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A 12-Week Aerobic Exercise Program Reduces Hepatic Fat Accumulation and Insulin Resistance in Obese, Hispanic Adolescents

Gert-Jan van der Heijden[1], Zhiyue J. Wang[1,2], Zili D. Chu[1], Pieter J.J. Sauer[3], Morey W. Haymond[1], Luisa M. Rodriguez[1] and Agneta L. Sunehag[1]

The rise in obesity-related morbidity in children and adolescents requires urgent prevention and treatment strategies. Currently, only limited data are available on the effects of exercise programs on insulin resistance, and visceral, hepatic, and intramyocellular fat accumulation. We hypothesized that a 12-week controlled aerobic exercise program without weight loss reduces visceral, hepatic, and intramyocellular fat content and decreases insulin resistance in sedentary Hispanic adolescents. Twenty-nine postpubertal (Tanner stage IV and V), Hispanic adolescents, 15 obese (7 boys, 8 girls; 15.6 ± 0.4 years; 33.7 ± 1.1 kg/m^2; 38.3 ± 1.5% body fat) and 14 lean (10 boys, 4 girls; 15.1 ± 0.3 years; 20.6 ± 0.8 kg/m^2; 18.9 ± 1.5% body fat), completed a 12-week aerobic exercise program (4 × 30 min/week at ≥70% of peak oxygen consumption (VO_2peak)). Measurements of cardiovascular fitness, visceral, hepatic, and intramyocellular fat content (magnetic resonance imaging (MRI)/magnetic resonance spectroscopy (MRS)), and insulin resistance were obtained at baseline and postexercise. In both groups, fitness increased (obese: 13 ± 2%, lean: 16 ± 4%; both $P <$ 0.01). In obese participants, intramyocellular fat remained unchanged, whereas hepatic fat content decreased from 8.9 ± 3.2 to 5.6 ± 1.8%; $P < 0.05$ and visceral fat content from 54.7 ± 6.0 to 49.6 ± 5.5 cm^2; $P < 0.05$. Insulin resistance decreased indicated by decreased fasting insulin (21.8 ± 2.7 to 18.2 ± 2.4 μU/ml; $P < 0.01$) and homeostasis model assessment of insulin resistance ($HOMA_{IR}$) (4.9 ± 0.7 to 4.1 ± 0.6; $P < 0.01$). The decrease in visceral fat correlated with the decrease in fasting insulin ($R^2 = 0.40$; $P < 0.05$). No significant changes were observed in any parameter in lean participants except a small increase in lean body mass (LBM). Thus, a controlled aerobic exercise program, without weight loss, reduced hepatic and visceral fat accumulation, and decreased insulin resistance in obese adolescents.

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The prevalence of obesity and obesity-related illnesses has increased dramatically in children and adolescents over the past decades. About 17% of American youth are obese (1). Of those who are obese, 30–50% have the metabolic syndrome (2), 30–40% have hepatic steatosis (3,4), and 15–30% of all newly diagnosed diabetic adolescents have obesity-related type 2 diabetes (5,6). This is a very serious public health concern requiring urgent prevention and treatment strategies.

Lifestyle interventions including various combinations of diet, exercise, and education programs have been shown to reduce obesity and its comorbidities (7–9). It is, however, difficult to determine which interventions are most efficient and best accepted by children and adolescents. Weight loss improves metabolic disturbances, but long-term compliance is often unsuccessful, resulting in weight regain. Improved insulin sensitivity and reduced abdominal fat accumulation have been reported in response to exercise with and without weight loss in children and adolescents (10–15). However, potential confounders such as age and pubertal stage of the participants, duration, intensity and type of exercise, and control of the diet preceding the pre- and postexercise measurements were often not well described. In addition, the effect of exercise on hepatic and intramyocellular fat were not measured.

The purpose of the present study was to determine the effects of a controlled, moderately intensive aerobic exercise program that would be acceptable to sedentary obese and lean adolescents. No additional dietary and lifestyle advice was provided, and there was no intent of weight loss. The study focused on Hispanic adolescents because of their high prevalence of obesity and its comorbidities (1,4,16). A group of sedentary lean

[1]Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA; [2]Department of Radiology, Children's Medical Center and University of Texas Southwestern Medical Center, Dallas, Texas, USA; [3]Department of Pediatrics, Beatrix Children's Hospital, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands. Correspondence: Agneta L. Sunehag (asunehag@bcm.tmc.edu)

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adolescents was included because sedentary lifestyle in itself might have negative metabolic effects (17). Further, effects of an exercise program in lean sedentary adolescents have not previously been reported.

