Left Ventricular Structure and Function in Obese Adolescents: Relations to Cardiovascular Fitness, Percent Body Fat, and Visceral Adiposity, and Effects of Physical Training

Brett M. Mitchell, MS; Bernard Gutin, PhD; Gaston Kapuku, MD, PhD; Paule Barbeau, PhD; Matthew C. Humphries, MS; Scott Owens, PhD; Sarita Vemulapalli, BS; and Jerry Allison, PhD

ABSTRACT. Objective. Little is known about the relations of fitness and fatness to left ventricular structure and function in obese adolescents. This project had 2 purposes: 1) to determine the correlations of cardiovascular fitness and adiposity to left ventricular parameters in obese adolescents; and 2) to see the effect of 8 months of physical training (PT) at low and high intensities.

Design. Obese 13- to 16-year-olds (N = 81) were tested at baseline and then randomly assigned to lifestyle education (LSE) alone, LSE plus moderate-intensity PT, or LSE plus high-intensity PT. Follow-up testing was conducted 8 months later. Because no significant differences were found between moderate-intensity and high-intensity PT, the groups were combined to form a LSE + PT group.

Intervention. Eight months of PT, offered 5 days per week with the target energy expenditure for all PT participants being 250 kcal/session, and LSE every 2 weeks.

Outcome Measures. Left ventricular mass divided by height to the 2.7th power (LVM/Ht2.7), midwall fractional shortening (MFS), and relative wall thickness (RWT) were measured using M-mode echocardiography. Cardiovascular fitness was measured by a maximal multistage treadmill test; percent body fat (%BF) with dual-energy radiography absorptiometry; and visceral adipose tissue (VAT) with magnetic resonance imaging.

Results. At baseline, high levels of VAT were associated with higher RWT (r = 0.30) and lesser MFS (r = -0.29). Compared with the LSE-alone group, the LSE + PT group significantly improved in cardiovascular fitness and decreased in %BF and VAT. However, there were no significant differences between groups on changes in LVM/Ht2.7, MFS, or RWT. Individual changes in cardiovascular fitness, %BF, and VAT did not correlate significantly with interindividual changes in left ventricular structure and function.

Conclusions. High levels of VAT were associated with unfavorable left ventricular structure and function. However, no evidence was provided that an 8-month PT program, which improved cardiovascular fitness and reduced general and visceral adiposity, improved left ventricular structure and function. Future studies consisting of longer training programs and/or greater weight reductions are needed to see whether the adverse left ventricular effects of obesity can be ameliorated by exercise training. Pediatrics 2002;109(5). URL: http://www.pediatrics.org/cgi/content/full/109/5/e73; obesity, physical training, visceral adiposity, ventricular function-left.

ABBREVIATIONS. CVF, cardiovascular fitness; %BF, percent body fat; VT, visceral adipose tissue; LVM, left ventricular mass; RWT, relative wall thickness; MFS midwall fractional shortening; PT, physical training; HR, heart rate; EE, energy expenditure; LSE, lifestyle education; AngII, angiotensin II.

Obesity and physical inactivity are modifiable lifestyle factors associated with cardiovascular disease, one of the major killers in the United States. The prevalence of obesity in American children is on the rise and presents a major public health concern. Unfavorable cardiovascular risk profiles are already present in children with low levels of cardiovascular fitness (CVF) and high levels of percent body fat (%BF) and visceral adipose tissue (VAT). In addition, adolescent obesity is strongly associated with adult obesity and may lead to type 2 diabetes, hypertension, or stroke. Left ventricular mass (LVM) and relative wall thickness (RWT), measures of left ventricular (LV) structure, and midwall fractional shortening (MFS), a measure of LV function, have been shown to be independent predictors of cardiovascular morbidity. Liao and colleagues found that increased levels of LVM divided by height to the 2.7th power (LVM/Ht2.7) was associated with increased risk of mortality in adults with or without coronary artery disease.

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participants were not randomly assigned to groups, and no between-groups analyses were performed. In obese adolescents, a weight- and %BF-reducing diet intervention did not elicit any changes in LV structure and function.\textsuperscript{17} We have previously shown that PT has a favorable influence on %BF and VAT in children.\textsuperscript{18} To our knowledge, no randomized, controlled studies have examined influences of PT on LV structure and function in obese adolescents.

