HIGHLIGHTED TOPIC | Role of Exercise in Reducing the Risk of Diabetes and Obesity

Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without Type 2 diabetes

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The prevalence of obesity and Type 2 diabetes (T2D) is already high and continues to rise (15, 25). It is well known that physical inactivity is a primary cause of obesity (16, 22, 24). Accordingly, adoption of a physically active lifestyle is now recognized as a cornerstone in the treatment and prevention of obesity (7, 27). Common to current obesity reduction guidelines is the assumption that the effectiveness of diet- and/or exercise-based strategies depends in large measure on weight loss. Indeed, it is recommended that diet and exercise induce a negative energy balance that corresponds to a reduction of ~1.5 lb (0.6 kg) per week (7). Furthermore, recent guidelines (19) highlight that weight loss should be a primary therapeutic strategy in all obese individuals who have T2D or are at risk for developing T2D. By definition, these guidelines (19) do not consider whether exercise alone is an effective strategy for obesity reduction even in the absence of weight loss. That weight loss is a desirable goal of obesity reduction is clear. However, the assumption that weight loss is the primary antecedent to lifestyle-induced benefit precludes, for example, the possibility that exercise could induce a reduction in waist circumference, a strong independent predictor of morbidity and mortality, without a corresponding reduction in body weight [e.g., body mass index (BMI)].

At present, little is known about the utility of regular exercise without corresponding weight loss as a strategy for the treatment of obesity. Our laboratory has recently reported that exercise without weight loss is associated with a significant reduction in abdominal fat in both obese men (29) and women (30), suggesting that regular exercise is associated with a clinically significant reduction in abdominal obesity without a corresponding change in BMI. Whether exercise without weight loss is associated with a reduction in total and/or abdominal obesity in T2D is unknown.

Emerging evidence suggests that the accumulation of lipid within skeletal muscle increases with obesity (9, 11, 13, 17) and that muscle lipid content is associated with insulin resistance in lean (26), obese (11, 12), and individuals with T2D (11). It has also been reported that both diet- (10, 13) or exercise-induced weight loss (5) are associated with diminished skeletal muscle lipid content. However, whether exercise without weight loss is associated with a reduction in this ectopic lipid marker of metabolic risk is lacking and warrants investigation.

This study was undertaken to determine the effects of exercise without weight loss on total and regional adiposity as well as skeletal muscle composition in lean men and in obese men with and without T2D. We hypothesized that exercise without weight loss would be associated with marked reduction in abdominal obesity and muscle lipid content in both obesity and T2D. Were this true, it would add important insight into the process by which the adoption of a physically
active lifestyle may attenuate health risk independent of weight loss.

MATERIALS AND METHODS

Subjects. Twenty-seven, middle-aged men (10 lean, 8 obese without T2D, and 9 obese with T2D) were recruited from Kingston via the general media. Of the 27 participants, 24 men (8 lean, 8 obese without T2D, and 8 obese with T2D) completed the study. Three men (2 lean, 1 obese with T2D) withdrew from the study citing time constraints associated with their employment. The metabolic data for this study are published elsewhere (21). Inclusion criteria for lean men were that BMI (weight in kg/height in m²) was <25.0 kg/m² with a waist circumference <94 cm. Obese men with or without T2D were abdominally obese with a BMI >27.0 kg/m² and a waist circumference of >100 cm. All subjects were weight stable (±2 kg) for 6 mo before the beginning of the study. Participants were nonsmokers who consumed on average fewer than two alcoholic beverages per day, led a sedentary lifestyle (no participation in any regular physical activity for past 6 mo), and took no medications known to affect the principal outcome measures. The obese group underwent an oral glucose tolerance test (OGTT) before the study participation to screen for normal glucose tolerance. Individuals with T2D were not taking insulin or insulin sensitizers and were free of other complications (e.g., cardiovascular disease, neuropathy, or retinopathy) as confirmed by their physicians. All subjects gave their fully informed and written consent before participation in the study, which was conducted in accordance with the ethical guidelines as set by Queen’s University.

Diet and exercise regimen. During the 4-wk baseline period, daily energy requirements for all subjects were determined by estimating resting energy expenditure and multiplying the obtained value by a factor of 1.5 (14). During the baseline period and throughout the study, all subjects followed a weight maintenance diet (55–60% carbohydrate, 15–20% protein, 20–25% fat). To allow us to test the hypothesis that significant obesity reduction could occur despite the absence of change in body weight (e.g., no change in BMI), during the 13-wk exercise intervention period, all subjects were asked to maintain body weight, and they consumed the calories required to compensate for the energy expended during the exercise sessions. Body weight was monitored during this period to determine the accuracy of the prescribed energy requirement and was adjusted accordingly so that body weight was maintained. Subjects kept daily, detailed food records for the duration of the entire study period (~17 wk) that were reviewed by the study dietician on a weekly basis to ensure compliance. The diet records were analyzed using a computerized program (Food Processor, Esha Research, Salem, OR). Body weight was measured before each exercise session throughout the program to ensure weight maintenance. All subjects were free living and consumed foods that were self-selected. No vitamins or other nutritional supplements were prescribed.