We hypothesized that a 12-week controlled aerobic exercise program without weight loss reduces visceral, hepatic, and intramyocellular lipid (IMCL) content and decreases insulin resistance in sedentary Hispanic adolescents.

METHODS AND PROCEDURES

Participants

After approval of the protocol by the Baylor College of Medicine Institutional Review Board for Human Subject Research and the General Clinical Research Center Advisory Board, lean and obese adolescents were recruited by local advertisement. Adolescents were screened and enrolled in the study after written assent from the participant and consent from the legal guardian were obtained.

Twenty-nine postpubertal (i.e., Tanner pubertal stage IV and V), Hispanic adolescents, 15 obese and 14 lean, were studied (**Table 1**). All obese participants had BMI >95th and all lean participants <85th percentile for age according to Centers for Disease Control and Prevention growth charts (18). Participants had been lean or obese for ≥5 years and reported stable body weight for at least 6 months. Only sedentary adolescents were included, defined by no school organized athletic program participation and <45 min light-to-moderate physical activity/week. All participants were Hispanic (parents and grandparents of Hispanic descent by self-report). The participants were in good health as determined by a medical history, a physical examination, and a standard blood chemistry analysis including blood lipids, liver and kidney function tests, hemoglobin, hematocrit, hemoglobin A1c, and fasting and 2-h postprandial glucose response. Participants were taking no medications including birth control pills and had no first-degree relatives with diabetes. Adolescents with morbid obesity (body fat % >50, sleep apnea, Pickwick syndrome, or cor pulmonale) were excluded.

Study design

Each participant was studied on two separate occasions: (i) the weekend before start of the exercise program (baseline), (ii) 3 days after the final exercise session of the 12–week exercise program (post). All procedures were identical on both study occasions.

To exclude effects of dietary intake on measurements obtained at baseline vs. postexercise, prior to both studies, each participant received an identical 7-day low-carbohydrate/high-fat diet at home (30% carbohydrate, 55% fat, and 15% protein; 20% of the total carbohydrate content as fructose) (19–21). Total energy intake was calculated to correspond to each individual's requirement according to the Institute of Medicine Dietary Reference Intakes (22). Nonconsumed food was examined for constituents, and the energy and macronutrient composition of the consumed food was calculated by difference (19–21). In order to measure the effect of exercise alone, participants were told not to make lifestyle and dietary changes during the exercise program. On day 7 of the diet period, the participants were admitted to the Metabolic Research Unit at the Children's Nutrition Research Center, Houston, TX. Participants were fasted overnight for 12 h (except for water). Following the fast, four blood samples were obtained for measurements of glucose, insulin, and alanine aminotransferase concentrations. Subsequently, the participants were transferred to the radiology department at Texas Children's Hospital for magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) of abdominal, hepatic, and intramyocellular fat content.

Exercise program

For the duration of 12 weeks, participants came to the physical therapy unit at Texas Children's Hospital twice a week for a 30-min aerobic exercise session on a treadmill, elliptical or a bicycle (dependent on the preference of the participant). Each exercise session was preceded by 10 min of warm-up and stretching, and followed by 10 min of cooldown and stretching. The exercise intensity level was designed to result in a heart rate corresponding to at least 70% of that obtained at peak oxygen consumption (VO_2peak) at baseline (see below), i.e., we aimed at maintaining heart rates >140 beats/min. Experienced exercise physiologists were responsible for the training sessions together with the principal investigator. Participants were instructed to perform a similar program (same duration and intensity) twice a week at home, i.e., a total of four exercise sessions per week, which amounted to 48 sessions in the total exercise program. To assure that the desired heart rate (exercise intensity) was achieved and maintained for 30 min, each participant wore a heart rate monitor, Polar S-710 (HealthCheck Systems, Brooklyn, NY) during all home and hospital exercise sessions. Information from the monitors was downloaded and evaluated on a weekly basis. Participants performed no exercise outside the program. The participants' weight was assessed twice a week in conjunction with the exercise sessions to assure weight stability.

