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Relationships of Body Composition to Cardiac Structure and Function in Adolescents with Down Syndrome are Different than in Adolescents Without Down Syndrome

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Abstract

Background: Median survival in Down Syndrome(DS) is 60 years, but cardiovascular disease risk and its markers such as left ventricular mass(LVM) have received limited attention. In youth, LVM is typically scaled to height^{^2.7} as a surrogate for lean body mass(LBM), the strongest

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predictor of LVM, but whether this algorithm applies to DS, a condition which features short stature, is unknown.

Methods: To examine the relationships of LVM and function with height, LBM, and moderate-to-vigorous physical activity (MVPA) in DS, DS youth aged 10–20y and age-, sex-, BMI-, race-matched nonDS controls underwent echocardiography for LVM, ejection fraction (EF), and left ventricular diastolic function (measured as E/E'); dual-energy x-ray absorptiometry (DXA)-measured LBM; accelerometry for MVPA.

Results: (DS vs. nonDS median [min-max]): DS had lower height (cm) (144.5 [116.7–170.3] vs. 163.3 [134.8–186.7]; $p < 0.0001$); LBM (kg) (33.48 [14.5–62.3] vs 41.8 [18.07–72.46], $p < 0.0001$); and LVM (g) (68.3 [32.1–135] vs 94.0 [43.9–164.6], $p < 0.0001$); similar EF (%) (65 [54–77] vs (64 [53–77], $p = 0.59$); and higher E/E' (8.41 [5.54–21.4] vs 5.81 [3.44–9.56], $p < 0.0001$). In $height^{2.7}$ -adjusted models, LVM was lower in DS ($\beta = -7.7$, $p = 0.02$). With adjustment for **LBM**, LVM was even lower in DS ($\beta = -15.1$, $p < 0.0001$), a finding not explained by MVPA. E/E' remained higher in DS after adjustment for age, height, HR, SBP, and BMI ($\beta = 2.6$, $p < 0.0001$).

Conclusions: DS was associated with stiffer left ventricles and lower LVM, the latter magnified with LBM adjustment. Scaling to $height^{2.7}$, the traditional approach for assessing LVM in youth, may underestimate LVM differences in DS. Whether lower LVM and diastolic function are intrinsic to DS, pathologic, or protective remain unknown.

Keywords

Down Syndrome; left ventricular mass; left ventricular diastolic function; body composition; echocardiogram

INTRODUCTION

Children with Down Syndrome (DS) now have a median life expectancy of about 60 years[1]. This achievement is partly attributable to improved health care including surgical intervention for congenital heart defects (CHD) which are present in approximately 50% of neonates with DS. CHD in children with DS is well-defined, but the effect of the 21st chromosome on cardiac function and cardiac muscle morphology is not. While the past several decades have witnessed this increased life expectancy, future risks for acquired heart disease and cardiac dysfunction have received limited attention. Indeed, individuals with DS are routinely excluded from both population-based and disease-based clinical research studies of acquired heart disease. Moreover, future risk of cardiovascular disease (CVD) in the setting of repaired CHD has largely been neglected in DS but has recently been recognized in the nonDS CHD population[2, 3]. Further highlighting the potential relevance of CVD for DS, individuals with DS are frequently classified as overweight or obese and have reduced physical activity[4–6], risk factors which could impact cardiac structure and function as well as long-term cardiac outcomes.

Left ventricular mass (LVM) and function are independent predictors of CVD and CVD-related mortality in adults[7]. Precursors of CVD are evident in childhood, and LVM has been pursued as a surrogate of CVD risk in youth in whom higher LVM is found with obesity and increased blood pressure[8–10]. LVM, as measured by echocardiography, is

frequently assessed in the clinical and research settings in children, but defining “increased” LVM in growing children has been challenging[11, 12]. Lean body mass (LBM) is a major determinant of LVM[13, 14]. Normative pediatric reference data for LVM adjust for HT[15], $HT^{2.7}$ [16], or body surface area (BSA) [16], as proxies for LBM[17, 18]. However, short stature and alterations in body proportions prevail in DS, and how well the “typical” relationships between height and LBM with LVM extend to children with DS is not known. Understanding these relationships in our growing population of children and adults with DS is important as standards derived from nonDS children may not be applicable.

