Effects of Aerobic Versus Resistance Exercise Without Caloric Restriction on Abdominal Fat, Intrahepatic Lipid, and Insulin Sensitivity in Obese Adolescent Boys. A Randomized, Controlled Trial

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The optimal exercise modality for reductions of abdominal obesity and risk factors for type 2 diabetes in youth is unknown. We examined the effects of aerobic exercise (AE) versus resistance exercise (RE) without caloric restriction on abdominal adiposity, ectopic fat, and insulin sensitivity and secretion in youth. Forty-five obese adolescent boys were randomly assigned to one of three 3-month interventions: AE, RE, or a nonexercising control. Abdominal fat was assessed by magnetic resonance imaging, and intrahepatic lipid and intramyocellular lipid were assessed by proton magnetic resonance spectroscopy. Insulin sensitivity and secretion were evaluated by a 3-h hyperinsulinemic-euglycemic clamp and a 2-h hyperglycemic clamp. Both AE and RE prevented the significant weight gain that was observed in controls. Compared with controls, significant reductions in total and visceral fat and intrahepatic lipid were observed in both exercise groups. Compared with controls, a significant improvement in insulin sensitivity (27%) was observed in the RE group. Collapsed across groups, changes in visceral fat were associated with changes in intrahepatic lipid (r = 0.72) and insulin sensitivity (r = −0.47). Both AE and RE alone are effective for reducing abdominal fat and intrahepatic lipid in obese adolescent boys. RE but not AE is also associated with significant improvements in insulin sensitivity. Diabetes 61:2787–2795, 2012

According to the recent National Health and Nutrition Examination Survey (2009–2010), a third (33.6%) of U.S. children and adolescents (12–19 years old) are overweight or obese (1). It is suggested that abdominal obesity, in particular visceral fat, is an important culprit for many obesity-related comorbidities in youth (2). In light of the secular increases in waist circumference (WC) among children and adolescents (3,4) and the finding that abdominal obesity is a stronger risk factor for insulin resistance and cardiometabolic diseases than BMI (5,6), effective intervention strategies are needed for targeting abdominal fat reduction in youth.

In adults, randomized, controlled studies have reported that regular exercise (performed for 30–60 min/day ≥3 days/week) is associated with significant reductions in abdominal fat and improvements in glycemia and insulin resistance in nondieting men and women (7–11). In obese adolescents, the utility of exercise alone (no caloric restriction) as a strategy for reducing obesity-related health risk is not clear. Although previous studies have examined the effect of aerobic exercise (12,13) or resistance training (14,15) on insulin sensitivity in obese children and adolescents, interpretation is limited because these studies did not include nonexercising controls (12,13,15) and did not measure ectopic fat (e.g., visceral obesity, liver fat, intramyocellular lipid (IMCL) mobilizations with exercise treatments (12,14)). Further, although it is generally accepted that regular physical activity provides substantial health benefits in obese adolescents, it is unclear which exercise modality is most beneficial for reducing comorbidities associated with obesity in adolescents. A recent meta-analysis (16) reported that aerobic exercise performed for 60 min 3 times/week improves LDL cholesterol and triglyceride concentrations in obese children, whereas combined exercise increases HDL concentration. Further, Suh et al. (17) demonstrated that in overweight Asian adolescents improvements in insulin sensitivity index (oral glucose tolerance test) were similar between aerobic and resistance training, and the improvements in the exercise training groups did not differ from those with diet alone. By contrast, adult studies have reported greater improvements in insulin sensitivity after aerobic versus resistance training (11,18).

We therefore conducted a randomized, controlled study to examine the effects of aerobic versus resistance exercise, without caloric restriction, on abdominal obesity, ectopic fat in the liver and skeletal muscle, and insulin action and secretion in obese adolescent boys. We hypothesized that in youth both aerobic and resistance exercise training would be associated with reductions in abdominal fat and improvements in insulin sensitivity and also the improvements in obesity-related risk factors would be greater in response to aerobic exercise than resistance exercise.