To avoid the acute effect of exercise on measurements obtained during the postexercise study, the last exercise session took place 3 days prior to the glucose, insulin, and MRI/MRS measurements.

Cardiovascular fitness

VO_2peak was measured at baseline and postexercise using a modified Bruce treadmill protocol. The treadmill test started at a speed of 1.7 mph. Subsequently, the speed and incline were gradually increased every 3 min until maximal exercise capacity of the participant was reached. Oxygen consumption was measured with a Vmax-229 metabolic cart (SensorMedics, Anaheim, CA). VO_2peak was determined using standard criteria, specifically, a heart rate >195 beats/min or a respiratory quotient >1.0 at peak exercise (21).

Body composition

Nonbone lean body (LBM) and fat mass (FM) were measured by dual-energy X-ray absorptiometry (QDR 11.2; Hologic, Bedford, MA) (19–21).

Abdominal fat content was measured by MRI, and intrahepatic and IMCL content (soleus muscle) by MRS using a Philips Achieva 1.5T whole body clinical scanner, software release 1.5 (Philips Healthcare, Best, the Netherlands).

The magnetic resonance image of abdominal fat, i.e., visceral (intra-abdominal) and subcutaneous (peripheral) fat content, was acquired in a single transversal slice at the level of the umbilicus as previously described (19,21). MRI data are expressed as cross-sectional area (cm^2).

A point-resolved spectroscopy single voxel technique was used to obtain the liver magnetic resonance spectra in a $3 \times 3 \times 3\,cm^3$ voxel, with repetition time/echo time = 5,000/31 ms, NSA = 32, and water suppression off. Data were analyzed using the scanner software to obtain the peak areas of water and lipids, respectively. The lipid signals were treated as one composite peak and integrated from 0.0 to 2.5 ppm after baseline correction. The result was expressed as the total lipid/water peak area ratio (%) (ref. 23) (**Figure 1**). Hepatic fat was considered normal if the MRS lipid peak/water peak was <5.6% and high if the MRS lipid peak/water peak was >5.6% (ref. 24).

A point-resolved spectroscopy chemical shift imaging technique was used for measuring IMCL, with repetition time/echo time = 1,500/31 ms, field of view = 120–160 mm, slice thickness = 10 mm, in-plane nominal voxel size $5 \times 5\,mm^2$, number of signal average = 1, and no water suppression. Presaturation multiple regional saturation technique pulses were used to suppress the lipid signal from outside the region of interest. The region of interest excluded tibia and fibula bone marrow and was positioned at the same height and location for both study occasions. The spectral map was overlaid on a T1-weighted localizer image using the "SpecTool" software (version 4.5; Philips Healthcare). Our MRS imaging method provided high spatial resolution data with good shim. There were several voxels inside the soleus muscle, but only spectra from voxels showing well-defined separation between extramyocellular lipid and

IMCL peaks were analyzed individually using jMRUI v3.0 (ref. 25) with the advanced magnetic resonance algorithm to obtain the peak areas as described by Szczepaniak *et al.* (26). The water and IMCL signals were quantified together from spectra acquired without water suppression. The average value of the IMCL/water ratio (%) from these spectra was used for statistical analysis.

Blood sampling and analyses

Blood samples were collected in EDTA tubes. Immediately after blood collection, samples were put on ice and span at 3,000 rpm for 10 min. Plasma was stored at −80 °C until final analysis. Glucose concentrations were measured using an enzymatic specific method (YSI glucose analyzer; YSI, Yellow Springs, OH) and insulin concentrations, by electrochemiluminescence using a Roche Elecsys 1010 analyzer (Roche Diagnostics, Indianapolis, IN).

Insulin resistance was calculated by the homeostasis model assessment, $HOMA_{IR}$ (fasting insulin (μU/ml) × fasting glucose (mmol/l) /22.5) (ref. 27).