Therefore, this study had several aims. First, we examined baseline relations of CVF, %BF, and VAT with various measures of LV structure and function. We hypothesized that unfavorable levels of LVM/HT\textsuperscript{2,7}, RWT, and MFS would be associated with high %BF and VAT, and low CVF. We then tested the effects of 8 months of PT on LV structure and function. We hypothesized that LSE + PT, especially high-intensity PT, would elicit greater improvements in LV structure and function than LSE alone. Lastly, we explored the degree to which individual differences in LV changes could be explained by individual variation in changes of CVF, %BF, and VAT, as well as PT-process variables such as PT attendance, heart rate (HR), and energy expenditure (EE) during PT.

METHODS

Participants and Design

Obese 13- to 16-year-old youths were recruited via flyers sent to parents of children who attended area schools. Youths and parents signed informed consents in accordance with procedures of our Human Assurance Committee. To be included, a child needed to have a triceps skinfold greater than the 85th percentile for gender, ethnicity, and age;\textsuperscript{19} not be involved in any other weight control or exercise program; and not have any physical activity restrictions.

Youths underwent baseline testing and were randomly assigned, within gender and ethnicity, to 1 of 3 experimental groups. One group engaged in biweekly lifestyle education (LSE) classes alone, the second group engaged in LSE plus moderate-intensity PT, while the third group engaged in LSE plus high-intensity PT. Full-testing sessions were again conducted after 8 months of the experimental period.

Measurement of LV Structure and Function

All LV measurements were conducted as described previously.\textsuperscript{20} In brief, LVM was calculated with a formula that has been validated for children with normal hearts:\textsuperscript{21} $LVM = 0.80 \times ([IVSD + LVDD + LVPWD\textsuperscript{2} – (LVDD\textsuperscript{2})] + 0.06)$, where IVSD = intraventricular septal dimension, LVDD = LV internal dimension during diastole, and LVPWD = LV posterior wall dimension. RWT was calculated as follows: $RWT = (IVSD + LVPWD)/LVDD$. MFS was calculated following the method described by de Simone et al\textsuperscript{a} as follows: $MFS = ([LVDD + LVPWD/2 + IVSD/2]–[IVDS + HS/2])/([LVDD + LVPWD/2 + IVSD/2]$, where LVDS = LV internal diameter in systole and HS/2 = assumed LV inner-shell myocardial thickness at end systole, taking into account the epicardial migration of midwall during systole in a spherical model.

Measurement of Body Composition and CVF

Details of the body composition, CVF, and VAT measurements are given elsewhere.\textsuperscript{20} Briefly, body weight (in shorts and T-shirt) and height (without shoes) were measured with an electronic scale and stadiometer. Total body composition was measured with dual-energy radiograph absorptiometry (Hologic QDR-1000, Waltham, MA, software version 6.0), and VAT was determined with a 1.5-Tesla magnetic resonance imaging system.

A multistage treadmill test was used to measure CVF. The treadmill test began at 2.5 mph and 0% grade for 2 minutes, speed increased to 3 mph for the next work rate, and then the grade was increased 2% every 2 minutes from then on, until the youth declined to continue despite encouragement. Our primary index of CVF was submaximal in nature; the $VO_2$ at a HR of 170 beats per minute ($VO_2$-170); the rationale for this index of fitness is provided elsewhere.\textsuperscript{25}

LSE

The 1-hour LSE sessions were offered to each youth once every 2 weeks for the 8-month intervention; youths were paid $5 for each LSE class attended. The LSE included the following: principles of learning and behavior modification, information about nutrition and PT, discussions of various aspects of the food consumption process, psychosocial factors related to obesity, and problem solving/coping skills. A licensed clinical psychologist who specializes in the treatment of eating disorders and obesity and who has experience in providing LSE to children, adolescents, and adults taught the LSE sessions.

PT

The PT was offered 5 days per week, except during the weeks when that group was scheduled for LSE on 1 day. Transportation was provided for each participant to attend the PT session at our facility. EE was held constant at 1045 kJ (250 kcal)/session regardless of group assignment. Participants randomized to the moderate-intensity PT group and high-intensity PT group exercised at HRs corresponding to 55% to 60% and 75% to 75% of peak $VO_2$, respectively. The number of minutes of exercise needed to expend 1045 kJ was established for each participant. Thus, the moderate-intensity group exercised for an average of 43 minutes, while the high-intensity group exercised for about 29 minutes.

Details of the exercise sessions and the estimation of EE have been described elsewhere.\textsuperscript{22} Activities included exercise on machines (ie, treadmills, bicycles, rows, and stair-stoppers), aerobics, basketball, badminton, kickball, and aerobic slide. As an incentive, each teenager was awarded points for maintenance of target HRs that were redeemed for prizes. To encourage attendance, each teenager was paid $1 for each PT class attended.