The Cardiometabolic Risk and Obesity in Adolescents with Down Syndrome study recruited youth with DS and a control cohort of typically developing children of comparable age, sex, race, and body mass index (BMI) to assess the relationship of BMI and other measures of adiposity with insulin resistance, dyslipidemia, physical activity, and CVD markers. The purpose of this report is 1) to assess the relationship of LVM with established predictors of LVM in youth (age, systolic blood pressure (SBP), heart rate (HR), and LBM) as well as surrogates of LBM, namely, HT, $HT^{2.7}$, and BSA in DS vs. controls, 2) to determine the impact of accelerometer-measured physical activity upon LVM after adjustment for established predictors, and 3) to compare LV systolic and diastolic function in DS and controls after adjustment for identified predictors. We hypothesized that LVM would be better explained by LBM than by HT, $HT^{2.7}$, and BSA in DS but did not expect LVM or LV function to differ in DS vs controls after adjustment for identified covariates.

METHODS

Adolescents with DS (n=154) and typically-developing youth (nonDS, n=102) of comparable age, sex, BMI-percentile, race, and ethnicity were recruited for a cross-sectional study examining body composition and cardiometabolic risk. The institutional review boards of Children’s Hospital of Philadelphia and Children’s National Health System approved all procedures. Parental consent and participant consent/assent, when appropriate, were obtained. AK had full access to all the data in the study and takes responsibility for its integrity and the data analysis.

Participants were males and females aged 10–20 years. Exclusion criteria included major organ system illness not related to DS (except diabetes mellitus), oncologic process, cyanotic or symptomatic CHD, pulmonary hypertension, pregnancy, genetic syndrome/medications known to affect glucose tolerance, insulin sensitivity, or lipids.

Weight was measured by digital electronic scale (Scaletonix), calibrated daily, and height was measured on a wall-mounted stadiometer (Holtain) with the participant in light clothing without shoes by trained research anthropometrists using standard techniques. Age- and sex-specific Z-scores were generated based on CDC 2000 growth charts[19] for weight (WT-Z), height (HT-Z), and BMI (BMI-Z) so that DS and nonDS groups were compared by the same reference. Overweight was defined as BMI between 85th and 95th-percentile and obesity as BMI ≥95th-percentile for age and sex. BSA was calculated as $[(HT(cm)*WT(kg))/3600]$.

Whole Body DXA was performed to measure body composition including whole body lean mass (LBM) and fat mass (FM), Hologic QDR2000 instrument (Bedford, MA). Subjects were scanned in fan beam mode using standard positioning techniques, and scans analyzed using Enhanced Whole Body *** V12.4 or V5.71A*** software provided by Hologic.

Blood pressure (BP) was measured after at least 5 minutes of rest in seated position on the right upper arm by automatic oscillometry (Dynamap, GE Healthcare). The average of the second and third measurement was used for analysis. Age and height-adjusted systolic BP-Z (SBP-Z) was calculated[20].

Echocardiograms were performed using M-mode and 2-dimensional (2D), color Doppler and tissue Doppler using Philips echocardiographic system and appropriate probe size. All images were interpreted by one pediatric cardiologist (MC) according to the American Society of Echocardiography[21, 22]. LVM was measured by area/length method using the apical four-chamber and parasternal short-axis views. LVM was calculated as $LV \text{ area} \times LV \text{ length} \times 1.05 \times 5/6$ [23]. Left ventricular ejection fraction (LVEF) was measured using the biplane disc method[23]. LV diastolic function was assessed by using the ratio of early transmitral flow velocity to early mitral annular velocity E/E' ; values from three sequential beats were averaged. Mitral valve regurgitation (MVR) was classified as none, trivial-to-mild, or moderate-to-severe. CHD history was collected from electronic medical record and by parent report and classified as absent, non-surgical, or surgical repaired.

