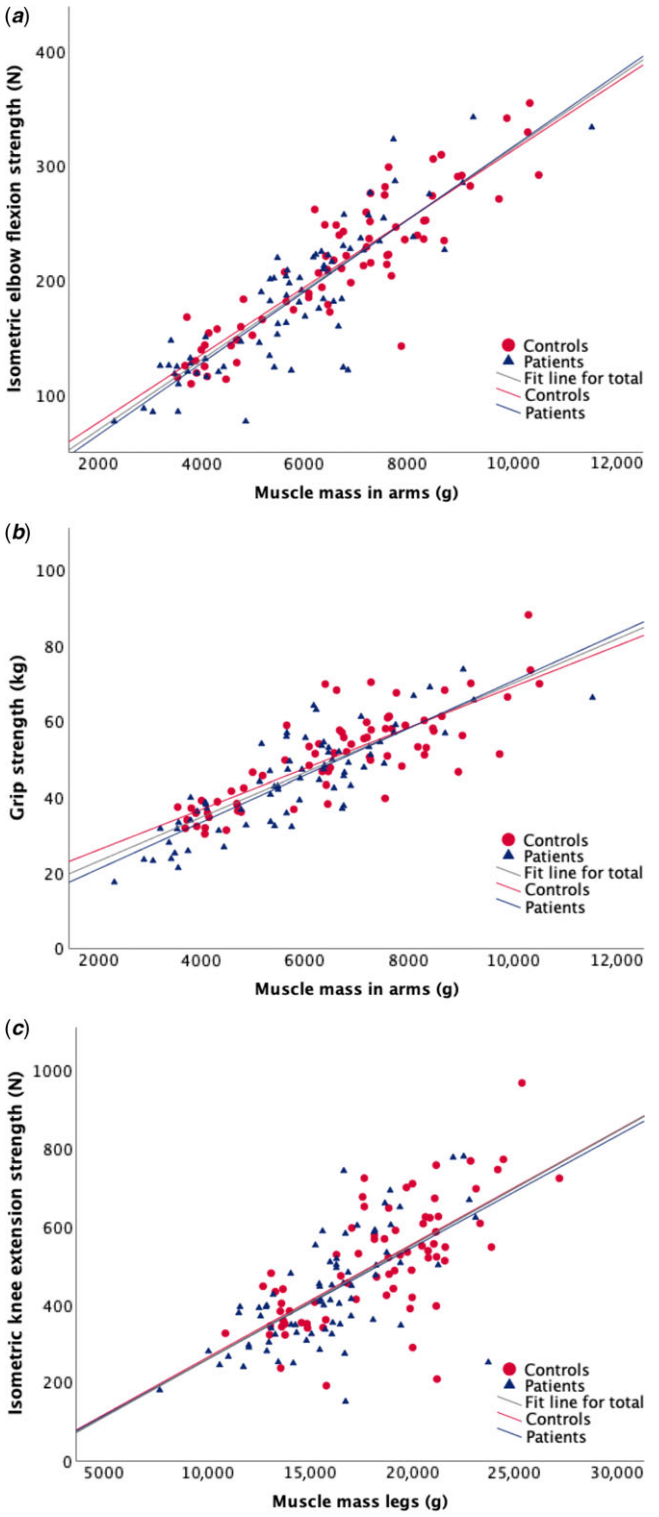

Figure 4. (***a–c***) (***a***) Correlations between isometric elbow flexion strength and the muscle mass in the arms, for patients ($r = 0.86$, $p < 0.001$) and controls ($r = 0.89$, $p < 0.001$). (***b***) Correlations between grip strength and the muscle mass in the arms for patients ($r = 0.84$, $p < 0.001$) and controls ($r = 0.81$, $p < 0.001$). (***c***) Correlations between isometric knee extension strength and the muscle mass in the legs for patients ($r = 0.64$, $p < 0.001$) and controls ($r = 0.68$, $p < 0.001$).

>40% (systemic ventricle). Therefore, further investigations are needed to clarify the prognostic impact of lower isometric muscle strength and lower skeletal muscle mass in adults with complex

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CHD. It may also be of importance to follow the development over time and to evaluate the ability for these patients to improve their isometric strength and possibly prevent further deterioration with interventions such as strength training. This may be of particular importance in the subgroup of patients with Fontan circulation since they are dependent on the skeletal muscle pump for venous return.[18]

Although the patients had lower limb muscle mass, there were no differences in BMI or activity level. Also, the patients were shorter but weighed similar as the controls. This suggests that other components of body composition than muscle mass may be deviant in patients with CHD. However, fat mass and bone mass were not addressed in the present work. The cause of the lower limb muscle mass in patients with CHD is probably multifactorial. One reasonable factor to consider is reduced physical activity; however, previous and present studies report that persons with CHD are physically active to the same extent as reference populations.[19,20] Patients with Fontan circulation and those with systemic right ventricles have a limited ability to increase systemic blood flow,[1] which could possibly impact muscle development. Another factor that could impact muscle development is the time with cyanosis prior to correcting or palliating surgery in patients with cyanotic heart lesions. It is currently unknown when in time the lower limb muscle mass first presents, and how it progresses over time, thus further research is needed.

The relation between limb muscle mass and produced force was similar in patients and controls with both groups showing strong correlations. This was also verified by the finding that the muscle force per unit of muscle mass did not differ between patients and controls. This leads one to question whether it is possible through strength training to increase muscle strength and muscle mass in this population. Therefore, there is a need for research regarding the effects of strength training in adults with complex CHD.

Although speculative, the strong correlation between isometric strength and skeletal muscle mass could have the potential to create a metric in a clinical setting. For example, a low performance in grip strength could indicate the need of assessing the body composition and more specifically the muscle mass with dual-energy x-ray absorptiometry, whereas a strong performance could represent a higher muscle mass. Additionally, it could be possible to follow the development of skeletal muscle mass over time by measuring progress or regress in isometric strength. However, further studies are needed before a clinical implementation.

Limitations

The cross-sectional design of the present study is a limitation since it only provides data of the present state, and thus there is no indication of the development of muscle strength and muscle mass over time. Therefore, we recommend that repeated measurements should be included in future study protocols. Another limitation is that the present study protocol did not include any data on cardiopulmonary exercise capacity, and there is a known relation between aerobic capacity and muscle performance.[4]

Conclusion

Impaired isometric muscle strength together with a proportional reduction in limb skeletal muscle is common in this young population with CHD. That the relationship between isometric muscle strength and limb muscle mass in adults with CHD was similar to controls indicates that the skeletal muscles have the same efficiency as in healthy subjects. Although speculative, if strength training proves efficient, this might in turn impact prognosis.

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Conflict of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008, and was approved by the regional Ethics Review Board, Umeå, Sweden (Dnr 2016-18-31M, 2016-462-32M, 2017-203-32M).

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