Statistical Analyses

The dependent variables were checked for normality before the analyses, and appropriate transformations applied when necessary. Our participants were not sampled to be representative of their particular gender-ethnicity subgroups; therefore, we did not draw any inferences concerning gender or ethnicity differences. However, we did adjust for gender and ethnicity in the analyses that evaluated the effects of LSE and PT. For analyses that involved ethnicity (ie, black/white), the 1 Hispanic subject was omitted, but this subject was included in other analyses (ie, correlations).

Pairwise associations among baseline measures were evaluated using the Pearson correlation coefficient. The significance level was set at 0.05.

The hypotheses dealing with the effects of PT were tested with an analysis of variance on the baseline to 8-month change scores. Both effectiveness and efficacy analyses were conducted. The effectiveness analyses used all participants assigned to the experimental groups who returned for posttesting, regardless of their compliance with the prescribed regimens. The efficacy analyses used only subjects who met preset criteria for appropriate exposure to the interventions; ie, maintenance of heart rates within 10 beats per minute of those prescribed for low- or high-intensity PT and attendance in the PT sessions of greater than 40% (ie, twice per week). To test the main hypothesis that the PT would lead to favorable changes in LVM/HT\textsuperscript{2,7}, RWT, and MFS, youths who met the 40% attendance criterion were combined into 1 LSE plus PT group and were compared with the LSE-alone group.

To explore correlates of individual variability in response to the interventions, we first examined correlates of change for all the participants in all groups for whom a baseline to postintervention difference score was available. Then we analyzed the PT participants alone to see whether individual differences in the changes of LV structure and function could be explained by PT-process variables such as PT-attendance, PT-HR, and PT-EE.
RESULTS

Baseline Characteristics and Relationships

Characteristics for the 81 participants before group assignment and intervention are presented in Table 1. There were no significant differences among the randomly assigned experimental groups, and there were no significant ethnicity or gender interactions with respect to the 3 main outcome variables (LVM/Ht2.7, RWT, and MFS).

Table 2 shows the baseline intercorrelations among variables. Because all participants were selected to be obese and inactive at baseline, the magnitude of correlations between %BF, CVF, and the LV variables was probably limited. Neither %BF nor CVF were significantly correlated with the LV variables. VAT was not highly correlated with CVF and %BF, but was significantly associated with unfavorable levels of RWT and MFS, suggesting that it provides somewhat independent information about whether this aspect of adiposity affects pathophysiological processes underlying CVD. In addition, RWT and MFS were inversely correlated (P < .001), indicating the association between LV structure and function.

Effects of the Interventions: PT

The average attendance of the LSE plus moderate-intensity PT and LSE plus high-intensity PT groups was very similar (51% and 56%, respectively). For the moderate-intensity group, the prescribed and attained HRs were similar (137 and 138 beats per minute, respectively). However, the high-intensity PT group achieved a mean HR that was lower (154 beats per minute) than the prescribed mean HR (167 beats per minute). Although the high-intensity group’s HR was significantly higher, PT-EE was not significantly different between the 2 groups (1049 beats per minute). Although the high-intensity group exercised for a shorter amount of time.

Effects of the Interventions: Efficacy Analyses

As presented more completely elsewhere,20 the LSE plus high-intensity PT group significantly improved CVF more than the LSE-alone group (P = .009), with the moderate-intensity PT group being intermediate between, and not significantly different from, the other 2 groups. However, the effectiveness analyses of %BF and VAT showed no significant differences among the 3 groups (data not shown).

We obtained an echocardiogram for 56 out of 61 participants who returned for posttesting. The range of increases for LVM over 8 months in all groups were between 7.2 and 14.0 g. The 3-group analyses found no significant group differences in changes for the LV variables (data not shown). Thus, we proceeded to conduct efficacy analyses using only subjects who met criteria for exposure to PT.

Effects of the Interventions: Efficacy Analyses

We initially set 2 criteria for adequate exposure to the specific doses of PT: attendance >40% and HR within 10 beats per minute of the prescribed HR zones. However, because of the difficulty we had in keeping participants in their target zones, the number of participants remaining in the PT groups who met both of these criteria fell to 9 and 8, compromising our ability to test the intensity hypothesis. For the LV variables, the F ratios for comparisons of the 3 groups did not achieve significance (data not shown). Therefore, this study provided no experimental evidence that the 2 PT intensities produced different degrees of change for LVM/Ht2.7, RWT, or MFS.