RESEARCH DESIGN AND METHODS

We conducted a 3-month randomized, controlled trial with a parallel group design. This study was conducted from November 2007 through October 2011 at Children’s Hospital of Pittsburgh (CHP) of University of Pittsburgh Medical Center. 48 boys were recruited from the Obesity and Diabetes Research Center, Baylor College of Medicine, Houston, Texas; the Division of Pediatric Endocrinology, Metabolism and Diabetes Mellitus, Children’s Hospital of Pittsburgh of UPMC, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; the Children’s Nutrition Research Center, Baylor College of Medicine, Houston, Texas; the Division of Pediatric Endocrinology, Metabolism and Diabetes Mellitus, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, Indiana; the School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada; and the Department of Clinical Research/AMSM, University of Bern, Bern, Switzerland. The study was approved by the institutional review boards at Children’s Hospital of Pittsburgh (CHP) of University of Pittsburgh Medical Center and Baylor College of Medicine. All participants were 12–19 years old and had abdominal obesity and insulin resistance (HOMA-IR >2.5). Participants were excluded if they had current smoking, had a history of drug or alcohol abuse, or had metabolic disease. Participants were randomly assigned to one of three arms: aerobic exercise (AE), resistance exercise (RE), or a nonexercising control (NC). The AE group exercised 60 min 5 days/week. The RE group performed 15 min 5 days/week of resistance training at >80% of maximum voluntary contraction. Both groups were instructed to maintain caloric intake throughout the study. Insulin sensitivity and secretion were evaluated by a 3-h hyperinsulinemic-euglycemic clamp and a 2-h hyperglycemic clamp. Changes in waist circumference (WC), abdominal fat, intrahepatic lipid, intramyocellular lipid (IMCL), and insulin sensitivity were evaluated. The changes in abdominal fat and intrahepatic lipid were assessed by proton magnetic resonance spectroscopy and magnetic resonance imaging, respectively. Insulin sensitivity and secretion were evaluated by a 3-h hyperinsulinemic-euglycemic clamp and a 2-h hyperglycemic clamp. Both AE and RE prevented the significant weight gain that was observed in controls. Compared with controls, significant reductions in total and visceral fat and intrahepatic lipid were observed in both exercise groups. Compared with controls, a significant improvement in insulin sensitivity (27%) was observed in the RE group.
REDUCTIONS IN ADIPOSITY AND INSULIN RESISTANCE WITH EXERCISE

Center. Obese (BMI ≥95th percentile) (19) adolescent boys were recruited by means of flyers posted in the city public transportation and posters placed on campus and from the Weight Management and Wellness Center at CHP. The investigation was approved by the University of Pittsburgh institutional review board. Parental consent and child assent were obtained for all participants before participation. Inclusion criteria included that the subjects be 12–18 years of age, pubertal (Tanner stages III–V), nonsmokers, nondiabetic, and physically inactive (no participation in structured physical activity for previous 3 months except school physical education classes). Exclusion criteria included participation in structured exercise, significant weight change (BMI >±5 kg/m²), endocrine disorders, syndromic obesity (e.g., Prader-Willi syndrome, anorexia nervosa, and celiac disease), and current use of medications known to influence glucose metabolism and body composition. Participants self-identified as black or white. Pubertal development was assessed according to Tanner criteria (genital development and pubic hair) by a certified nurse practitioner. All participants underwent a complete physical examination and routine hematological and biochemical tests at the Pediatric Clinical and Translational Research Center at CHP.

Randomization was performed after completing two baseline overnight admissions at CHP for assessments of insulin sensitivity and secretion and of body composition. Staff members who were not involved in the study randomly selected pieces of paper from a container with group assignments. Subjects were randomly assigned, with a completely randomized design and cell sizes of 16, to one of three groups: aerobic exercise, resistance exercise, or a nonexercise control group. Participants were compensated for two inpatient admissions for baseline evaluations (§150 total) and for another two inpatient admissions for postintervention evaluations (§200 total). For exercise training groups, we compensated $5 per session for travel (e.g., either bus ticket for a subject or parking for parents) to attend each exercise session and the compensation was made after finishing both post intervention clamp tests.

Dietary regimen. At baseline, subjects participated in a 1-h individual nutrition session, wherein the study nutritionist taught proper food selection and preparation. During this session, daily energy requirements for all subjects were determined by estimating resting energy expenditure and multiplying the obtained value by a factor of 1.2 (20). All subjects were asked to follow a weight maintenance diet (55–60% carbohydrate, 15–20% protein, and 20–25% fat) during the intervention period to allow the assumption that any changes in abdominal fat and insulin sensitivity were consequent to the effects of regular exercise alone without caloric restriction. Adherence to this regimen was determined by examination of body weight before each exercise session. If weight deviated significantly (>4% of initial weight on two consecutive weeks), nutrition counseling was provided to identify the deviation.

