Reductions in visceral fat during weight loss and walking are associated with improvements in $\dot{V}O_2_{\text{max}}$

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Received 9 November 1999; accepted in final form 8 August 2000

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The accumulation of fat in visceral depots, independent of total body obesity, is associated with the development of dyslipidemia, hypertension, glucose intolerance, and hyperinsulinemia in women (10, 13, 36). These metabolic abnormalities increase the risk for cardiovascular disease (19) and diabetes (25), which are the leading causes of death among older women (16, 31).

Several studies show that lifestyle interventions, including hypocaloric dieting for weight loss (WL) and/or aerobic exercise training (AEx), reduce abdominal obesity and cardiovascular disease risk factors (4, 14, 33, 37). However, only a few studies use computed tomography (CT) or magnetic resonance imaging to document whether these interventions preferentially decrease visceral adipose tissue area (VAT). In the hypocaloric WL studies, there was a preferential loss of VAT compared with abdominal subcutaneous adipose tissue area (SAT) in premenopausal women (20, 39), postmenopausal women (32), and men (20, 27, 29). However, hypocaloric WL often reduced lean body mass (LBM) (20, 32), which resulted in a decline in resting metabolic rate (20). Other studies have shown that AEx training blunts the loss of LBM (10, 30). The effects of AEx on the preferential loss of VAT are variable and may be affected by the magnitude of the improvement in maximal oxygen uptake ($\dot{V}O_2_{\text{max}}$). Schwartz et al. (30) showed a 25% reduction in VAT with a 22% increase in $\dot{V}O_2_{\text{max}}$ during AEx in old men, whereas a 17% decrease in VAT was associated with a 18% increase in $\dot{V}O_2_{\text{max}}$ in young men. This suggests that the reduction in VAT may be more pronounced with greater improvements in $\dot{V}O_2_{\text{max}}$. However, Despres et al. (9) reported an 11% decrease in SAT and no change in VAT after an AEx program that increased $\dot{V}O_2_{\text{max}}$ by 15% in premenopausal women. Thus, although AEx seems to reduce VAT and preserve LBM in some studies, the best treatment for visceral and total body obesity may be a combined program of hypocaloric WL and AEx.

The few studies that examined the effects of a combination of hypocaloric WL and AEx showed that the loss of VAT and body weight was similar to that observed with hypocaloric dieting alone and that LBM was preserved (1, 28, 29). There are no studies examining the effect of changes in $\dot{V}O_2_{\text{max}}$ during a hypocaloric WL and walking program on changes in VAT and SAT in postmenopausal women. We hypothesized that postmenopausal women who show the greatest improvement in $\dot{V}O_2_{\text{max}}$ during a 6-mo hypocaloric WL and walking intervention would lose the most VAT.

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METHODS

Subject selection. All subjects were healthy, obese (body mass index \(>27 \text{ kg/m}^2\)) postmenopausal women (no menstruation for at least 1 yr, with follicle-stimulating hormone \(>30 \text{ IU/l}\)). The women were sedentary (\(<20 \text{ min of AEx, 2 times/wk}\)), weight stable (\(<2.0-\text{kg weight change in past year}\)), and had not smoked for at least 5 yr. None of the women was on estrogen or hormone replacement therapy in the previous year or medications affecting lipids, glucose metabolism, or blood pressure. All women provided informed consent to participate in the study according to the guidelines of the University of Maryland Institutional Review Board for Human Research.

Initial screening evaluations included a medical history, physical examination, fasting blood profile, 2-h oral glucose tolerance test, 12-lead resting electrocardiogram, and a treadmill exercise test according to the Bruce protocol (6a). Subjects with evidence of diabetes (2), hypertension (blood pressure \(>140/90 \text{ mmHg}\)), hyperlipidemia (triglyceride \(>400 \text{ mg/dl}\)), heart disease, liver disease, renal or hematologic disease, cancer, other medical disorders, or orthopedic limitations that would affect physical activity were excluded. Sixty-four women met the criteria and were enrolled in the study.