Physical activity was measured using Sensewear Mini accelerometer, Body Media (Pittsburgh, PA). Participants were instructed to wear the activity monitor armband for 23 hours/day over 7 consecutive days, except during water activities, on the left arm halfway between the shoulder and elbow with the sensor over the triceps. A visual picture was provided to demonstrate placement. The SenseWear Mini armband contains a tri-axial accelerometer, two galvanic skin response sensors, a skin temperature sensor, a heat flux sensor and a near-body temperature sensor. Sex, age, height, weight, and sensor data are incorporated into proprietary algorithms to estimate physical activity intensity, duration, and energy expenditure. Average daily moderate-to-vigorous physical activity (MVPA, defined as ≥ 3 METS) was included in these analyses if data were available for ≥ 20 hours/day for ≥ 2 weekdays and ≥ 1 weekend day.

Continuous variables were summarized as median [minimum; maximum] and were compared between DS and non-DS using the two-sample *t* test or Wilcoxon rank sum test, as appropriate. Categorical variables were summarized as count and percentage and compared using the chi-squared test. The relationship of potential covariates (age, black race, HT, $HT^{2.7}$, BSA, SBP, HR, LBM or appendicular LBM, FM) and LVM were first examined separately in DS and nonDS using graphical inspection and Pearson or Spearman correlation depending upon normality. The Fisher z transformation for correlations coefficients was used to test whether HT, $HT^{2.7}$, BMI, BSA, and LBM were similarly correlated with LVM in DS and nonDS. Group-specific linear regression models were developed to determine the relationships of LVM with independent predictors in DS and nonDS. Combined models were then used to determine if DS was associated with differences in LVM after adjusting for covariates including MVR- and CHD-status.

Interaction terms between DS-status and predictors (e.g. LBM, age, MVPA) were included in models to assess whether they associate differently with LVM in DS and nonDS, and the likelihood ratio test was then used to assess whether the model with the interaction term was stronger than the model excluding the interaction. This same approach was used to assess the association of DS with E/E' as well as the contribution of MVPA to LVM in DS vs nonDS controls. P value<0.05 was considered statistically significant and p<0.1 is highlighted in regression models. Statistical analyses were performed with STATA (version 15.0; Stata Corp., College Station, TX).

RESULTS

LVM was available in 136 adolescents with DS (60M/76F) and 101 nonDS controls (41M/60F). As expected, age, BMI, and obesity-status were not different, but DS participants were shorter ($p<0.0001$) and had lower LBM ($p<0.0001$) and appendicular-LBM ($p<0.0001$), Table 1. Moderate-to-severe MVR was present in 2 youth with DS. History of CHD (ranging from patent ductus arteriosus to AV canal defects) was present in 86 (67.6%), 46 of whom had undergone repair. LVM did not differ between DS with vs. without CHD ($p=0.47$) or between surgically-repaired vs without CHD ($p=0.41$).

LVM was lower in DS ($p<0.0001$) compared to the nonDS cohort, Table 1. LVM was positively correlated ($p<0.0001$) with age, HT, $HT^{2.7}$, BSA, LBM, (Figure 1), BMI, appendicular-LBM, and SBP and negatively correlated with HR in both DS and nonDS (data not shown). In nonDS, the correlation of LVM with 1) LBM was similar to that with 2) HT ($p=0.14$) and 3) $HT^{2.7}$ ($p=0.26$) but lower with 4) BSA ($p<0.0001$). In contrast, in DS, LVM was more strongly correlated with 1) LBM than with 2) HT ($p=0.035$), 3) $HT^{2.7}$ ($p=0.036$), and 4) BSA ($p<0.0001$), Figure 1. Correlations of LVM with BMI were lower than with LBM in nonDS and DS ($p<0.0001$ for both), data not shown.