All subjects participated in a 13-wk aerobic exercise intervention that consisted of either walking or light jogging on a treadmill for 60 min, five times per week, at a moderate intensity (~60% of peak oxygen uptake [VO2]). Energy expenditure during exercise program was determined using the heart rate and VO2 data obtained from the pretreatment graded exercise test, and it was adjusted using the subsequent test results performed at weeks 4 and 8. Heart rate was monitored every 5 min during exercise session using an automated heart rate monitor (Polar Oy, Kempele, Finland). All exercise sessions were by appointment and were supervised.

Cardiorespiratory fitness. Peak VO2 was determined using a graded maximal treadmill test that employed a constant walking speed and the use of standard open-circuit spirometry techniques (SensorMedics, Yorba Linda, CA) at baseline and during the 4th, 8th, 12th, and 13th wk of the intervention. Peak VO2 was attained when at least two of the following three criteria were achieved: no increase in VO2 despite further increases in treadmill grade, a heart rate at or above age predicted maximum (220 − age), and/or a respiratory exchange ratio in excess of 1.0.

Anthropometric measurements. Anthropometric measurements were taken at baseline and during the 13th wk of the intervention. Body mass was measured on a balance scale calibrated to the nearest 0.1 kg with the subjects dressed in standard T-shirts and shorts. Barefoot standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Waist circumference was obtained at the level of the last rib using standard procedures described previously (32). Thigh circumference was measured on the right leg at the midpoint between the inguinal crease and superior edge of the patella. The average value of two measurements was used in the analyses.

Measurement of total and regional body composition by magnetic resonance imaging. Whole body (~46 equidistant images) magnetic resonance imaging (MRI) data were obtained with a General Electric, 1.5-T magnet using an established protocol (32) at baseline and during the 13th wk of the intervention. Once acquired, the MRI data were transferred to a stand-alone workstation for analysis using specially designed computer software (Tomovision, Montreal, PQ, Canada), the procedures for which have been described previously (31, 32). Total fat and skeletal muscle were determined using all 46 images. Visceral and abdominal subcutaneous fat was calculated using the five images extending from 5 cm below to 15 cm above L4–L5. Lower body fat and skeletal muscle was identified as all fat and skeletal muscle distal to the femoral head. Adipose tissue (fat) and skeletal muscle were converted to mass units (kg) by multiplying the volumes by the assumed constant density for fat (0.92 kg/l) and fat-free skeletal muscle (1.04 kg/l) (39).

Measurement of muscle composition by computed tomography. Computed tomography (CT) images were obtained on a Toshiba Aquilion scanner (Toshiba America Medical Systems, Tustin, CA) using 220 mA, a 512 × 512 matrix, and 48-cm field of view at baseline and during the 13th wk of the intervention. Using external landmarks, two contiguous transverse images (10 mm thick) were acquired at the mid-point between the inguinal crease and superior edge of the patella. All muscle composition analyses were based on the average values for the two images. CT is capable of differentiating tissues on the basis of their attenuation characteristics, which are a function of tissue density and chemical composition. Because fat has a negative attenuation value, a lower mean attenuation value is indicative of greater fat deposition within the muscle. CT-measured muscle attenuation has been previously validated against muscle biopsy-measured muscle lipid content (9). Mean skeletal muscle attenuation was measured as the mean attenuation value for all pixels within the range of 0–100 Hounsfield units (HU) using commercially available software (Slice-O-Matic, Tomovision) as previously described (11, 12). Skeletal muscle was subdivided into the low- and high-density muscle. Low-density muscle was defined as muscle within the range of 0–30 HU, and high-density muscle was defined as muscle within the range of 31–100 HU. The test-retest coefficient of variation for two CT scans is <1% (9).

Statistical analysis. A one-way ANOVA was performed to examine group differences at baseline. A repeated-measures ANOVA (group × time) was used to evaluate main effect and group interactions for all dependent variables. When the ANOVA P value was <0.05, a Tukey’s post hoc comparison test was used to locate treatment and/or group differences. Statistical procedures were performed using SPSS version 11.0 (SPSS, Chicago, IL). All data are presented as means ± SD.