Dietary control. Before beginning the intervention, the women completed an initial 7-day food record to provide information about their dietary habits. All women met weekly with a registered dietitian for 8–10 wk and were instructed in the principles of the American Heart Association Step 1 diet to establish dietary control before research testing. Subjects were weight stable (\(<0.50-\text{kg weight change on this diet for at least 2 wk before retesting}\). The dietitian monitored compliance by weekly review of 7-day food-exchange records and 24-h dietary recalls.

Research testing. Measurements of body composition and aerobic fitness were performed before and after a 6-mo WL and walking program. Waist-to-hip ratio was measured in duplicate and calculated as the ratio of the minimal waist circumference to the circumference at the maximal gluteal protuberance. A total body scan was performed using dual-energy X-ray absorptiometry (model DPX-L, Lunar Radiation, Madison, WI) to determine percent body fat, nonosseous LBM, and fat mass. A single-slice CT scan taken midway between L4 and L5 was performed using a GE Hi-Light CT scanner to measure VAT and SAT, as previously described (22).

\(\text{V}\dot{O}_2\text{max}\) was measured during a modified Balke protocol (3a). Treadmill speed remained constant at the speed that elicited 70% of heart rate maximum with 0% grade. The elevation was increased by 2% every 2 min for the first 4 min and then by 2% every minute until maximal exhaustion. Oxygen uptake (\(\text{V}\dot{O}_2\)), carbon dioxide production, and minute ventilation were obtained every 20 s using a Sensormedics metabolic measurement cart (model 2900, Yorba Linda, CA). Heart rate was determined electrocardiographically throughout the tests. Two of three criteria had to be met for achievement of \(\text{V}\dot{O}_2\text{max}\): 1) maximal heart rate \(\pm 10 \text{ beats/min of age-predicted maximal heart rate (heart rate } = 220 - \text{ age)\), 2) respiratory exchange ratio of at least 1.10, and 3) plateau in \(\text{V}\dot{O}_2\) (\(<2.0 \text{ ml.kg}^{-1}.\text{min}^{-1}\) ). \(\text{V}\dot{O}_2\text{max}\) was calculated from the average of the three highest 20-s collections.

Hypocaloric WL and walking intervention. During the 6-mo WL intervention, women met weekly with a registered dietitian for instruction in the principles of a hypocaloric diet (250–350 kcal/day deficit) that followed the American Heart Association Step 1 guidelines. The program focused on eating behavior, stress management, control of portion sizes, modification of binge eating, and other adverse habits. The dietitian monitored compliance by weekly review of 7-day food exchange records. In addition, women were instructed to walk 3 days/wk at a target heart rate of 50–60% of heart rate reserve for 30–45 min. The women walked 1 day/wk on a treadmill at our exercise facility under the supervision of an exercise physiologist, during which time heart rate was determined with a heart rate monitor, and they walked the other 2 days on their own. After the 6-mo intervention, the women continued the walking program but were weight stabilized (\(<0.5-\text{kg change}\) on a eucaloric diet for a period of 2 wk before retesting.

Statistics. Standardized residual plots and standardized residual vs. predicted value plots for all variables were used to examine the assumption of independence. No violations of regression or ANOVA assumptions were identified, and all data analyses were completed using SPSS for Windows. Analysis of covariance (ANCOVA) was used to adjust \(\text{V}\dot{O}_2\text{max}\) for LBM at baseline and after the intervention (34). Change values were defined as the difference between the postintervention values and the baseline values, and relative change (%) was calculated by expressing the change value as a function of the baseline value. The absolute change in \(\text{V}\dot{O}_2\text{max}\) was adjusted for baseline \(\text{V}\dot{O}_2\text{max}\) using ANCOVA. Correlations between response variables and their respective baseline values were determined using Pearson correlation analysis. Response variables that significantly correlated with their baseline value were adjusted using ANCOVA. One-way ANOVA was used to determine differences between variables before and after intervention and to determine statistically significant differences between women who improved \(\text{V}\dot{O}_2\text{max}\) (highest 3 quartiles) and women who did not improve \(\text{V}\dot{O}_2\text{max}\) (lowest quartile). Statistically significant relationships between change in \(\text{V}\dot{O}_2\text{max}\) and body composition were determined using Pearson correlation analysis. Multiple-regression analysis was used to determine independent predictors of the change in VAT. Data are presented as means \(\pm \text{SE}\), and the level of significance was set at \(P < 0.05\) for all analyses.