The next effort was to determine if LVM differed in DS and nonDS after adjustment for their shorter stature using $HT^{2.7}$ (the traditional approach) or LBM (for which $HT^{2.7}$ is a surrogate). First, DS-status-specific models adjusted for age-, HR-, SBP-, MVR-, CHD-, and black-status were developed, Table 2. As expected, $HT^{2.7}$ was associated with LVM in both DS (β -coefficient=14.1, $p<0.0001$, $R^2=0.65$) and nonDS (β -coefficient=21.7, $p<0.0001$, $R^2=0.67$). In a combined $HT^{2.7}$ -adjusted model, DS was associated with lower LVM compared to nonDS (β -coefficient= -7.70 g; $p=0.02$), Table 2. Because $HT^{2.7}$ may not accurately depict LBM in the setting of DS-related short stature and altered body proportions, LBM was substituted for $HT^{2.7}$. Unexpectedly, with adjustment for LBM, the lower LVM in DS was magnified (β -coefficient= -15.1 g; $p<0.0001$), Table 2. In models that included both LBM and $HT^{2.7}$, $HT^{2.7}$ remained associated with LVM in nonDS ($p=0.002$) but not in DS ($p=0.93$), and LVM remained lower in DS (-12.4 g). With simultaneous inclusion of both LBM and $HT^{2.7}$, the association of $HT^{2.7}$ with LVM approached significance only in nonDS ($p=0.088$) and LVM remained lower in DS (12.4 g, $p<0.0001$). With substitution of appendicular-LBM for whole body LBM, LVM remained lower in DS vs nonDS (β -coefficient= -14.12 g; $p<0.0001$). No interactions between DS-status and age or LBM were found (data not shown). These results were not altered with exclusion of two

children with DS and moderate-severe MVR. After adjustment for $HT^{2.7}$ or LBM, sex was not associated with LVM, and, thus, was not included in models.

Because increased BMI is a CVD risk factor, the relationship of BMI to LVM in DS and nonDS was also assessed. BMI was positively associated with LVM in both DS (β -coefficient=0.71, $p<0.0001$; $R^2=0.67$) and nonDS (β -coefficient=0.73, $p=0.007$; $R^2=0.70$). Additionally, because BMI is more readily measured than body composition, BMI was substituted for LBM in the regression model. In this combined model, LVM remained lower in DS vs nonDS (β -coefficient= -26 , $p<0.0001$; $R^2=0.63$). Similarly, with substitution of BSA for LBM, LVM remained lower in DS vs nonDS (β -coefficient= -15.55 $p<0.0001$; $R^2=0.70$).

Accelerometry data were available in a subset of study participants. DS youth ($n=73$) tended to engage in less MVPA than nonDS ($n=57$): 73 (0–290) vs 109 (4–339) min, but the difference did not reach significance, $p=0.07$. DS youth had lower LVM ($\beta= -13.94$, $p<0.0001$; $R^2: 0.80$) even after adjustment for MVPA, Supplemental Figure 1.

LVEF was similar in DS and nonDS youth ($p=0.9$) while E/E' was higher in DS vs nonDS ($p<0.0001$), Table 1.

In nonDS controls, E/E' was positively correlated with BMI ($\rho=0.25$, $p=0.016$), FM ($\rho=0.25$, $p=0.016$), and SBP ($\rho=0.24$, $p=0.016$) but not with age, LBM, HT, or LVM. In contrast, in DS, E/E' was negatively correlated with age ($\rho=-0.23$, $p=0.011$) and HT ($\rho=-0.22$, $p=0.013$) but not correlated with BMI ($p=0.68$), SBP ($p=0.22$), FM ($p=0.30$), LBM ($p=0.21$), or LVM ($p=0.21$). E/E' remained higher in DS after adjustment for age, HT, HR, SBP, black-, MVR-, and CHD-status, and either BMI or FM (both models: $p<0.0001$). Higher E/E' persisted ($p<0.0001$) in DS after exclusion of DS individuals with moderate-severe VR and/or CHD treated with surgical repair. Normalized E/E' ($1/(\text{square root } (E/E'))$) yielded similar results, and, thus, E/E' is used to demonstrate differences in Figure 2.

DISCUSSION

This study demonstrated lower LVM, similar LVEF, and higher E/E' in adolescents and young adults with Down Syndrome compared to youth without Down Syndrome of similar age, gender, BMI, and race. These findings were independent of the presence of well-repaired congenital heart disease in the Down Syndrome cohort.