Exercise regimen. The exercise groups exercised at either the downtown Pittsburgh YMCA exercise facility or the exercise laboratory at CHP for 3 months. All exercise sessions were by appointment and were directly supervised by physical education graduate students. The aerobic exercise program required participants to exercise three times per week for 60 min/session (including 5 min warm-up and 5 min cool down) with treadmills, ellipticals, or stationary bikes. Aerobic exercise programs progressively increased in duration and intensity to 60 min at 75–80% of Vo2peak by week two. Participants wore a heart rate monitor (Polar Oy, Kempele, Finland) during the exercise sessions to ensure achievement of the target heart rate. Energy expenditure was estimated with the heart rate–Vo2 relationship observed during the Vo2peak test. The heart rates were translated into estimated energy expenditure according to the assumption that 1 L oxygen equals 5 kcal of energy expenditure (21). The heart rate range associated with 60–75% of Vo2peak was determined from the baseline maximal oxygen uptake test for each subject. The relationship between the heart rate and Vo2 was reevaluated during the subsequent maximal treadmill tests at weeks 4 and 8 to reassess the heart rate–energy expenditure relationship.

The resistance program included a series of 10 whole-body exercises three times per week. Each exercise was performed three times for a total of 30 repetitions. The resistance included leg press, leg extension, leg flexion, chest press, latisissumus pull down, seated row, biceps curl, and triceps extension with stack weight equipment. In addition, a single set each of push-ups and sit-ups were performed. For the first 4 weeks, participants performed one or two sets of 8–12 repetitions at 60% of baseline repetition maximum (RM) with proper lifting techniques. During weeks 4–12, subjects performed two sets of 8–12 repetitions to fatigue. Subjects took 1–2 min of rest between sets. Control subjects were asked to maintain their current leisure time activity (no participation in structured physical activities). To reduce dropouts and maintain adherence, participants were given the opportunity to participate in exercise sessions after the completion of postintervention evaluations.

Anthropometrics. Body weight was measured to the nearest 0.1 kg, and height was measured to the nearest 0.1 cm. WC was measured at the level of the last rib by standard procedures (22), and the average of two measures was used in the analyses.

Oral glucose tolerance test. Participants reported to the Pediatric Clinical and Translational Research Center after an overnight fast (minimum 8 h) for the baseline clamp test (1.75 g/kg, maximum 75 g). Blood samples were obtained at −15, 0, 15, 30, 60, 90, and 120 min for determination of glucose and insulin levels.

Measurement of β-cell function and insulin sensitivity by the clamp technique. Participants underwent hyperglycemic and hypoglycemic-euglycemic clamps on two separate days chosen at random, separated by 1–3 weeks before the intervention and 1 week after the intervention. A 2-h hyperglycemic clamp (12.5 mmol/l) was performed from 9:00–11:00 a.m. to evaluate first- and second-phase insulin secretion as described previously (23). On a separate visit, a 3-h 80 mmol/min hyperinsulinemic-euglycemic clamp was performed to measure insulin sensitivity as reported elsewhere (24). Plasma glucose was clamped at 5.6 mmol/l with a variable-rate infusion of 20% dextrose based on arterialized plasma glucose determinations every 5 min. Insulin sensitivity was calculated by dividing insulin-stimulated glucose disposal rate by the steady-state plasma insulin concentration during the last 30 min of the clamp. In the exercise groups, postexercise clamp measurements were obtained 12 and 13 weeks after exercise. Each clamp measurement was obtained 48–72 h after exercise to control for the well-established effects of acute exercise on glucose uptake (25). To avoid the potential detaining effect on insulin sensitivity, participants in the exercise groups were asked to maintain their current level of exercise between the clamp measurements (between 12 and 13 weeks), which amounted to a total of 39 exercise sessions in both exercise programs. One control subject did not complete the post intervention clamp tests.

Biochemical measurements. Plasma glucose was measured by the glucose oxidase method with a glucose analyzer (YSI Inc., Yellow Springs, OH), and the insulin concentration was determined by radioimmunoassay (26).

Total and abdominal fat and skeletal muscle mass. Fat free mass was assessed by dual energy X-ray absorptiometry using Lunar iDXA (GE Healthcare, Madison, WI). Whole-body magnetic resonance imaging (MRI) data were obtained with a 3.0-T MRI scanner (Magnetom TIM Trio; Siemens, Erlangen, Germany) to quantify total adipose tissue (AT), skeletal muscle, and visceral and abdominal subcutaneous fat as shown previously (22,26).

Muscle tissue water content as an internal reference according to the literature (27). Because of technical difficulties, IMCL and intrahepatic lipid were only measured in a subset of participants (10 control, 10 aerobic, and 9 resistance). IMCL was measured in the tibialis anterior muscle of the right leg with a 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Repositioning of the subject and placement of the coil and voxels were carefully monitored on the localizer images to ensure that the repeat scan was performed in the same location. Spectra were acquired with a PRESS sequence with a repetition time (TR) of 2.0 s, number of averaged spectra 128, and an echo time (TE) of 30 ms. A voxel (12 × 11 × 18 mm3) was placed in the tibialis anterior muscle, carefully avoiding vascular structures and AT deposits within the voxels. The proton magnetic resonance spectra were acquired with water suppression for the determination of IMCL, and one single shot was acquired without water suppression for the determination of intrahepatic lipid by proton magnetic resonance spectroscopy. Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens). Whole-body magnetic resonance imaging (BMI) was performed at 3.0-T MRI system (TIM Trio) with a CP extremity coil (Siemens).
**Statistical analysis.** The primary outcome of the study was visceral fat at 3 months after intervention. We selected a sample size 14 to provide a statistical power of 95% to detect a difference of 0.56 kg in visceral fat (30) between any two groups at 3 months with a repeated measures ANCOVA at an $\alpha$ of 0.05. We increased the sample size to 16 to allow for withdrawals.

