# Cardiovascular Fitness and the Metabolic Syndrome in Overweight Latino Youths

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**ABSTRACT**

SHAIBI, G. Q., M. L. CRUZ, G. D. C. BALL, M. J. WEIGENSBERG, H. A. KOBAISSI, G. J. SALEM, and M. I. GORAN. Cardiovascular Fitness and the Metabolic Syndrome in Overweight Latino Youths. *Med. Sci. Sports Exerc.*, Vol. 37, No. 6, pp. 922–928, 2005. **Purpose:** To determine whether cardiovascular fitness ($\dot{V}O_{2max}$) is associated with the metabolic syndrome and its individual features in overweight Latino youths. **Methods:** A total of 163 overweight Latino boys and girls (body mass index (BMI) percentile = 97.0 ± 3.1; age = 11.2 ± 1.7 yr) with a family history of Type 2 diabetes participated in this investigation. The metabolic syndrome was defined as having three or more of the following risk factors: abdominal obesity, high blood pressure, low HDL-cholesterol, high triglycerides, and impaired glucose tolerance. $\dot{V}O_{2max}$ was determined by a progressive treadmill test to exhaustion, and body composition was assessed using dual energy x-ray absorptiometry. **Results:** $\dot{V}O_{2max}$ was not correlated with any individual risk factor of the metabolic syndrome after adjusting for gender, age, and body composition in partial analysis. Furthermore, ANCOVA revealed that children with zero, one, two, or three or more risk factors did not differ in regards to fitness levels. **Conclusion:** $\dot{V}O_{2max}$ is not independently associated with the metabolic syndrome or any individual feature in overweight youths of Latino ethnicity after controlling for differences in confounding variables. **Key Words:** OBESITY, CHILDREN, $\dot{V}O_{2MAX}$, INSULIN RESISTANCE SYNDROME, PHYSICAL FITNESS, TYPE 2 DIABETES

The prevalence of overweight in youths has increased dramatically in recent years, especially among children of ethnic minority groups (26). Recent data suggest that among Latino children, the prevalence of overweight (body mass index (BMI) ≥ 95th percentile for age and gender) has approximately doubled in the past 10 yr, such that 23.4% of Latino youths ages 12–19 yr are overweight (23). Childhood obesity is a multisystem disorder with corresponding comorbidities including hypertension, dyslipidemia, impaired glucose tolerance, and Type 2 diabetes. Furthermore, we (8) and others (7) have recently shown that 30% of overweight youths exhibit a constellation of these cardiovascular disease and diabetes risk factors known as the metabolic syndrome. The metabolic syndrome, as defined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III), is the clustering of three or more of the following risk factors: elevated blood pressure, hypertriglyceridemia, low HDL cholesterol, abdominal obesity, and hyperglycemia (2). While the underlying pathophysiology linking the individual features of the metabolic syndrome is thought to be insulin resistance, studies in the adult population suggest that low levels of physical fitness may play an important mediating role.

Several cross-sectional studies in the adult population suggest that cardiovascular fitness ($\dot{V}O_{2max}$) is inversely associated with the metabolic syndrome. Lakka et al. (22) studied 1069 middle-aged men who participated in the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) and found that, after adjusting for age, those subjects in the lowest tertile for $\dot{V}O_{2max}$ were 6.4-fold more likely to have the metabolic syndrome compared with men in the highest tertile: This relationship remained significant even after adjusting for BMI. The authors concluded that poor cardiovascular fitness was not only associated with the metabolic syndrome, but could be considered a feature of the syndrome. Similarly, Kullo and colleagues (20) found that men in the lowest quartile for cardiovascular fitness had an age- and BMI-adjusted odds ratio of 5.67 for the presence of the metabolic syndrome compared with subjects in the highest fitness quartile. Although these cross-sectional studies used standard definitions of the metabolic syndrome, causality can only be inferred from prospective investigations.

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Submitted for publication August 2004.
Accepted for publication February 2005.