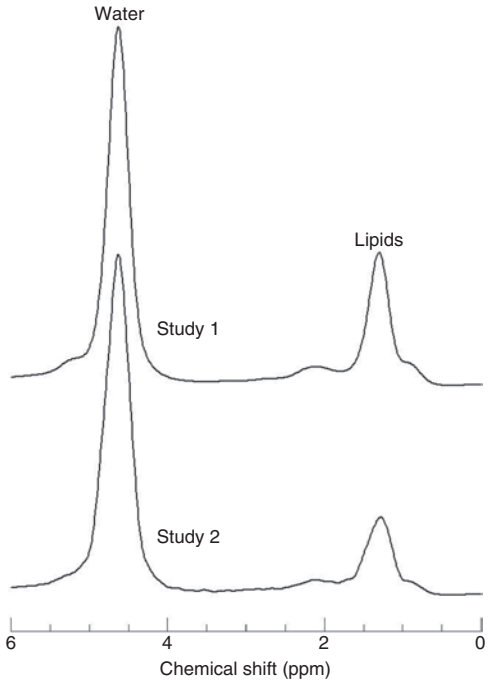

Figure 1 Representative liver spectra of an obese participant at baseline (study 1) and postexercise (study 2).

Statistical methods

Data are presented as mean ± s.e. Repeated measures ANOVA (SPSS 17.0; SPSS, Chicago, IL) was used to assess the effects of exercise, groups (lean vs. obese participants and obese participants with high hepatic fat vs. normal hepatic fat), and the interaction between groups and exercise. Unpaired *t*-test was used to assess differences between groups at baseline and post the exercise program after detection of interaction. Within-group differences (i.e., baseline vs. postexercise) were assessed by paired *t*-test. Regression analysis was used to test for correlations between variables. A $P < 0.05$ was considered statistically significant.

RESULTS

Obese and lean participants

Cardiovascular fitness. Obese and lean participants completed 91 ± 2% and 87 ± 2% of the total exercise program (48 sessions), respectively (ns), at 86 ± 2% and 85 ± 1% of their heart rate at baseline VO_2peak, respectively (ns). Total VO_2peak increased by 13 ± 2% in obese ($P = 0.0002$) and 16 ± 4% in lean adolescents ($P = 0.002$) (**Table 1**).

Energy intake. Prior to both study occasions, dietary compliance was not different in either lean or obese participants. Total energy intake was virtually identical on both study occasions in the obese (baseline: 2,725 ± 165; post: 2,695 ± 170 kcal/day) and in the lean participants (baseline: 2,318 ± 49; post: 2,314 ± 81 kcal/day). The macronutrient distribution was also identical on both study occasions and corresponded completely to that designed.

Table 1 Participant characteristics (mean ± s.e.)

	Obese		Lean		Interaction (P value)[$]
	Baseline	Post	Baseline	Post	
N	15		14		
Boy/girl	7/8		10/4		
Age (years)	15.6 ± 0.4		15.1 ± 0.3		
Tanner stage IV/V	3/12		5/9		
Weight (kg)	91.7 ± 3.5	91.2 ± 3.5	57.2 ± 2.7[###]	58.0 ± 2.9*[###]	0.083
BMI (kg/m^2)	33.7 ± 1.1	33.4 ± 1.1	20.6 ± 0.8[###]	20.7 ± 0.8[###]	0.175
Body fat %	38.3 ± 1.5	37.3 ± 1.6*	18.9 ± 1.5[###]	18.6 ± 1.6[###]	0.286
Lean body mass (kg)	54.6 ± 2.7	55.3 ± 2.8	44.7 ± 2.3[##]	46.0 ± 2.4*[#]	0.409
Fat mass (kg)	35.2 ± 2.0	34.2 ± 2.1*	10.9 ± 1.0[###]	10.9 ± 1.1[###]	0.048
Glucose (mmol/l)	5.0 ± 0.1	5.0 ± 0.1	5.1 ± 0.1	5.0 ± 0.1	0.696
Insulin (μU/ml)	21.8 ± 2.7	18.2 ± 2.4***	7.3 ± 0.9[###]	6.7 ± 0.9[###]	0.001
$HOMA_{IR}$	4.9 ± 0.7	4.1 ± 0.6***	1.7 ± 0.2[###]	1.5 ± 0.2[###]	0.003
ALT (U/l)	39 ± 4	35 ± 3	27 ± 1[##]	27 ± 2	0.083
VO_2peak l/min	2.45 ± 0.15	2.75 ± 0.18***	2.17 ± 0.14	2.47 ± 0.12**	0.975

ALT, alanine aminotransferase; $HOMA_{IR}$, homeostasis model assessment of insulin resistance; VO_2peak, peak oxygen consumption.
Different from baseline within each group: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. Different between obese and lean participants: #$P < 0.05$, ##$P < 0.01$, ###$P < 0.001$. $ANOVA two-way interaction.