To test the study hypothesis that PT would lead to favorable changes in LV variables in obese adolescents, 1 LSE plus PT group was formed of all youths who attended PT at least 2 days per week; this group was then compared with the LSE-alone group.

<table>
<thead>
<tr>
<th>TABLE 1. Baseline Characteristics: Mean (Standard Deviation)</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Age (y)</td>
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<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight (kg)</td>
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<tr>
<td>CV fitness</td>
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<tr>
<td>Body composition</td>
</tr>
<tr>
<td>VAT (cm³)</td>
</tr>
<tr>
<td>LV structure and function</td>
</tr>
<tr>
<td>LVM (g)</td>
</tr>
<tr>
<td>LVM/Ht2.7 (g/m²7)</td>
</tr>
<tr>
<td>RWT (cm)</td>
</tr>
<tr>
<td>MFS (%)</td>
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</tbody>
</table>

* P < .05 for males compared with females.
† P < .05 for whites compared with blacks.
baseline and 8-month values and changes for the main outcome variables from those who attended >40% are shown in Table 3. Details of the CVF and body composition results are provided elsewhere.20 In brief, the LSE + PT group showed more favorable changes over the 8-month intervention than the LSE-alone group. However, no significant group differences were found for any of the LV variables.

Correlates of Change

Table 4 shows the correlations among change scores; these were calculated to determine whether individual differences in changes in fitness and adiposity, regardless of group membership, would explain individual variability in response to the interventions. However, individual changes in CVF, %BF, or VAT did not correlate with individual changes in LV structure and function. In the analysis that included only the participants who engaged in PT (N = 40), the bivariate correlations between change in LVM/HI, RWT, and MFS were not significantly correlated with any of the 3 PT-process variables (PT-attendance, PT-HR, and PT-EE).

It is noteworthy that individual changes in RWT and MFS were highly correlated, providing additional support for the idea that these indices of LV structure and function are associated.

DISCUSSION

This study showed that a PT program that was sufficient to improve CVF and to reduce general and visceral adiposity in obese adolescents did not elicit favorable changes in adiposity-related LV structure or function; thus, the main hypothesis of the study was not supported. This result is consistent with those of other studies that failed to find that exercise or weight loss enhanced LV structure or function.14 However, a study of obese adults who lost large amounts of weight after gastroplasty did show improved LVM and RWT.14 Thus, the relatively modest reductions in adiposity that we produced may have been insufficient to have beneficial effects on LV structure and function. Furthermore, we were unable to show that individual variability in LV changes were explained by individual variability in changes of fitness and adiposity.

Interventions that last longer and/or elicit greater reductions in adiposity may be needed to improve LV structure and function in obese youths. Future studies involving more obese youths (>95th percentile for triceps skinfold) and better attendance rates may result in favorable improvements in LV measures. With respect to our attendance rates, we reported the overall percentage, which included children who dropped out midway through the 8-month program. Therefore, it is difficult to analyze our attendance rates and to categorize them (ie, “low”) as there are insufficient studies for comparison. Obert and colleagues found LV changes in nonobese youths using >80% heart rate maximum exercise intensity.16 A higher exercise intensity and/or greater EE per exercise session, such as that seen in Obert’s study, may result in favorable changes. Exercise sessions in our current studies are being performed at the schools of the children, rather than at our institute, to improve attendance. Other indices of LV function (ie, diastolic function), which seem to provide information about early aspects of cardiac pathophysiology, may be more sensitive to changes in fitness and adiposity early in life.

At baseline, we did not find any significant correlations between %BF and LV variables as reported previously,17,22 most likely because all youths were in the obese category. Nonetheless, we did find that visceral adiposity was associated with unfavorable LV structure and function, suggesting another pathway through which this fat depot has deleterious effects on CV health, starting in youth. In adults, previous studies reported that VAT was correlated with LVM and LV internal dimension during diastole.24,25

Cardiovascular involvement (ie, hypertension, increased LVM, cardiac malfunction) can be identified in early stages of obesity. Possible rationales may include volume overload or humoral activation. Obesity may activate the renin-angiotensin-system; a local renin-angiotensin system has been identified within adipose tissue.26–28 Cooper et al29 found that the angiotensin-convert enzyme and angiotensinogen were increased in obese subjects, implying an increased production of angiotensin II (Ang II). It has been recognized that Ang II elicits vaso-