RESULTS

Exercise attendance for all groups averaged 98% (range 91–100%; Table 1). The groups did not differ (P > 0.1) in average duration, intensity, and energy expended per exercise session.
Anthropometric and skeletal muscle composition measurements. Body weight did not change (P > 0.1) with exercise within any group (Table 2). However, waist circumference was significantly reduced (P < 0.01) within each group, and these changes were not different between groups (P > 0.1; Table 2). Cardiorespiratory fitness increased (P < 0.01) in all groups, and these improvements were not different between groups (P > 0.05; Table 2). A small but significant increase (P < 0.01) in thigh circumference was also observed independent of group (Table 2). CT measurements reveal that high-density muscle area (cm²) increased (P < 0.01) within all groups, and these changes were not different (P > 0.1) within each group, and these improvements were not different between groups (P > 0.05). The relative (%) reduction in abdominal fat was greater (P < 0.01) than that observed within the lower body for both obese and T2D groups (Fig. 2A). The relative (%) reduction in abdominal fat was significantly greater (P < 0.01) than that observed in the lower body regardless of group (Fig. 2B).

DISCUSSION

The effects of exercise without weight loss on total and abdominal adiposity and skeletal muscle mass and composition were examined in previously sedentary, lean men and in obese men with and without T2D. Our primary finding is that, despite the absence of weight loss, moderate-intensity exercise is associated with significant reductions in total and abdominal fat in both obesity and T2D. Furthermore, we observed a reduction in skeletal muscle lipid content independent of group. These findings are encouraging and have important implications for the development of public health policy. Indeed, combined with the observation that exercise without weight loss is associated with a decrease in metabolic risk (3, 6), they provide the basis for an improved therapeutic strategy for the treatment of abdominal obesity and the reduction in health risk; findings that are directly relevant for the one in two Americans who are overweight or obese.

Our finding that 3 mo of exercise without weight loss was associated with a marked reduction in both total (~6%) and abdominal subcutaneous fat was observed within all groups (P < 0.05), and these changes were not different (P > 0.1) between groups (Fig. 1A). For visceral fat, significant reduction was observed within all groups (P < 0.01); however, the reduction in visceral fat within the obese and T2D groups was significantly greater (P < 0.01) than the lean group (Fig. 1A). Expressed in relative terms (%), significant reduction in visceral fat was observed within all groups (P < 0.05), and these changes were not different (P > 0.1) between groups (Fig. 1B). In contrast to the observations based on absolute values, significant reduction in abdominal subcutaneous fat was observed within the lean and obese groups only (P < 0.05; Fig. 1B).

Lower body vs. abdominal fat distribution. The absolute (kg) reduction in abdomen fat was greater (P < 0.01) than that observed within the lower body for both obese and T2D groups (Fig. 2A). The relative (%) reduction in abdominal fat was significantly greater (P < 0.01) than that observed in the lower body regardless of group (Fig. 2B).

Table 1. Summary of exercise training sessions

<table>
<thead>
<tr>
<th>Duration, min</th>
<th>Lean</th>
<th>Obese</th>
<th>T2D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>66.0 ± 0.2</td>
<td>58.8 ± 1.8</td>
<td>59.4 ± 0.7</td>
</tr>
</tbody>
</table>