Baseline comparison of obese vs. lean participants

In addition to higher body weight, BMI, body fat %, body FM, and lean body mass (**Table 1**), obese participants had higher subcutaneous, visceral, hepatic, and intramyocellular fat content as compared to lean participants (**Figure 2**).

Although both obese and lean participants were normoglycemic, with no difference in plasma glucose concentration between the groups, obese participants had three times higher fasting insulin concentration and $HOMA_{IR}$, indicating they were more insulin resistant (**Table 1**).

Effects of the exercise program in obese participants

In response to the exercise program, total body weight, BMI, and lean body mass did not change significantly. There was, however, a small but significant decrease in FM ($P = 0.03$) and body fat % ($P = 0.02$) (**Table 1**).

Abdominal fat distribution. Visceral fat content decreased ($P = 0.03$), whereas subcutaneous fat content remained unchanged (**Figure 2**).

Hepatic fat content. In the whole group of obese participants, hepatic fat content decreased ($P = 0.04$) (**Figure 2**). This change was primarily attributed to the decrease in hepatic fat content in the five participants (33%) with high hepatic fat content, in whom hepatic fat decreased by 40, 44, 64, 42, and 26%, respectively. At baseline, participants with high hepatic fat had higher visceral fat content ($69.4 \pm 6.2\,cm^2$) compared to participants with normal hepatic fat content ($47.3 \pm 7.5\,cm^2$) ($P = 0.04$).

In the whole group of obese participants, hepatic fat content was directly correlated with alanine aminotransferase concentrations (baseline: $R^2 = 0.56$; $P = 0.03$; post: $R^2 = 0.67$; $P = 0.008$). Only in the participants with high hepatic fat, did the exercise-related decrease in alanine aminotransferase concentration reach significance (baseline: 47 ± 8; post: 41 ± 8 U/l; $P = 0.04$).

Intramyocellular fat content. The exercise program did not have any effect on IMCL (**Figure 2**).

Insulin resistance. Fasting plasma glucose concentration did not change in response to the exercise program. Fasting plasma insulin concentration and $HOMA_{IR}$ decreased in all obese participants ($P = 0.0001$ and $P = 0.0007$, respectively), indicating decreased insulin resistance (**Table 1**). The decrease in $HOMA_{IR}$ was a result of the decrease in insulin concentration. Therefore, we chose to use fasting insulin concentration to represent insulin resistance in all correlation analyses.

Fasting insulin concentration was directly correlated with visceral fat content (baseline: $R^2 = 0.47$; $P = 0.005$; post: $R^2 = 0.52$; $P = 0.003$), and the reduction in insulin concentration correlated with the decrease in visceral fat content ($R^2 = 0.40$; $P = 0.01$).

In addition, fasting insulin concentration correlated with hepatic fat content (both at baseline and postexercise: $R^2 = 0.31$; $P = 0.03$). Participants with high hepatic fat content had higher insulin concentrations (baseline: 33.03 ± 3.40; post: $27.15 \pm 3.84\,\mu U/ml$) compared to participants with normal hepatic fat content (baseline: 16.20 ± 2.03; post: $13.75 \pm 1.80\,\mu U/ml$) (baseline: $P = 0.0006$; post: $P = 0.003$). Insulin concentration did not correlate with IMCL.

Effects of the exercise program in lean participants

Except for a small but significant weight increase ($P = 0.04$), accounted for by an increase in lean body mass ($P = 0.01$), FM, body fat %, and visceral, subcutaneous, hepatic, and intramyocellular fat content did not change significantly in response to the exercise program (**Table 1** and **Figure 2**). In addition, plasma glucose, insulin, and alanine aminotransferase concentrations did not change significantly. $HOMA_{IR}$ decreased in 10/14 of the lean participants, whereas it increased in 4. This points to an improvement in insulin sensitivity although the overall decrease in $HOMA_{IR}$ did not reach significance ($P = 0.09$).