0195-9131/05/3706-0922/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1029/01.mss.0000170472.75214.53

Longitudinal results from the KIHD cohort suggest that poor cardiovascular fitness may predict the development of the metabolic syndrome. In 4-yr follow-up analysis, Laaksonen et al. (21) found that after adjusting for age and BMI, men with baseline $\dot{V}O_{2max}$ in the bottom tertile were two thirds as likely to develop the metabolic syndrome compared with those in the top tertile. To date, only one longitudinal investigation has examined the efficacy of aerobic exercise training for treatment of the metabolic syndrome. Katzmarzyk and colleagues (18) evaluated data from the HERITAGE Family Study and found that 20 wk of aerobic exercise training decreased the overall prevalence of the ATP III–defined metabolic syndrome in the cohort from 16.9 to 11.8%. Moreover, nearly one third of the participants ($N = 32$) who had the metabolic syndrome at baseline were no longer classified as having the metabolic syndrome after training. Collectively, the cross-sectional, longitudinal, and intervention studies support the notion that, in adults, cardiovascular fitness is a key correlate of the metabolic syndrome phenotype.

Little is known about the relationship between cardiovascular fitness and metabolic risk in children. Although obesity, insulin resistance/Type 2 diabetes, and the metabolic syndrome are clearly present and interrelated in younger populations, it is not clear how fitness may mediate these relationships. Thus, the objectives of the present study were 1) to investigate the associations between $\dot{V}O_{2max}$ and the individual features of the metabolic syndrome, and 2) to establish differences in $\dot{V}O_{2max}$ between children with and without the metabolic syndrome using the ATP III definition in overweight Latino youths.

## METHODS

**Sample.** The 163 children who participated in the present investigation are part of the University of Southern California (USC) SOLAR (Study of Latino Adolescents at Risk) Diabetes Project. The study is an ongoing longitudinal investigation to explore risk factors for the development of Type 2 diabetes in at-risk youths. For purposes of this article, the term Latino refers to children whose ethnic origins can be traced back to Spanish-speaking regions of Latin America including Mexico, Central America, and South America. Approximately 70% of the SOLAR children were of Mexican descent, with the remaining of Central American or mixed Mexican–Central American heritage. This group was selected for the SOLAR Diabetes Project because of the high rates of obesity, insulin resistance, and Type 2 diabetes in this population. Participants were recruited from the greater Los Angeles County through community health clinics, health fairs, and word of mouth, and were required to meet the following inclusion criteria at baseline: 1) Latino ethnicity (all four grandparents of Latino descent); 2) age 8–13 yr; 3) a family history of Type 2 diabetes (sibling, parent, or grandparent); and 4) age and gender BMI ≥ 85th percentile based on the standards of the Centers for Disease Control and Prevention. Children were excluded if they had a previous major illness, including Type 1 or 2 diabetes, took medications, or had a condition known to influence body composition, insulin action, or insulin secretion. This study was approved by the USC institutional review board. Written informed consent and assent were obtained from all parents and children before any testing procedures. Data from this cohort have been reported previously (4,8,11).

## PROTOCOL

**Outpatient screening visit.** Children arrived at the USC General Clinical Research Center (GCRC) in Los Angeles County Hospital at approximately 8:00 a.m. after an overnight fast. Physical maturation was assessed by a pediatrician according to the criteria of Marshall and Tanner (27). Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer, and weight was measured to the nearest 0.1 kg using a medical balance beam scale. Subjects ingested 1.75 g of oral glucose solution per kilogram of body weight (to a maximum of 75 g). Blood samples were taken via antecubital vein catheter for measurement of glucose before and 2 h after glucose load. Impaired glucose tolerance (IGT) was defined as a 2-h postchallenge plasma glucose value of at least 140 and less than 200 $mg \cdot dL^{-1}$ (1).

At least 7 d after the outpatient screening visit, children were admitted for an inpatient visit in the afternoon to the GCRC at the Los Angeles County Hospital, where they underwent a brief physical examination and completed body composition, anthropometry, and cardiovascular fitness measures. The following morning, blood was drawn after an overnight fast for analysis of plasma lipids.