One possible explanation for the lower LVM observed in DS may relate to their shorter stature. In typically developing youth, LBM is the strongest determinant of LVM[13–15], but $height^{2.7}$ is traditionally used as a surrogate for LBM since height scales to LBM and is more readily measured than LBM. In explanatory models that included $height^{2.7}$ but not LBM, LVM tended to be lower in DS. Unexpectedly, the lower LVM in youth with DS was magnified after adjustment for LBM or appendicular mass. These data raise concern that algorithms derived from nonDS populations that scale LVM to $height^{2.7}$ may overestimate predicted LVM in DS. Moreover, short stature and alterations in body composition are common in other congenital conditions associated with cardiac defects (e.g. Turner Syndrome, 22q11.2 deletion) and chronic childhood disorders in which the heart can be

secondarily impacted (chronic kidney disease). The convention of adjusting LVM for height^{2.7} as a substitute for LBM may be similarly problematic in these conditions. Because BMI and BSA are easily quantitated clinically, we substituted BMI as well as BSA for DXA-derived measures of body composition. BMI-adjusted models ($R^2=0.63$) and BSA-adjusted models ($R^2=0.70$) were less well fit than the LBM-adjusted models ($R^2=0.76$). However, adjustment for either BMI or BSA magnified the LVM differences between DS and nonDS compared to the height^{2.7}-adjustment. Additional studies should consider whether in clinical practice scaling to BSA is preferable to scaling to height^{2.7} in youth with DS.

Another potential contributor to the lower LVM in DS is chronically low levels of physical activity. Indeed, decreased physical activity is well-recognized in youth and adults with DS[46]; gross motor delays, poor coordination, anatomical differences, and easy fatigue have been implicated. Moreover, peak aerobic capacity is reduced in DS and time to exhaustion is shorter[24–27]. In adult athletes, physical training and greater fitness are associated with higher LVM and enhanced LV diastolic function[28–30]. In obese adolescents enrolled in the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) Study, LVM was associated with LBM and cardiorespiratory fitness, as measured by a submaximal test with cycle ergometry[31]. While moderate-to-vigorous physical activity trended toward lower in the DS cohort, lower LVM remained even after adjustment for this reduced cardiovascular physical activity.

Higher LVM is an independent predictor of CVD and CVD-related mortality in adults[32]. The extent to which lower than predicted LVM relates to outcomes in DS vs. nonDS is not known. Even more basic, the impact of acquired CVD on DS outcomes is not presently known. DS has been deemed to confer a cardioprotective effect based upon a 1977 autopsy study of five institutionalized adults with DS in whom atheroma was absent[33]. More recently, a study identified lower carotid intima-media thickness in 52 adults with DS despite higher CRP and percent body fat[34]. In contrast, epidemiologic data suggest DS is associated with increased CVD-related mortality[35]. Thus, the utility of LVM as well as other traditional markers in delineating cardiovascular disease risk needs more rigorous assessment.

Not surprisingly, LV ejection fraction was not different between groups. EF is a measure of systolic ventricular performance; low EF is associated with cardiomyopathy, ventricular injury, myocardial ischemia, and infarction. In general, these cardiac issues are not a concern in the DS population. DS is not associated with cardiomyopathy, and in individuals with CHD, LVEF is usually normal unless significant residual cardiac defects are present. Moreover, EF is neither dependent upon body habitus nor typically a reflection of physical fitness.

In contrast, diastolic function may be a reflection of the health of the cardiovascular system. The E/E' ratio measured by color Doppler and tissue Doppler imaging is a surrogate for LV diastolic function. Diastolic dysfunction is observed in populations with obesity, hypertension, exposure to smoking, sedentary lifestyle and aging[36–40]. In obese adolescents enrolled in the TODAY Study, FM was positively associated with E/E' (i.e.

worse LV diastolic function)[31]. The finding of higher E/E' in DS vs nonDS adolescents suggests stiffer left ventricles are present in DS; this difference was present regardless of underlying CHD status. Since the study is cross-sectional, we cannot determine if poorer LV diastolic function may underlie the reduced stamina frequently witnessed in youth and adults with DS or if diastolic function alterations are secondary to DS or altered physical activity. The contribution of overexpression of chromosome 21 genes (including variant and mutant forms of COL6A1 and COL6A2 among others) to congenital cardiac defects has been sought[41–43], but how this overexpression may affect LV diastolic function has not been considered.