RESULTS

Dropout rate and adherence to the walking intervention. We report data on the 40 women who completed the WL and walking intervention. Reasons for dropout included illness, relocation, personal reasons, and/or time constraints of participation. All women had follicle-stimulating hormone values \(>30 \text{ IU/l}\) and baseline physical characteristics of the 24 women who dropped out were not different from those of the 40 women who completed the study (data not shown). Exercise attendance to the supervised exercise session was 78% (range 36–100%), and average exercise intensity was 73% of the maximum predicted heart rate reserve.

Effects of the intervention (Table 1). These obese (body mass index \(=31 \pm 1 \text{ kg/m}^2\)) and sedentary (\(\text{V}\dot{O}_2\text{max }19 \pm 1 \text{ ml.kg}^{-1}.\text{min}^{-1}\)) women were age 62 \(\pm 1\) yr and postmenopausal (12 \(\pm 2\) yr since last menstrual period) at baseline. Body weight, percent body fat, fat mass, waist circumference, hip circumference, VAT, and SAT decreased significantly (\(P < 0.01\)) after the 6-mo intervention. Because both waist and hip circumference decreased to the same magnitude, the waist-to-hip ratio did not change. On average, nonosse-
ous LBM did not change during the intervention, but there was a wide range of individual changes (LBM -2.6–2.5 kg). Therefore, all analyses using VO<sub>2max</sub> were covaried for LBM. VO<sub>2max</sub> increased an average of 7%, expressed as liters per minute adjusted for LBM; however, the response to the intervention was variable (range -6–20%).

Effects of changes in VO<sub>2max</sub> on VAT. VAT and SAT response to the intervention significantly correlated with their respective baseline values. Thus VAT and SAT absolute response variables were adjusted for the baseline value using ANCOVA. To examine the effects of the change in VO<sub>2max</sub> on the change in VAT, we divided participants into quartiles on the basis of their absolute change in VO<sub>2max</sub> covaried for the initial value (Fig. 1). The 10 women in the quartile with the smallest improvement in VO<sub>2max</sub> (-0.01 ± 0.01 l/min) were compared with the 30 women in the upper three quartiles who showed a combined improvement in VO<sub>2max</sub> of 10 ± 1% (0.15 ± 0.01 l/min; P < 0.001). Absolute and relative change in body weight, percent body fat, total fat mass, and SAT did not differ between groups. However, the absolute and relative change in VAT was significantly greater (P < 0.01 and P < 0.02, respectively) in women who improved VO<sub>2max</sub> (VAT = -31 ± 3 cm<sup>2</sup>; -20 ± 2%) compared with women who did not improve VO<sub>2max</sub> (VAT = -13 ± 4 cm<sup>2</sup>; -10 ± 3%) (Fig. 2).

In bivariate analysis, absolute (covaried for initial value) as well as relative reductions in VAT correlated negatively with the changes in VO<sub>2max</sub> (r = -0.47; P < 0.01 and r = -0.38; P < 0.02, respectively) but were not related to changes in body weight (r = 0.22; P = not significant) or total fat mass (r = 0.29; P = 0.08). In multiple-regression analysis with the change in VO<sub>2max</sub> and fat mass in the analysis, both the change in VO<sub>2max</sub> (r<sup>2</sup> = 0.22; P < 0.01) and in fat mass (r<sup>2</sup> = 0.08; P = 0.05) independently predicted the change in VAT (Fig. 3, A and B, respectively). Furthermore, 30% of the variance in the decline in VAT was explained by the change in VO<sub>2max</sub> and fat mass. There was no relationship between change in VO<sub>2max</sub> and change in other indexes of obesity. Thus the relationship between change in VAT and VO<sub>2max</sub> was independent of the magnitude of total weight or fat lost.