**Anthropometry and blood pressure.** Height, weight, and waist circumference (at the umbilicus) were recorded to the nearest 0.1 cm, 0.1 kg, and 0.1 cm, respectively. Sitting blood pressure was measured on two separate days using the right arm after the subject had rested quietly for 5 min. On each occasion, three readings of blood pressure were obtained, and the average was recorded (3).

**Body composition.** Total body composition (fat mass and FFM, i.e., soft lean tissue mass) was determined by a whole-body dual-energy x-ray absorptiometry (DEXA) scan using a Hologic QDR 4500W (Bedford, MA).

**Cardiovascular fitness.** Children completed an all-out progressive treadmill test to exhaustion as previously described (28). After being familiarized with the equipment, the children practiced walking on the motorized treadmill until they were able to walk without holding the railings. Once comfortable, the children walked for 4 min at 0% grade and 4 $km \cdot h^{-1}$, after which the treadmill grade was raised to 10%. Each ensuing work level lasted 2 min, during which the grade was increased by 2.5%. The speed remained constant until a 22.5% grade was reached; beyond that point, speed increased by 0.6 $km \cdot h^{-1}$ every 2 min until the subject reached exhaustion. Respiratory gasses were collected and measured via open circuit spirometry and analyzed on a MedGraphics $CardiO_2$ combined exercise system (St. Paul, MN). HR was measured continuously throughout the test using a Polar Vantage XL HR monitor (Port Washington, NY). $\dot{V}O_{2max}$ was defined as the highest oxygen uptake attained over the final 1.5 min of the protocol. Criteria for $\dot{V}O_{2max}$ included the achievement of at least two of the following: HR $\geq$ 195 bpm, RER $>$ 1.0, and a plateau in oxygen consumption defined as an increase of oxygen uptake less than 2 $mL \cdot kg^{-1} \cdot min^{-1}$ with a concomitant increase in workload.

**Data expression.** Cardiovascular fitness is a general term often used to characterize an individual's performance during a standardized exercise test or protocol. The maximal amount of oxygen consumed relative to some index of body size (e.g., $\dot{V}O_2$ divided by total body mass) is typically the primary outcome measure. Much debate exists surrounding appropriate units of expression when comparing individuals of varying body composition, stature, and age. We chose to express cardiovascular fitness in absolute terms ($L \cdot min^{-1}$), and statistically adjusted for measures of body composition, gender, and age. This was done despite the fact that $\dot{V}O_{2max}$ is traditionally expressed relative to total body mass. We have previously observed that the latter methods of data expression may lead to spurious conclusions regarding fitness and measures of disease risk in overweight Latino youths because of the strong relationship between body mass and disease (4). By controlling for body composition in the statistical model, we obtain information regarding the relationship between fitness and the metabolic syndrome without adding a confounding term to the dependent variable. For the purposes of comparing results with previous publications, we also present results of $\dot{V}O_{2max}$ expressed as the ratio of the volume of oxygen consumed per minute relative to total body mass ($mL \cdot kg^{-1} \cdot min^{-1}$) and total fat-free mass (FFM) ($mL \cdot kg\ FFM^{-1} \cdot min^{-1}$). For clarity's sake, we refer to the three methods of $\dot{V}O_{2max}$ expression as 1) $\dot{V}O_{2max}$ adjusted ($\dot{V}O_{2max}$-A), where total fat mass, total lean tissue mass, gender, and age are statistically adjusted for; 2) $\dot{V}O_{2max}$ divided by body mass ($\dot{V}O_{2max}$-BM); and 3) $\dot{V}O_{2max}$ divided by FFM ($\dot{V}O_{2max}$-FFM).