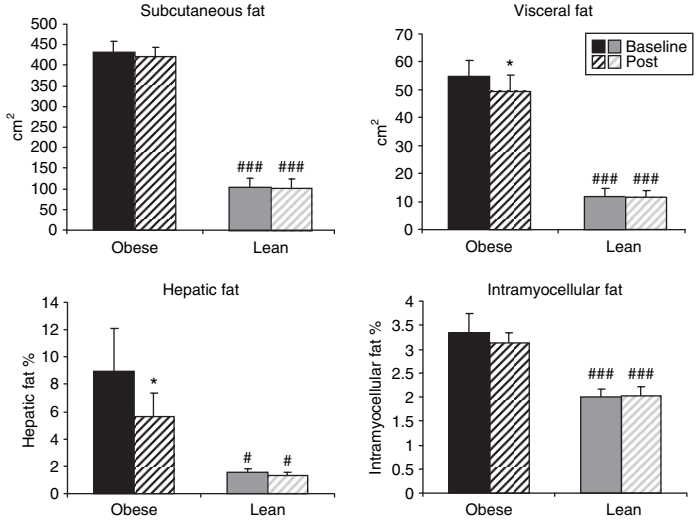

Figure 2 Subcutaneous, visceral, hepatic, and intramyocellular fat content at baseline and postexercise program (mean ± s.e.). Different from baseline within each group: $^*P < 0.05$. Different between obese and lean participants: $^{\#}P < 0.05$, $^{\#\#\#}P < 0.001$.

DISCUSSION

The present study demonstrates that a 12-week aerobic exercise program (four times 30 min per week) without weight loss or change in BMI, results in increased cardiovascular fitness, reduced visceral and hepatic fat content, and decreased insulin resistance in sedentary, postpubertal, obese, Hispanic adolescents. Subcutaneous and intramyocellular fat content remained unchanged.

Both obese and lean adolescents complied very well with the designed program with no difference between the groups. As a result, both groups increased their fitness to the same extent in response to the program.

In sedentary lean participants, the exercise program did not significantly change body composition (total FM, percent body fat, and subcutaneous, visceral, hepatic, and intramyocellular fat content) except for a small but significant increase in body weight due to an increase in lean body mass. Although insulin resistance measured by $HOMA_{IR}$ decreased in 10/14 lean participants, the change in the whole lean group did not reach significance. In a recent review, Shaibi *et al.* (28) discussed that increased cardiovascular fitness might have an independent effect on decreasing insulin resistance, especially in boys (28). Thus, the increased fitness is an important result of the exercise program in these sedentary lean adolescents.

In obese participants, in addition to increased fitness, the exercise program (without weight loss) resulted in a substantial decrease in hepatic fat, particularly in adolescents with high hepatic fat content. The high prevalence of fatty liver in obese adolescents (3,4) and its potential to progress to liver inflammation, fibrosis, and cirrhosis (nonalcoholic fatty liver disease) (29) is of great concern. Our results indicate that aerobic exercise might be an effective way to counteract the development of this harmful disease. To our knowledge, these are the first data on the effect of an exercise program (without additional interventions) on hepatic fat content in children and adolescents. Only a couple of studies in adults have previously addressed this issue (30–32). Perseghin *et al.* (30) showed reduced prevalence of fatty liver in more as compared to less physically active individuals (30). In addition, Larson-Meyer *et al.* (31) found that 6-month caloric restriction with or without exercise decreased liver fat content. The findings of both studies (30,31) are in agreement with our results. In contrast, Devries *et al.* (32) reported no effects on hepatic fat content and insulin sensitivity in response to a 12 wk aerobic exercise program with gradual increase from light-to-moderate intensity. The intensity of the exercise program in the Devries study (32) might have been insufficient to affect liver fat content.

Intramyocellular fat content remained unchanged in response to the exercise program despite decreased insulin resistance. In adults, reports on the relationship between intramyocellular fat content and insulin resistance are inconclusive (33). In children and adolescents, a direct correlation has been reported between insulin resistance and intramyocellular fat (34–36). We did not observe any correlation between insulin resistance and intramyocellular fat content. However, intramyocellular fat content was significantly higher (baseline 68%; post 53%) in the insulin-resistant obese as compared with the insulin-sensitive lean participants. Kelley and Mandarino described that a failure to increase lipid oxidation during fasting leads to intramyocellular fat deposition in obese individuals, subsequently contributing to patterns of insulin resistance (37). In agreement with our results, Bruce *et al.* (38) reported decreased insulin resistance despite unchanged intramyocellular fat content after exercise training in obese adults. A possible explanation for this paradox is that exercise increases the oxidative capacity in the muscles and intramyocellular lipid is used as a fuel source (38,39).