A one-way ANOVA was performed to examine group differences at baseline. We examined the effect of the intervention with an intent-to-treat analysis for only randomized subjects with baseline data. Missing follow-up data values were estimated by multiple imputations procedure (Proc mi) with 100 imputations (31). Repeated measures ANOVA was used to determine treatment differences with the imputed data. Two participants had missing baseline images for skeletal muscle and visceral and abdominal subcutaneous fat and were excluded from the intent-to-treat analyses.

We also examined the effect of the exercise intervention with as-treated analyses in participants who had complete baseline and follow-up data. Least squared means difference post hoc tests were used to determine differences between the control and intervention groups. The relationships between changes in total and abdominal fat and insulin sensitivity were evaluated by Pearson correlation coefficients.

$P$ values of less than 0.05 were accepted to indicate statistical significance. All analyses were performed with commercially available software (SAS, version 9.2; SAS Institute Inc, Cary, NC). Unless otherwise indicated, data are expressed as mean (SE).

**FIG. 1. Participant flow diagram.** All subjects assigned to each group (including subjects who discontinued the study) were included in intent-to-treat analyses.
RESULTS

Adherence. Of the 45 boys randomized, 43 completed their assigned treatment (Fig. 1). Two subjects (one each in aerobic and control groups) did not complete the study because of lack of interest. We excluded one control subject from data analyses who was found to be taking metformin during the intervention period. Average (mean ± SD) attendance at the exercise sessions was >99% in both the aerobic (99.7 ± 0.8%) and resistance (99.0 ± 2.1%) groups, and average exercise durations were similar between the aerobic (57.7 ± 1.2 min/session) and resistance (59.4 ± 3.6 min/session) exercise groups. In the aerobic exercise group, the mean heart rate was 153.8 ± 7.2 bpm (range, 144–175 bpm) and energy expenditure was 713.9 ± 166.4 kcal/session (range, 303–943 kcal/session).

Baseline characteristics. There were no significant differences between groups for baseline variables (Table 1).

Changes in fitness. Compared with controls, cardiorespiratory fitness increased significantly (P < 0.05) by similar magnitudes in the aerobic and resistance exercise (aerobic, 5.7 ± 1.2 min/session) exercise groups. Compared with controls, muscular strength increased significantly (P < 0.05) in the aerobic exercise group but not in the aerobic exercise group.

Changes in body weight and WC. After 3 months, both aerobic and resistance exercise (aerobic, −0.04 ± 0.8 kg; resistance, −0.6 ± 0.8 kg) prevented the significant weight gain that was observed in controls (2.6 ± 0.1 kg) (Table 2). A significant (P < 0.05) reduction in WC was observed in both exercise groups compared with controls. There was a small but significant decrease in BMI in the resistance exercise group but not the aerobic group.

Changes in total fat and skeletal muscle mass. Compared with controls, a significant (P < 0.05) reduction in total adiposity (%) was observed in the exercise groups (Table 2). A significant increase in total skeletal muscle mass (1.4 ± 0.3 kg; P = 0.01) was observed in the resistance exercise group alone compared with controls.

Changes in abdominal fat, intrahepatic lipid, and IMCL. Comparing with controls, significant (P < 0.05) reductions in abdominal subcutaneous and visceral fat (kg) were observed in both the aerobic and resistance exercise groups (Table 2 and Fig. 2A). Compared with controls, intrahepatic lipid (%) was reduced (P < 0.05) in the aerobic (−1.9 ± 1.0%) and resistance (−2.0 ± 1.0%) exercise groups by similar magnitudes (Fig. 2B). No significant within or between group changes in IMCL were observed in any group.