Several limitations are worth noting. Measures of physical fitness were not performed, and, thus, we are unable to correlate either LVM or LV diastolic function with cardiorespiratory fitness. Indeed, increased LVM is well-recognized in athletes and is considered a physiologic adaptation to increased demand[44]; how well cardiac muscle can adapt to accommodate increased aerobic demand in DS remains unknown. Additionally, the percentage of the DS population with some form of CHD was higher than expected at 61% vs 50%. The extent to which this enrichment represents the population of a tertiary care center is not known, but patients followed by primary care centers and from the local community were actively recruited. Only 33% of the DS population studied underwent surgical repair and differences in echocardiogram outcomes were not explained by CHD status, suggesting the data are generalizable to adolescents and young adults with DS. The cross-sectional nature of this study precludes any assessments of changes in LVM and LV function over time. Finally, LVM was measured in a relatively young cohort and its link if any with cardiovascular morbidity and mortality cannot be determined from this study.

CONCLUSION

In summary, this study has identified lower LVM and altered diastolic function in youth and young adults with DS compared to nonDS individuals. Neither the mechanisms underlying these differences nor the relevance of the findings to adult CVD outcomes are yet known. The combination of chronic sedentary lifestyle and diastolic dysfunction may interact to contribute to this phenotype. Moreover, the finding of lower LVM and diastolic dysfunction for DS youth with congenital cardiac defects is novel. Genetic differences that affect the anatomical structure of the heart could also be affecting the morphologic development and function even in the absence of anatomical disease. The impact of DS on cardiac remodeling and long-term outcomes after surgical repair compared to nonDS CHD survivors should be explored. Longitudinal studies in children and adults could provide greater insight into the role of LVM as an intermediary for later CVD in DS. An improved understanding of cardiovascular health in DS is necessary for optimizing care for this growing and aging population while the concerns raised regarding scaling to height in DS may also be relevant for other conditions in which short stature and alterations in body composition feature.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Relationship of Left Ventricular Mass with LBM and Surrogates of LBM in Youth with Down Syndrome and Typically Developing Youth Matched for Age, Sex, Race, and BMI.

HT, HT^{2.7}, BSA, and LBM are all highly correlated with LVM in DS (x) and nonDS (●).

In nonDS, the correlation between LVM and LBM was not different than the correlation of LVM with HT ($p=0.14$) or HT^{2.7} ($p=0.26$) but correlated less strongly with BSA ($p<0.0001$). In contrast, in DS, LVM was more strongly correlated with LBM than with HT ($p=0.035$) (and by extension HT^{2.7} ($p=0.036$)) and BSA ($p<0.0001$).

Figure 2. Comparison of Left Ventricular Diastolic Function, as Measured by E/e', in Youth with Down Syndrome and Typically Developing Youth Matched for Age, Sex, Race, and BMI.

LV diastolic function was worse in DS regardless of CHD disease status [(x no CHD), (+ h/o CHD not requiring surgical repair), (h/o CHD repaired surgically)] compared to matched controls (●). Models adjusted for age, HT, BMI, SBP, black- and MVR-status.

Table 1.