**DISCUSSION**

The results of this study show that a 6-mo WL and walking program in obese postmenopausal women results in reductions in VAT that are related to the magnitude of the increase in VO<sub>2max</sub>. Women who had an average 10% increase in VO<sub>2max</sub> reduced VAT by an average of 20%, whereas those who did not increase VO<sub>2max</sub> decreased VAT by only 10%, despite comparable reductions in fat mass. In addition, the combined increase in VO<sub>2max</sub> and the decrease in fat mass explained 30% of the variance in the decrease of VAT with WL and walking. This suggests that women who raise VO<sub>2max</sub> the most during a WL and walking program will lose the greatest amount of VAT.

Previous studies have not addressed the relationship between the change in VAT and the change in VO<sub>2max</sub>.

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**Table 1. Effect of hypocaloric diet and walking on body composition and fitness levels**

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>Δ</th>
<th>%Δ</th>
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<tr>
<td>Weight, kg</td>
<td>81 ± 2</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-8 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>47 ± 1</td>
<td>-4 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-4 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>38 ± 1</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-7 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>39 ± 1</td>
<td>0 ± 1</td>
<td>0 ± 1</td>
</tr>
<tr>
<td>Waist, cm</td>
<td>94 ± 1</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hip, cm</td>
<td>113 ± 2</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.83 ± 0.01</td>
<td>-0.01 ± 0.01</td>
<td>-1 ± 1</td>
</tr>
<tr>
<td>Visceral fat, cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>156 ± 6</td>
<td>-26 ± 3&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-17 ± 2&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>Subcutaneous fat, cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>431 ± 18</td>
<td>-75 ± 7&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>-17 ± 2&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2max&lt;/sub&gt;, l/min</td>
<td>1.56 ± 0.04</td>
<td>0.10 ± 0.01&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>6 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2max&lt;/sub&gt;Adj,LBM, l/min</td>
<td>1.61 ± 0.05</td>
<td>0.11 ± 0.01&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>7 ± 1&lt;sup&gt;Δ&lt;/sup&gt;</td>
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Values are means ± SE for 40 subjects. VO<sub>2max</sub> maximal O<sub>2</sub> uptake. VO<sub>2max,Adj,LBM</sub> maximal O<sub>2</sub> uptake adjusted for lean body mass using analysis of covariance; Δ, change; %Δ, percent change. *P < 0.001.

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**Fig. 1. Quartiles based on the change in maximal O<sub>2</sub> uptake (VO<sub>2max</sub>). Values are means ± SE.**

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**Fig. 2. Percent change in body weight, percent body fat, fat mass (FM), subcutaneous adipose tissue area (SAT), and visceral adipose tissue area (VAT) by women who did not improve VO<sub>2max</sub> from the lowest quartile (open bars) vs. women who improved VO<sub>2max</sub> from the highest 3 quartiles (hatched bars). Values are means ± SE. *P < 0.02.**
during a WL and walking program, but our findings are in agreement with the four studies that report data on the combined influence of WL and AEEx on VAT. Ross et al. showed significant reductions in VAT, SAT, and body weight and increases in V\( \dot{O}_2 \) max 28 and 29). In these studies, there was a 10-12 kg loss of body weight in both men and women. Men decreased VAT by 39% and improved V\( \dot{O}_2 \) max by 14%, and women decreased VAT by 34% with an 8% increase in V\( \dot{O}_2 \) max. Although the difference in response between groups is quite small, the group that lost the most VAT had the greatest improvement in V\( \dot{O}_2 \) max. Two other studies showed a reduction in VAT with hypocaloric WL and AEEx, but neither study measured V\( \dot{O}_2 \) max 1, 7). Conway et al. 7) reported a 30 and 34% VAT reduction in obese black and white women, respectively. Abe et al. 1) reported a 38% reduction in VAT in young women instructed to exercise one to two times per week.