TABLE 1

Subject characteristics at baseline

| Characteristics                  | Control (n = 13) | Aerobic exercise (n = 16) | Resistance exercise (n = 16) | P value |
|----------------------------------|-----------------|--------------------------|-----------------------------|---------|
| Black/white/mixed (n)            | 6/6/1           | 9/7/0                    | 7/9/0                       | 0.69    |
| Puberty, III/IV/V (n)            | 2/3/8           | 1/4/11                   | 6/1/9                       | 0.65    |
| Anthropometric                   |                 |                          |                             |         |
| Age (years)                      | 14.8 ± 1.4      | 15.2 ± 1.9               | 14.6 ± 1.5                  | 0.596   |
| Body weight (kg)                 | 100.0 ± 14.4    | 106.5 ± 19.3             | 97.7 ± 10.8                 | 0.251   |
| BMI (kg/m²)                      | 33.9 ± 4.2      | 36.6 ± 5.9               | 34.5 ± 2.4                  | 0.224   |
| WC (cm)                          | 99.3 ± 10.3     | 105.2 ± 11.2             | 101.1 ± 8.0                 | 0.270   |
| DXA                              |                 |                          |                             |         |
| FFM (kg)                         | 58.9 ± 8.1      | 62.7 ± 9.6               | 56.1 ± 6.8                  | 0.091   |
| MRI                              |                 |                          |                             |         |
| Total adiposity (%)              | 42.7 ± 8.3      | 43.2 ± 4.9               | 43.8 ± 6.1                  | 0.895   |
| Total AT (kg)*                   | 43.2 ± 12.4     | 46.5 ± 12.1              | 43.4 ± 9.0                  | 0.679   |
| Skeletal muscle (kg)*            | 27.4 ± 4.8      | 30.7 ± 5.3               | 27.2 ± 4.0                  | 0.994   |
| Visceral AT (kg)*                | 1.2 ± 0.4       | 1.5 ± 0.5                | 1.4 ± 0.6                   | 0.413   |
| Abdominal subcutaneous AT (kg)*  | 6.7 ± 2.5       | 7.8 ± 2.5                | 6.8 ± 1.8                   | 0.306   |
| Intrahepatic lipid (%)†          | 2.2 ± 2.2       | 4.7 ± 4.0                | 2.9 ± 2.4                   | 0.190   |
| IMCL (nmol/kg wet weight)†       | 2.6 ± 1.6       | 3.4 ± 1.5                | 2.2 ± 1.0                   | 0.194   |
| Metabolic                        |                 |                          |                             |         |
| Fasting glucose (mg/dL)          | 96.9 ± 5.0      | 95.9 ± 4.2               | 94.8 ± 4.3                  | 0.461   |
| Fasting insulin (μU/mL)          | 32.9 ± 13.6     | 38.3 ± 21.2              | 27.6 ± 7.3                  | 0.152   |
| First-phase insulin (μU/mL)      | 244.3 ± 136.0   | 292.7 ± 164.8            | 213.9 ± 119.0               | 0.295   |
| Second-phase insulin (μU/mL)     | 270.1 ± 158.1   | 344.0 ± 219.3            | 241.4 ± 93.4                | 0.210   |
| Insulin sensitivity‡             | (mL/kg/min per μU/mL) | 2.7 ± 1.2          | 2.2 ± 1.0                   | 2.9 ± 1.0 | 0.159 |
| Disposition index                | 545.3 ± 206.7   | 538.9 ± 341.8            | 545.5 ± 201.7               | 0.997   |
| Fitness                          |                 |                          |                             |         |
| VO2peak (L/min)                  | 3.0 ± 0.6       | 3.1 ± 0.8                | 3.0 ± 0.5                   | 0.849   |
| VO2peak (mL/kg/min)              | 30.0 ± 4.3      | 29.0 ± 4.8               | 30.4 ± 5.0                  | 0.706   |
| Chest press RM (kg)              | 49.3 ± 13.1     | 59.4 ± 15.9              | 49.6 ± 13.8                 | 0.099   |
| Leg press RM (kg)                | 61.2 ± 13.5     | 68.5 ± 14.5              | 63.6 ± 12.5                 | 0.340   |
| Muscular strength index          | 1.1 ± 0.2       | 1.2 ± 0.2                | 1.2 ± 0.3                   | 0.547   |

Data are means ± SD except as marked. DXA, dual energy X-ray absorptiometry. FFM, fat-free mass. *Total adiposity, skeletal muscle, visceral AT, and abdominal subcutaneous AT (all in kilograms) were quantified in 14 subjects in the exercise exercise group as a result of missing data during data transfer. †Control, 10 aerobic, and 9 resistance. §Resistance n = 15 as a result of intravenous issue during the clamp.
TABLE 2
Absolute changes in total and regional body composition and fitness after 3 months