Study Participant Demographics, Anthropometrics, and ECHO Characteristics

	Down Syndrome (N=136)	Control (N=102)	p-value
Age, yr	14.6 (10.01; 20.99)	14.78 (10.17; 20.99)	0.99
Sex, M/F	60/76	42/60	0.63
Black/non-black	26/110	24/78	0.41
Weight, kg	53.3 (21.5; 109.8)	66.7(27.2; 121.4)	<0.0001
Weight-Z	0.26 (−3.27; 2.81)	1.34(−2.36; 3.61)	<0.0001
Height, cm	144.57 (116.73; 170.27)	163.17 (134.8; 186.7)	<0.0001
Height-Z	−2.37 (−4.74; 0.82)	0.38 (−1.99; 2.57)	<0.0001
Height ^{^2.7} , m ^{^2.7}	3.76 (2.24; 5.40)	2.70 (1.52; 4.21)	<0.0001
BMI, kg/m ²	25.47(14.53; 50.55)	25.02 (14.23; 44.63)	0.97
BMI-Z	1.39 (−1.52; 2.95)	1.32 (−1.98; 2.82)	0.57
BMI Percentile Category, N (%)			
<i>Obese</i>	55 (41)	40 (40)	0.50
<i>Overweight</i>	30 (22)	22 (22)	
<i>Non-Obese/Non-Overweight</i>	50 (37)	39 (39)	
LBM, kg	33.5 (14.5; 65.3)	42.2 (18.1; 72.5)	<0.0001
LBMI-Z	0.51 (−2.28; 2.86)	0.57 (−2.87; 2.76)	0.12
Appendicular LBM, kg	13.7 (5.4; 29.5)	18.9 (7.6; 34.9)	<0.0001
HR, bpm	73 (47; 113)	74.5 (46; 103)	0.59
SBP, mm Hg	105 (80; 139)	109 (89; 138)	0.04
SBP-Z	0.01 (−104.96; 2.88)	−0.11 (−2.47; 2.38)	0.10
Mitral Valve Prolapse, N (%)			
<i>Trivial-Mild</i>	52 (39)	34 (34)	0.27
<i>Moderate-Severe</i>	2 (1)	0	
LVM, g	68.3 (32.1; 135)	94.0 (43.9; 164.6)	<0.0001
LV Ejection Fraction (%)	65 (54; 77)	64 (53; 77)	0.59
E/E' (121 DS, 95 nonDS)	8.41 (5.54; 21.4)	5.81 (3.44; 9.56)	<0.0001

For continuous variables: median (min; max)

BMI body mass index

HR heart rate

BMI-Z body mass index standard deviation score

LBM lean body mass

LBMI-Z lean body mass index standard deviation score

LVM left ventricular mass

LV left ventricle

SBP systolic blood pressure

SBP-Z systolic blood pressure standard deviation score

Comparison of LVM and its Relationship with Height^{2.7} and LBM in Adolescents with DS and Typically-Developing nonDS Controls

Table 2.

	Left Ventricular Mass (g)									
	HT ^{2.7} -adjusted			LBM-adjusted			HT ^{2.7} & LBM-adjusted			Appendicular LBM-adjusted
	DS	Controls	DS vs Controls	DS	Controls	DS vs Controls	DS	Controls	DS vs Controls	DS vs Controls
R²	0.66	0.67	0.71	0.71	0.73	0.76	0.71	0.74	0.76	0.75
Constant	-1.4	-63.5***	-19.7	14.4	13.4	22.7	13.7	-4.37	13.3	22.7
HT^{2.7} (m^{2.7})	13.7***	21.7***	18.3***	--	--	--	0.51	6.86*	4.27	-
LBM (kg)	--	--	--	1.12***	1.72***	1.45***	1.1***	1.37***	1.24***	-
Appendicular LBM (kg)	--	--	--	--	--	--	--	--	--	2.83***
Age (y)	2.53***	0.61	1.79***	1.35**	-0.87	0.42	1.35**	-0.93	0.44	0.78**
SBP (mmHg)	0.22*	0.80***	0.40***	0.23**	0.49***	0.30***	0.22*	0.53***	0.30***	0.33**
HR (bpm)	-0.39***	-0.23*	-0.31***	-0.39***	-0.40***	-0.36***	-0.38***	-0.35**	-0.33***	-0.37***
Trivial-minimal MVR	3.98	2.5	1.1	1.80	6.32**	3.54*	1.76	5.46*	3.10	3.43
Mod-severe MVR	0.31	--	-0.34	4.79	--	4.93	4.70	--	4.19	6.82
CHD w/o surgery	3.6	--	3.35	2.78	--	2.01	2.79	--	2.20	2.33
CHD w/surgery	6.22*	--	6.46*	5.33*	--	4.88	5.35	--	5.10	5.42*
Black	5.67*	-0.43	3.35	0.46	-13.5***	-5.86***	0.55	-10.4**	-4.46*	-7.83***
Down Syndrome	--	--	-7.70	--	--	-15.1	--	--	-12.40	-14.12
			p=0.02			p<0.0001			p<0.0001	p<0.0001

(shown are partial β -coefficients for each independent variable and R^2 for each model)***
p<0.01**
p<0.05*
p<0.1

BMI body mass index

CHD congenital heart defect

FM fat mass

SBP systolic blood pressure

MVR mitral valve regurgitation

LBM lean body mass

HR heart rate

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