Table 2. Anthropometric, MRI, and CT variables pre- and posttreatment

<table>
<thead>
<tr>
<th></th>
<th>Lean Pretreatment</th>
<th>Lean Posttreatment</th>
<th>Obese Pretreatment</th>
<th>Obese Posttreatment</th>
<th>T2D Pretreatment</th>
<th>T2D Posttreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>47.5 ± 6.7</td>
<td>47.1 ± 8.1</td>
<td>51.0 ± 8.0</td>
<td>51.0 ± 8.0</td>
<td>51.0 ± 8.0</td>
<td>51.0 ± 8.0</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73.9 ± 6.6</td>
<td>73.5 ± 6.6</td>
<td>97.6 ± 8.9*</td>
<td>97.2 ± 8.9</td>
<td>93.5 ± 7.6*</td>
<td>93.9 ± 8.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.5 ± 1.3</td>
<td>24.3 ± 1.2</td>
<td>32.4 ± 1.6*</td>
<td>32.2 ± 1.7</td>
<td>29.9 ± 3.2*</td>
<td>30.1 ± 3.4</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>89.2 ± 4.6</td>
<td>86.5 ± 4.7‡</td>
<td>108.4 ± 4.3*</td>
<td>105.8 ± 3.8‡</td>
<td>106.3 ± 6.4*</td>
<td>103.6 ± 5.7‡</td>
</tr>
<tr>
<td>Thigh circumference, cm</td>
<td>51.2 ± 1.0</td>
<td>52.2 ± 1.0</td>
<td>57.8 ± 3.6*</td>
<td>58.7 ± 4.0‡</td>
<td>54.2 ± 3.9</td>
<td>56.0 ± 4.9‡</td>
</tr>
<tr>
<td>MRI measurements, kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total skeletal muscle</td>
<td>27.7 ± 3.5</td>
<td>28.0 ± 3.3</td>
<td>32.9 ± 3.9*</td>
<td>33.3 ± 4.1</td>
<td>32.7 ± 3.9*</td>
<td>33.6 ± 4.1‡</td>
</tr>
<tr>
<td>Total fat</td>
<td>20.7 ± 3.9</td>
<td>19.5 ± 3.9</td>
<td>35.8 ± 2.4*</td>
<td>33.8 ± 4.4</td>
<td>30.1 ± 4.5*</td>
<td>28.4 ± 2.7‡</td>
</tr>
<tr>
<td>Total fat-to-muscle ratio</td>
<td>1.38 ± 0.34</td>
<td>1.49 ± 0.37</td>
<td>0.92 ± 0.10</td>
<td>0.99 ± 0.11‡</td>
<td>1.11 ± 0.22</td>
<td>1.21 ± 0.23‡</td>
</tr>
<tr>
<td>Abdominal fat</td>
<td>4.5 ± 1.1</td>
<td>4.0 ± 1.0</td>
<td>9.2 ± 1.2</td>
<td>8.3 ± 1.11§</td>
<td>7.5 ± 1.3</td>
<td>6.7 ± 1.5§</td>
</tr>
<tr>
<td>Lower body skeletal muscle</td>
<td>15.8 ± 1.8</td>
<td>16.2 ± 1.2</td>
<td>18.5 ± 1.9</td>
<td>18.9 ± 2.0‡</td>
<td>18.1 ± 2.3</td>
<td>19.1 ± 2.4‡</td>
</tr>
<tr>
<td>Lower body fat</td>
<td>7.9 ± 1.2</td>
<td>7.6 ± 1.2</td>
<td>12.3 ± 2.3</td>
<td>12.0 ± 2.4‡</td>
<td>9.1 ± 2.5</td>
<td>8.8 ± 2.5‡</td>
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<tr>
<td>CT muscle composition (midthigh)</td>
<td></td>
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<tr>
<td>Low-density muscle, cm²</td>
<td>34.8 ± 15.3</td>
<td>29.8 ± 11.1</td>
<td>58.2 ± 18.4*</td>
<td>57.0 ± 17.2</td>
<td>52.5 ± 15.6</td>
<td>56.2 ± 19.5</td>
</tr>
<tr>
<td>High-density muscle, cm²</td>
<td>259.3 ± 22.0</td>
<td>265.6 ± 24.2</td>
<td>267.0 ± 20.0</td>
<td>275.7 ± 15.2‡</td>
<td>271.7 ± 41.7</td>
<td>285.7 ± 46.9‡</td>
</tr>
<tr>
<td>Mean muscle attenuation, HU</td>
<td>55.8 ± 3.2</td>
<td>56.4 ± 2.7</td>
<td>51.3 ± 2.0*</td>
<td>53.0 ± 3.1‡</td>
<td>52.3 ± 2.9*</td>
<td>53.0 ± 3.2‡</td>
</tr>
<tr>
<td>Peak VO₂, ml·kg⁻¹·min⁻¹</td>
<td>42.6 ± 5.8</td>
<td>53.1 ± 3.7</td>
<td>32.7 ± 3.5*</td>
<td>39.3 ± 4.0</td>
<td>33.0 ± 4.4*</td>
<td>42.2 ± 7.6‡</td>
</tr>
</tbody>
</table>

Values are means ± SD. MRI, magnetic resonance imaging; CT, computed tomography; BMI, body mass index; HU, Hounsfield units. Note: CT data in the lean group were analyzed in 7 individuals due to technical difficulties. *Significantly different from the lean group at pretreatment, P < 0.01. †Significantly different from the obese group at pretreatment, P < 0.05. ‡Significant treatment differences (pretreatment vs. posttreatment) within group, P < 0.01. §Significant treatment differences (pretreatment vs. posttreatment) compared with lean group, P < 0.01.
visceral fat (~17%) in middle-aged lean men and obese men is consistent with previous observations in obese men (29) and women (30) and in black and white men and women across a wide range of adiposity (41). That regular exercise with no weight loss was associated with a substantial reduction in total and abdominal fat in men with T2D is a novel finding and underscores the potential therapeutic value of this treatment strategy. Furthermore, our findings agree with others (35) and suggest that daily exercise without caloric restriction performed for 45–60 min at a moderate intensity is associated with substantial reductions in total and abdominal obesity. However, these findings are countered by a similar study by Segal et al. (33), who report that 12 wk of aerobic exercise without weight loss is not associated with changes in total adiposity (hydrostatic weighing) in the lean, obese, and individuals with T2D. Although we cannot be certain, it is possible that the disparate findings are explained by methodological differences because it is well established that the use of hydrostatic weighing using two-compartment models is prone to error and confounds interpretation (4).