|                        | Control (n = 11, ITT = 13) | Aerobic exercise (n = 15, ITT = 16) | Resistance exercise (n = 16, ITT = 16) |
|------------------------|-----------------------------|------------------------------------|---------------------------------------|
|                        | Value | Value | P value | Value | Value | P value | Value | Value | P value |
| ITT analysis (n = 45)  |       |       |         |       |       |         |       |       |         |
| Body weight (kg)       | 2.6 ± 1.0 | 0.04 ± 0.8 | 0.039 | -0.6 ± 0.8 | 0.009 |
| BMI (kg/m²)            | 0.3 ± 0.3 | -0.3 ± 0.3 | 0.191 | -0.6 ± 0.3 | 0.047 |
| WC (cm)                | 1.1 ± 1.0 | -2.0 ± 0.9 | 0.027 | -3.2 ± 0.9 | 0.001 |
| Fat free mass (kg, DXA)| 1.38 ± 0.39 | 1.23 ± 0.34 | 0.774 | 2.11 ± 0.33 | 0.152 |
| Total adiposity (%)    | 0.02 ± 0.6 | -2.6 ± 0.6 | 0.002 | -2.5 ± 0.6 | 0.004 |
| Total AT (kg)          | 1.2 ± 0.9 | -3.0 ± 0.8 | 0.001 | -2.5 ± 0.8 | 0.002 |
| Skeletal muscle (kg)   | 0.5 ± 0.3 | 1.0 ± 0.3 | 0.155 | 1.4 ± 0.3 | 0.01 |
| Visceral AT (kg)       | 0.2 ± 0.1 | -0.1 ± 0.04 | <0.0001 | -0.2 ± 0.04 | <0.0001 |
| Abdominal subcutaneous AT (kg)| 0.2 ± 0.2 | -0.5 ± 0.1 | 0.004 | -0.4 ± 0.1 | 0.005 |
| Liver fat (%)          | 0.9 ± 0.7 | -1.9 ± 1.0 | 0.049 | -2.0 ± 1.0 | 0.047 |
| IMCL (mmol/kg ww)      | 0.7 ± 0.5 | 1.0 ± 0.6 | 0.087 | -0.05 ± 0.5 | 0.909 |
| VO2peak (L/min)        | 0.2 ± 0.1 | 0.9 ± 0.1 | <0.0001 | 0.7 ± 0.1 | <0.0001 |
| VO2peak (mL/kg/min)    | -0.04 ± 1.1 | 9.1 ± 0.9 | <0.0001 | 7.7 ± 0.9 | <0.0001 |
| Chest press RM (kg)    | 0.13 ± 1.3 | 2.1 ± 1.1 | 0.28 | 13.6 ± 1.1 | <0.0001 |
| Leg press RM (kg)      | 4.6 ± 5.9 | 0.6 ± 5.5 | 0.79 | 25.8 ± 6.8 | 0.0001 |
| Muscular strength index| 0.02 ± 0.1 | 0.2 ± 0.2 | 0.36 | 1.0 ± 0.2 | <0.0001 |
| Per protocol analysis (n = 42) |       |         |         |       |         |         |       |         |         |
| Body weight (kg)       | 2.7 ± 0.9 | 0.04 ± 0.8 | 0.039 | -0.6 ± 0.8 | 0.011 |
| BMI (kg/m²)            | 0.3 ± 0.3 | -0.3 ± 0.3 | 0.179 | -0.5 ± 0.3 | 0.047 |
| WC (cm)                | 1.2 ± 1.0 | -1.9 ± 0.9 | 0.028 | -3.2 ± 0.8 | 0.002 |
| Fat free mass (kg, DXA)| 1.42 ± 0.38 | 1.25 ± 0.33 | 0.748 | 2.13 ± 0.32 | 0.160 |
| Total adiposity (%)    | 0.02 ± 0.6 | -2.7 ± 0.6 | 0.004 | -2.5 ± 0.6 | 0.004 |
| Total AT (kg)          | 1.2 ± 0.9 | -3.1 ± 0.8 | 0.001 | -2.8 ± 0.6 | 0.003 |
| Skeletal muscle (kg)   | 0.5 ± 0.3 | 1.0 ± 0.3 | 0.170 | 1.5 ± 0.2 | 0.008 |
| Visceral AT (kg)       | 0.2 ± 0.1 | -0.1 ± 0.04 | <0.0001 | -0.2 ± 0.04 | <0.0001 |
| Abdominal subcutaneous AT (kg)| 0.2 ± 0.2 | -0.5 ± 0.1 | 0.005 | -0.1 ± 0.1 | 0.006 |
| Liver fat (%)          | 0.9 ± 0.7 | -1.1 ± 0.7 | 0.061 | -1.2 ± 0.6 | 0.042 |
| IMCL (mmol/kg ww)      | 0.7 ± 0.5 | 1.1 ± 0.5 | 0.639 | -0.03 ± 0.4 | 0.231 |
| VO2peak (L/min)        | 0.1 ± 0.1 | 0.9 ± 0.1 | <0.0001 | 0.7 ± 0.1 | <0.0001 |
| VO2peak (mL/kg/min)    | -0.1 ± 1.0 | 9.0 ± 0.9 | <0.0001 | 7.6 ± 0.9 | <0.0001 |
| Chest press RM (kg)    | 0.3 ± 1.3 | 2.1 ± 1.1 | 0.29 | 13.7 ± 1.1 | <0.0001 |
| Leg press RM (kg)      | 4.7 ± 5.8 | 6.6 ± 5.0 | 0.81 | 29.8 ± 6.8 | 0.0002 |
| Muscular strength index| 0.03 ± 0.10 | 0.2 ± 0.2 | 0.37 | 1.0 ± 0.1 | <0.0001 |