**Definition of the metabolic syndrome.** According to the ATP III, the presence of the metabolic syndrome is defined as having at least three of the following abnormalities: abdominal obesity measured via waist circumference, triglycerides $\geq$150 $mg \cdot dL^{-1}$, HDL-cholesterol $<$40 $mg \cdot dL^{-1}$ in men and $<$50 $mg \cdot dL^{-1}$ in women, blood pressure $\geq$130/85 mm Hg, and a serum fasting glucose $\geq$110 $mg \cdot dL^{-1}$. Because there is no current definition of the metabolic syndrome in children, we (8) have recently defined the metabolic syndrome in this pediatric cohort as having at least three of the following features: abdominal obesity measured (waist circumference of at least 90th percentile for age, gender, and Latino ethnicity from National Health and Nutrition Examination Survey III (NHANES III) data provided by Fernandez et al. (unpublished data, 2003), hypertriglyceridemia (triglycerides $\geq$90th percentile for age and gender) (15), low HDL-cholesterol (HDL-cholesterol $\leq$10th percentile for age and gender) (15), elevated blood pressure (systolic or diastolic blood pressure $>$90th percentile adjusted for height, age, and gender) (3), and impaired glucose tolerance (1).

**Assays.** Blood samples taken during the oral glucose tolerance test were separated for plasma and immediately transported on ice to the Los Angeles County–USC Medical Center Core Laboratory, where glucose was analyzed with a Dimension clinical chemistry system using the *in vitro* hexokinase method (Dade Behring, Deerfield, IL). During the inpatient visit, fasting blood samples were taken and centrifuged immediately to obtain plasma, and aliquots were frozen at −70ºC until assayed. Fasting triglycerides and HDL-cholesterol were measured using the Vitro chemistry DT slides (Johnson and Johnson Clinical Diagnostics Inc., Rochester, NY).

**Statistics.** Gender differences in physical, metabolic, and fitness characteristics were examined using independent sample *t*-tests. Variables that were not normally distributed were log transformed ($\dot{V}O_{2max}$, $\dot{V}O_{2max}$-BM, total fat mass, total FFM, percentage of fat, systolic blood pressure, diastolic blood pressure, waist circumference, triglycerides, HDL-cholesterol, and fasting glucose). Untransformed data are presented for ease of interpretation. Associations between $\dot{V}O_{2max}$ and the individual features of the metabolic syndrome were explored using partial correlation analysis. Variables known to influence either $\dot{V}O_{2max}$ or the metabolic syndrome (gender, age, total fat mass, and FFM) were adjusted in the partial analysis ($\dot{V}O_{2max}$-A). For comparison purposes, we also present simple Pearson correlations with fitness expressed relative to total body mass ($\dot{V}O_{2max}$-BM) and FFM ($\dot{V}O_{2max}$-FFM). Group differences in $\dot{V}O_{2max}$ across children with zero, one, two, or three or more features of the metabolic syndrome were established by using ANCOVA adjusting for gender, age, total fat mass, and FFM. Differences relative to total body mass and FFM were also explored by using ANOVA. All analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, IL) with a Type I error set at $P < 0.05$.

## RESULTS

Descriptive characteristics of the subjects separated by gender are presented in Table 1. Girls were more physically mature than boys and had higher total fat mass and percentage of body fat and lower diastolic blood pressure and fasting glucose compared with boys (all $P$ values $< 0.05$). Additionally, girls had lower $\dot{V}O_{2max}$ than boys regardless of whether data were expressed in absolute terms, relative to total body mass, or relative to FFM.

**Cardiovascular fitness and the components of the metabolic syndrome.** Partial Pearson correlation analysis revealed that after adjusting for gender, age, total fat mass, and FFM, no feature of the metabolic syndrome was significantly associated with $\dot{V}O_{2max}$. Given the potential for gender and maturation to influence fitness and the features of the metabolic syndrome, subanalyses were run separately in boys and girls (adjusting for maturation) as well as separately in pre-/early pubertal youths (Tanner stages 1 and 2) and mid-/postpubertal youths (Tanner stages 3–5) (adjusting for gender). No significant associations were observed in either case. Simple correlation analysis revealed

TABLE 1. Physical, metabolic, and fitness characteristics of participants.