That there was a smaller reduction in abdominal subcutaneous fat in our study is in agreement with our laboratory’s previous finding (29) indicating that change in fat distribution in response to exercise favors a reduction in visceral fat. Preferential reduction in visceral fat also has been observed with weight loss induced by either diet or exercise (28). The preferential reduction in visceral fat is consistent with previous reports demonstrating that omental and mesenteric adipocytes are more sensitive to the lipolytic stimulation of catecholamines compared with the abdominal subcutaneous adipocytes (8). Furthermore, the marked reduction in adipose tissue from the abdomen region compared with the lower body region was expected because, during exercise, evidence suggests that lipid mobilization from the abdominal region is greater compared with the femoral region (1).

Whereas waist circumference is positively associated with higher health risk, a growing body of evidence suggests that having a larger thigh or hip circumference is associated with lower health risk (23, 36–38). Although not firmly established, it is postulated that a greater lean body mass in the lower body may confer health benefits (34). Accordingly, our observation that exercise without weight loss was associated with an increase in thigh circumference consequent with an increase in lower body skeletal muscle suggests an alternative pathway by which exercise without weight loss may reduce health risk.

Our finding that regular exercise without weight loss results in a reduction in skeletal muscle lipid content coincident with an increase in skeletal muscle mass in both obesity and T2D extends the recent observation by Kim et al. (18), who examined the effect of 12 wk of aerobic exercise without weight loss on intramuscular triglycerides content in a small number (n = 10) of elderly Asian men with impaired glucose tolerance. In that study, regular exercise (3 times per week) was associated with a significant reduction in intramuscular triglycerides and an increase in GLUT4 protein expression and fatty acid oxidation capacity (β-hydroxyacyl-CoA dehydrogenase) as measured by percutaneous biopsy. Together, these observations reinforce the utility of exercise without weight loss as a strategy to improve skeletal muscle morphology, independent of age, race, and obesity.

In the present study, the participants exercised for ~60 min, 5 days/wk. This duration of exercise is within the current public
health guidelines that recommend all adults should engage in moderate-intensity physical activity (30–60 min of brisk walking) on all or most days of the week (7, 27). However, it is important to note that the levels of fat loss (e.g., obesity reduction) observed in this study are less than those generally observed in response to exercise-induced weight loss (29, 35). This reinforces current guidelines that recommend diet (caloric restriction) and/or exercise-induced weight loss as the principal therapy for overweight and obese individuals in the prevention and management of T2D (19). However, the findings here extend these guidelines and provide substantial support for the recommendation that exercise without weight loss represents another strategy for obesity reduction. This is good news and may be used to encourage and counsel those who appear resistant to substantial weight loss despite considerable effort. Stated differently, health care professionals should recognize that exercise without weight loss is not a failure when obesity reduction is the desired outcome. To the contrary, combined with the knowledge that exercise is associated with substantial health benefits independent of obesity (40), exercise without weight loss is a useful strategy for reducing obesity and related comorbid conditions: a win-win scenario.

Limitations of this study warrant mention. First, our observations are based on recently diagnosed men with T2D who were not taking insulin or insulin sensitizers. Whether similar findings would be observed in T2D individuals who have developed other complications (e.g., cardiovascular disease or neuropathy) is unclear. Second, our study consists of a homogeneous sample of Caucasian men. Whether our findings remain true for women or other ethnic groups is unknown. In conclusion, the results of this study suggest that moderate-intensity exercise without weight loss or calorie restriction is associated with significant reductions in total fat, visceral fat, and skeletal muscle lipid content in both obesity and T2D. Combined with the observation that abdominal obesity conveys a significant health risk (2) and that increased cardiopulmonary fitness is associated with a reduction in morbidity and mortality independent of BMI (20, 40), our findings have important public health implications. Indeed, they augment current guidelines and provide compelling evidence that engaging in regular physical activity (~60 min of walking or light jogging on all or most days of the week) is another effective means of reducing obesity and related comorbid conditions.

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