Data are means ± SE. Values for the control group are imputed means ± SE. Change values for the intervention groups are the difference as compared with control with SE. P values are as compared with the control group. DXA, dual energy X-ray absorptiometry; FFM, fat-free mass; ITT, intent-to-treat.

Collapsed across all groups, changes in abdominal fat (r = 0.73) and visceral fat (r = 0.67) were associated (P < 0.001) with the corresponding change in WC. Further, collapsed across all groups (n = 26), the change in visceral fat was significantly related to the corresponding change in intrahepatic lipid (r = 0.72; P < 0.001).

Changes in insulin action and secretion. Compared with controls, insulin sensitivity improved significantly in the resistance exercise group (0.8 ± 0.2 mL/kg/min per μU/mL; P = 0.009), and this remained significant when data were expressed per unit of fat-free mass (Table 3 and Fig. 2C). No significant changes in insulin secretion during the hyperglycemic clamp, disposition index (first-phase insulin × insulin sensitivity), and oral glucose tolerance (data not shown) were observed in any groups (Table 3). Collapsed across groups, the change in insulin sensitivity was significantly related to the corresponding changes in visceral AT in kilograms (r = -0.47; P = 0.003).

DISCUSSION
We examined the effects of aerobic versus resistance exercise alone without caloric restriction on abdominal obesity, ectopic fat, and insulin sensitivity and secretion in previously sedentary obese adolescent boys. This is the first randomized trial in the adolescent age group designed specifically to investigate the role of regular exercise alone on obesity-related risk factors with criterion measures including whole-body MRI, proton magnetic resonance spectroscopy, and the 2-h hyperglycemic and 3-h hyperinsulinemic-euglycemic clamp techniques. The primary finding is that both aerobic and resistance exercise performed for 180 min per week without caloric restriction resulted in significant reductions in total fat, visceral adiposity, WC, and intrahepatic lipid and in improvement in cardiorespiratory fitness in obese adolescent boys. Furthermore, resistance exercise was effective in improving insulin sensitivity, skeletal muscle mass, and muscular strength. Our findings have important health implications and provide therapeutic strategies to health care professionals for the treatment of childhood obesity and the reduction in insulin resistance in moderately obese boys.

Our finding that regular exercise, independent of modality, is associated with significant reductions in intrahepatic lipid in previously sedentary obese adolescent boys.
boys is noteworthy, given that nonalcoholic fatty liver disease is a common feature of childhood obesity (32) and that increased liver fat is strongly associated with insulin resistance and hypertriglyceridemia in adolescents (33). Although the pathogenesis of nonalcoholic fatty liver in obese adolescents remains unclear, our observation that visceral fat is associated with intrahepatic lipid ($r = 0.55$) at baseline and that changes in visceral fat are related to corresponding changes in intrahepatic lipid ($r = 0.72$) suggests a possible link between the two fat depots.

In this study, we did not observe significant changes in IMCL content in response to either aerobic or resistance exercise training, despite improved in vivo insulin sensitivity. This is consistent with previous studies reporting no changes in IMCL after aerobic training in previously sedentary obese adults (34,35) and adolescents (36) despite improvements in insulin resistance. The implication of a lack of association between changes in IMCL and insulin sensitivity with exercise training is unclear, as cross-sectional studies have demonstrated significant relationships between IMCL and insulin resistance in individuals with obesity (37), type 2 diabetes (T2D) (38), and a family history of T2D (39). Some suggest that IMCL content per se is metabolically inert and is not likely to be a determinant of insulin resistance in skeletal muscle (35). Others have demonstrated that skeletal muscle quality, such as oxidation capacity of muscle and muscle fiber type distribution, plays a role in the association between excess IMCL and insulin resistance in obesity (40,41).