**TABLE 3.** Comparisons Between LSE Alone and LSE + PT: Mean (SEM)

<table>
<thead>
<tr>
<th>Variable</th>
<th>LSE Alone (n = 15)</th>
<th>LSE + PT (n = 20)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Month 8</td>
</tr>
<tr>
<td>CVF (mL/kg/min)</td>
<td>20.1 (1.1)</td>
<td>19.8 (1.0)</td>
</tr>
<tr>
<td>%BF (%)</td>
<td>45.5 (1.6)</td>
<td>45.3 (1.7)</td>
</tr>
<tr>
<td>VAT (cm³)</td>
<td>296 (29)</td>
<td>286 (29)</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>129.3 (6.8)</td>
<td>143.3 (9.1)</td>
</tr>
<tr>
<td>LVM/HI²7 (g/m²²)</td>
<td>32.9 (2.0)</td>
<td>34.9 (1.9)</td>
</tr>
<tr>
<td>IVSD (cm)</td>
<td>0.786 (0.017)</td>
<td>0.797 (0.025)</td>
</tr>
<tr>
<td>LVPWD (cm)</td>
<td>0.775 (0.023)</td>
<td>0.806 (0.030)</td>
</tr>
<tr>
<td>LVIDD (cm)</td>
<td>4.93 (0.12)</td>
<td>5.11 (0.10)</td>
</tr>
<tr>
<td>RWT (cm)</td>
<td>0.32 (0.01)</td>
<td>0.32 (0.01)</td>
</tr>
<tr>
<td>MFS (%)</td>
<td>21.2 (0.6)</td>
<td>20.9 (0.5)</td>
</tr>
</tbody>
</table>

IVSD indicates intraventricular septal thickness (diastole); LVPWD, left ventricular posterior wall thickness (diastole); LVIDD, left ventricular internal diameter (diastole).

*P < .05 compared with LSE alone.
constrictive and trophic effects in the cardiovascular system. Therefore, increased levels of Ang II may be a potential pathway leading to obesity-related cardiovascular complications. Also, insulin resistance and leptin levels have been suggested as alternate pathways contributing to obesity-related cardiac dysfunction. Leptin, produced by adipocytes, increases cardiac contraction via nitric oxide production and may contribute to obesity-related cardiac dysfunction.

CONCLUSION
VAT was associated with unfavorable LV structure and function. However, despite producing favorable changes in fitness and general and visceral adiposity, we did not provide evidence that an 8-month LSE plus PT program produced favorable changes in LV structure and function compared with LSE alone. Thus, interventions that are more intensive and last longer than 8 months, and/or produce greater changes in general and visceral adiposity may be necessary before significant favorable effects on obesity-associated LV variables can be seen in obese youths.

ACKNOWLEDGMENT
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REFERENCES

TABLE 4. Correlations of Change Scores for All Participants Who Returned for Posttesting (n = 56); Correlations for PT-Process Variables Are Shown for Those Who Engaged in PT (n = 40)

<table>
<thead>
<tr>
<th>Δ%BF</th>
<th>ΔVAT</th>
<th>ΔLVM/Ht2.7</th>
<th>ΔRWT</th>
<th>ΔMFS</th>
<th>PT-Att</th>
<th>PT-HR</th>
<th>PT-EE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.52*</td>
<td>0.33*</td>
<td>0.09</td>
<td>0.10</td>
<td>−0.14</td>
<td>0.32*</td>
<td>0.42*</td>
<td>0.37*</td>
</tr>
<tr>
<td>0.35*</td>
<td>−0.12</td>
<td>−0.15</td>
<td>0.25</td>
<td>−0.21</td>
<td>−0.28</td>
<td>−0.23</td>
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<tr>
<td>−0.09</td>
<td>−0.13</td>
<td>0.04</td>
<td>−0.04</td>
<td>−0.03</td>
<td>−0.24</td>
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<tr>
<td>0.05</td>
<td>−0.09</td>
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<td>0.24</td>
<td>0.12</td>
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<tr>
<td>−0.68*</td>
<td>0.27</td>
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<td>−0.12</td>
<td>0.03</td>
<td>−0.13</td>
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<td>0.06</td>
<td>0.18</td>
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<td>0.26</td>
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ΔCVF indicates change in oxygen consumption at HR of 170 beats per minute; Δ%BF, change in percent body fat; ΔVAT, change in VAT; ΔLVM/Ht2.7, change in LVM/height2.7; ΔRWT, change in RWT; ΔMFS, change in MFS; PT-Att, attendance at PT sessions; PT-HR, average HR taken from all PT sessions; PT-EE, average EE during PT sessions.

* P < .05.


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