A likely explanation for the association between the change in V\( \dot{O}_2 \) max and VAT is the role of V\( \dot{O}_2 \) max response as an indicator of free-living physical activity. Broach et al. 6) reported a positive association between higher levels of peak V\( \dot{O}_2 \) and greater volitional and nonvolitional (i.e., fidgeting) physical activity energy expenditure. Thus free-living daily physical activity most likely contributed to the increase in V\( \dot{O}_2 \) max measured during the 6-mo intervention in this population of obese sedentary women. Furthermore, this increase in daily free-living activity also may elevate catecholamine levels during activity for a long period of time, which could affect regional fat cell metabolism and be one mechanism for the decrease in VAT.

There are other potential mechanisms by which the improvement in V\( \dot{O}_2 \) max is associated with a greater reduction in VAT. Several studies show that exercise training increases circulating catecholamine levels 3) and in vitro catecholamine-stimulated lipolysis in isolated adipocytes from SAT 8, 22). Also, exercise blunts the reduction in lipolysis of SAT typically seen with weight loss 24). In addition, VAT is more lipolytically sensitive than SAT at rest 12, 21, 26), which may be due to the combined effects of greater \( \beta_3 \)-adrenergic receptor affinity and binding and a reduced action of \( \alpha_2 \)-adrenoceptor sensitivity 18, 35). Because exercise stimulates lipolysis in SAT, and VAT is more lipolytically active than SAT, lipolysis may be more pronounced in VAT with walking in those women who improve V\( \dot{O}_2 \) max the most. In addition, there is a decline in circulating levels of insulin during acute exercise 11), as well as after exercise training 17). Therefore, the reduction of the antilipolytic action of insulin on VAT 5) may also contribute to the effect of walking on VAT area. Finally, in vivo studies show that the reesterification of free fatty acids by adipose tissue declines during exercise 15, 38), and, therefore, free fatty acid mobilization from VAT may be increased in women who improved V\( \dot{O}_2 \) max with the walking program. Thus the lower antilipolytic effect of insulin and increased free fatty acid mobilization after walking, combined with a rise in catecholamines as a result of regular physical activity, might explain, at least in part, the larger reductions in VAT area observed in women who increased V\( \dot{O}_2 \) max by walking.

There are several limitations to this study that warrant comment. The exercise sessions were supervised only 1 day/wk; hence, although participants were instructed to exercise a total of 3 days/wk, we did not accurately monitor compliance or intensity of exercise on the nonsupervised days. Because of the varied degrees of compliance to walking and variations in walking intensity among the women in this study, there was a large interindividual variation in V\( \dot{O}_2 \) max response. This afforded us the opportunity to test our hypothesis. However, to determine whether some biological mechanism related to increases in V\( \dot{O}_2 \) max mediate the preferential loss of VAT, it would be necessary to rigorously control the frequency, intensity, and duration of exercise during the intervention period so that all subjects performed similar amounts of work.
Well-controlled studies will need to be designed to determine the optimal dose of exercise necessary to reduce upper body fat in obese postmenopausal women. Another limitation of this study is that the results may only be applicable to obese postmenopausal women. Finally, because the relationship between the increase in VO₂max and the decrease in VAT is a correlation, it does not prove cause and effect. We do not know whether women lost more VAT because they improved VO₂max more or whether the greater loss in VAT during WL and walking resulted in greater improvements in VO₂max.

The results of this study indicate that postmenopausal women who manifest greater improvements in VO₂max during a 6-mo walking and WL program show greater reductions in VAT, despite a similar reduction in body weight, fat mass, and SAT. This has potential health benefits for obese postmenopausal women because VAT is independently correlated with Type 2 diabetes, hypertension, and hyperlipidemia, which are major risk factors for cardiovascular disease in this population (9, 13). Future studies will need to control the frequency, intensity, and duration of the AEx program during WL to determine the optimal exercise prescription needed to promote the greatest health benefits.

We appreciate the assistance of our dietitians, exercise physiologists, and nursing staff in the Division of Gerontology with the WL program, exercise supervision, and research testing. We especially thank all of the women who participated in this research study.

The study was supported by National Institutes on Aging Grants T32 AG-002109, R29 AG-14066, K01 AG-00685, and K07 AG-00680; National Institute of Nursing Research Grant R01 NR-03514; and the Department of Veterans Affairs Geriatric Research, Education, and Clinical Center (Baltimore, MD).

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