It has been shown that weight loss induced by either exercise or diet improves insulin sensitivity (9,42). Our data extend these observations and suggest that regular

![FIG. 2. Absolute changes in visceral fat (A), intrahepatic lipid (B), and insulin sensitivity (C) for each intervention group. *P values are as compared with the control group (intent-to-treat analyses). FFM, fat-free mass.](image-url)
exercise without caloric restriction is associated with 19% and 28% improvements in insulin sensitivity in the aerobic and resistance exercise groups, respectively. It has been reported that improvements in insulin sensitivity are associated with improvements in aerobic fitness (34) and skeletal muscle mass (43) in adult men. Thus the significant improvements in insulin sensitivity in the resistance group observed in the current study are likely explained in part by significant increases in skeletal muscle mass with training. In the aerobic group, there were similar significant improvements in aerobic fitness but smaller and non-significant improvements in skeletal muscle mass and insulin sensitivity. Further, it is important to consider that insulin sensitivity was measured 48–72 h after the last exercise session, and this may have contributed to the inability to observe a significant improvement in insulin sensitivity. Nevertheless, the improvements in insulin sensitivity within the exercise training groups are explained by reductions in total fat ($r = -0.43$; $P < 0.05$) and visceral adiposity ($r = -0.42$; $P < 0.05$), highlighting the importance of adiposity reduction to improve insulin sensitivity in adolescents.

We did not observe improvements in insulin secretion in the exercise training groups. Because our study participants were nonobese, it is reasonable to believe that they had appropriate β-cell function to compensate for insulin resistance and maintain euglycemia, and thus regular exercise alone would have little effect on insulin secretion in this nonobese adolescent population. It is currently unclear whether regular exercise alone is effective in improving insulin secretion in adolescents with impaired β-cell function and prediabetes or T2D.

In the current study, obese adolescent boys complied well with the prescribed exercise regimens, resulting in high attendance rates in both aerobic (99.7 ± 0.8%) and resistance (90.0 ± 2.1%) groups. This observation suggests that our exercise regimen (three times/week or 180 min/week) is feasible and effective for obese adolescent boys. Anecdotally, however, there were differences in how much the boys enjoyed the exercise intervention. In the aerobic group, the participants found the exercise to be boring, whereas those in the resistance group were much more enthusiastic and seemingly enjoyed the exercise intervention. Given the superior improvements with resistance exercise and the enjoyment factor, we propose therefore that resistance exercise may be a better mode of exercise for moderately obese boys of this age group.

The limitations of this study warrant mention. Although this is the first study in adolescents to use state-of-the-art methodologies to examine the effects of different exercise modalities without caloric restriction on adiposity reduction and insulin resistance, our observations are based on healthy pubertal moderately obese adolescent boys, who were black or white. Whether our findings would remain true in girls, other ethnic groups, or youth at different pubertal developmental stages is unknown. This was a tightly controlled efficacy study, and all exercise was completed under supervision, and thus our findings cannot be generalized to the general population of obese adolescent boys. Supervision, access, cost, and the support received during the study may have helped to improve compliance; however, the high level of compliance allowed us to assess more effectively the effects of exercise training on our outcomes of interest. During the study, leisure time physical activity was not measured with pedometers or accelerometers, and although subjects were asked to log their energy intake, this was not completed by a significant portion of subjects and was generally done very poorly.

In our study, subject recruitment was an ongoing process during the entire study period. Seasonal variations and age have been shown to affect physical activity patterns in youth (44). In addition, although our findings from a short-term exercise intervention are encouraging, evidence regarding the benefits of long-term exercise on obesity-related health outcomes in youth is unclear. In adults, the findings from short-term (<4 months) exercise intervention
studies generally report higher energy expenditure and thus much greater reductions in body weight and total fat than long-term (>6 months) exercise intervention studies (45). It is unclear whether the health benefits and compliance observed in our study can be maintained long-term in obese adolescents. Finally, biomarkers such as retinol binding protein 4 and inflammatory factors have not been analyzed, which is also a limitation of the study. Examining biomarkers is important, as they are useful in illuminating the potential cross talk between organs in our efforts to identify risk factors for diabetes and cardiovascular disease (46,47).

In summary, both aerobic and resistance exercise without caloric restriction are effective for reducing abdominal fat and intrahepatic lipid in moderately obese adolescent boys. Resistance exercise but not aerobic exercise is also associated with significant improvements in insulin sensitivity.

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S.L. designed the study, obtained funding, researched data, and wrote the manuscript. F.B. and T.H. researched data and reviewed the manuscript. J.K. performed statistical analyses and provided critical revision of the manuscript. C.B. together with S.L. established the magnetic resonance spectroscopy protocol at the University of Pittsburgh and assisted in magnetic resonance spectroscopic data analyses and interpretations. S.A. obtained funding, researched data, and provided critical revision of the manuscript. S.L. is the guarantor of this work and, as such, had full access to all the data in this study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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