Several investigators have measured the effect of aerobic exercise programs on insulin resistance and body composition in children. Nassis *et al.* (10) reported that a 12-week aerobic exercise program (3 × 40 min/week; Average exercise intensity: HR 161 ± 2 beats/min) without weight loss, decreased insulin resistance in sedentary overweight and obese girls (9–15 years). Similarly, Bell *et al.* (11) reported that an 8-week combined aerobic and resistance exercise program (3 × 60 min/week) without weight loss resulted in decreased insulin resistance and reduced waist circumference in sedentary obese children and adolescents (9–16 years). Although both studies (10,11) differed from ours with regard to the pubertal stage of the participants, the effects of exercise on insulin resistance were similar to our results. However, diets preceding the measurements and physical activity outside the program were not controlled, and abdominal, hepatic, and intramyocellular fat content were not measured. Finally, the exercise program by Bell *et al.* (11) included both aerobic and resistance exercise, thus, precluding evaluation of the individual effects of these two different types of exercise.

With regard to body composition, Gutin and Owens (12) observed that in 7–11-year-old obese children, a 12-week aerobic exercise program (~4 × 40 min/week at HR ~157 beats/min) attenuated growth-related increase in visceral fat accumulation in comparison to a nonexercising control group. In another study in obese adolescents (13–16 years), Gutin *et al.* (13) demonstrated that an 8-month program of physical activity (>2×/week at moderate or vigorous intensity) combined with lifestyle education (1-h sessions every 2 weeks) decreased visceral fat content. Both study results are in line with our findings. Our results indicate that exercise without weight loss results in decreased visceral but not subcutaneous fat content. We postulate that this is due to the fact that visceral fat is more metabolically active (40).

In the obese participants, fasting insulin concentration was strongly and consistently correlated with visceral fat content but not with body weight, BMI, body fat %, or total, subcutaneous, or intramyocellular fat content. In addition, the decrease in visceral fat content resulting from the exercise program was significantly correlated with the decrease in insulin concentration. The results from other published studies investigating the relationship between abdominal fat distribution and insulin sensitivity in children and adolescents are conflicting (36,41–44). Some studies have found a relationship between insulin sensitivity and visceral fat (36,43), whereas others have reported a relation between insulin sensitivity and subcutaneous fat (41,42),

or with both visceral and subcutaneous fat deposits (44). One possible reason for these inconsistencies might be differences in pubertal stage of the participants. However, the mechanism for the contribution from visceral and subcutaneous fat to insulin resistance is still an unresolved issue. It has been speculated that defective differentiation of subcutaneous fat and/or increased inflammation in visceral fat might be involved (40,45).

We also demonstrated that in the whole group of obese participants, fasting insulin concentration was directly correlated with hepatic fat content. Further, the obese participants with high hepatic fat were significantly more insulin resistant than those with normal hepatic fat content. This is in agreement with reports by Burgert *et al.*(3) and Deivanayagam *et al.* (46). In addition, the latter group (46) observed that obese adolescents with hepatic steatosis had higher visceral fat content compared with those without hepatic steatosis. Overall, our data indicate a metabolic interaction between abdominal fat, specifically visceral and hepatic fat, and insulin resistance.

In summary, our results demonstrate that sedentary, postpubertal, obese and lean Hispanic adolescents comply very well with a controlled 12-week aerobic exercise program (4 × 30 min/week at a heart rate corresponding to ~85% of VO_2peak) without additional dietary and lifestyle advice, or weight loss. In both lean and obese participants, the program resulted in increased fitness. In addition, in obese participants, the program resulted in decreased visceral and hepatic fat accumulation, and decreased insulin resistance. More research is warranted to investigate the promising potential of exercise to prevent and treat nonalcoholic fatty liver disease in obese adolescents.

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DISCLOSURE

The authors declared no conflict of interest.

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