| | Boys (*N* = 91) Mean ± SD (Range) | Girls (*N* = 72) Mean ± SD (Range) | Total (*N* = 163) Mean ± SD | 95% CI of the Difference |
|---|---|---|---|---|
| Age (yr) | 11.3 ± 1.6 (7.9–13.9) | 11.1 ± 1.8 (8.0–14.5) | 11.2 ± 1.7 | −0.3 to 0.7 |
| Height (cm) | 150.2 ± 10.9 (122.1–175.8) | 149.4 ± 11.5 (128.05–170.5) | 149.9 ± 11.1 | −2.6 to 4.4 |
| Weight (kg) | 62.3 ± 16.8 (29.3–115.0) | 65.3 ± 20.7 (35.9–117.4) | 64.0 ± 18.6 | −8.4 to 3.6 |
| Tanner stage (1–5) | 1.84 ± 1.2** (1–5) | 2.9 ± 1.4 (1–5) | 2.3 ± 1.4 | −1.5 to −0.7 |
| BMI ($kg \cdot m^{-2}$) | 27.4 ± 4.6 (19.7–45.0) | 28.6 ± 5.6 (20.0–44.2) | 27.9 ± 5.0 | −2.7 to 0.5 |
| BMI percentile | 96.9 ± 3.2 (86.4–99.8) | 97.0 ± 3.0 (88.9–99.9) | 97.0 ± 3.1 | −1.1 to 0.9 |
| Waist circumference (cm) | 87.7 ± 11.6 (65.9–123.5) | 87.0 ± 14.5 (52.5–125.5) | 87.4 ± 12.9 | −3.5 to 4.8 |
| Total fat mass (kg) | 23.0 ± 8.4 (7.6–53.3) | 26.2 ± 10.6 (10.9–55.5) | 24.4 ± 9.5 | −62.4 to −0.2 |
| Total fat-free mass (kg) | 37.5 ± 9.8 (21.2–69.7) | 36.7 ± 10.1 (20.8–61.7) | 37.2 ± 9.9 | −22.8 to 39.1 |
| Total percent fat | 36.5 ± 6.6** (11.2–52.1) | 39.8 ± 5.4 (25.9–49.3) | 38.0 ± 6.3 | −5.1 to −1.3 |
| Fasting glucose ($mg \cdot dL^{-1}$) | 93.2 ± 6.6* (79.0–111.0) | 90.4 ± 7.4 (76.0–119.0) | 92.0 ± 7.1 | 0.6 to 5.0 |
| 2-h glucose ($mg \cdot dL^{-1}$) | 125.3 ± 16.2 (93.0–166.0) | 128.3 ± 17.7 (81.0–174.0) | 126.7 ± 16.9 | −8.3 to 2.3 |
| Systolic blood pressure (mm Hg) | 110.3 ± 10.1 (88.0–147.0) | 109.3 ± 9.8 (85–131) | 109.9 ± 9.9 | −2.0 to 4.2 |
| Diastolic blood pressure (mm Hg) | 64.5 ± 6.1** (51.0–83.5) | 61.3 ± 5.4 (50.0–74.0) | 63.1 ± 6.0 | 1.3 to 4.9 |
| HDL-cholesterol ($mg \cdot dL^{-1}$) | 36.6 ± 9.2 (23.0–85.0) | 36.7 ± 7.5 (22.0–60.0) | 36.7 ± 8.5 | −2.8 to 2.5 |
| Triglycerides ($mg \cdot dL^{-1}$) | 115.7 ± 62.0 (32.0–368.0) | 102.6 ± 44.3 (38–271) | 109.9 ± 55.1 | −3.4 to 29.5 |
| $\dot{V}O_{2max}$ ($L \cdot min^{-1}$) | 2.3 ± 0.6* (1.3–4.3) | 2.0 ± 0.5 (1.1–3.2) | 2.2 ± 0.6 | 0.1 to 0.4 |
| $\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) | 37.3 ± 6.9** (20.7–61.0) | 32.2 ± 5.3 (22.9–46.6) | 35.0 ± 6.7 | 3.1 to 7.0 |
| $\dot{V}O_{2max}$ ($mL \cdot kg\ FFM^{-1} \cdot min^{-1}$) | 61.6 ± 6.4** (38.4–76.6) | 56.2 ± 6.0 (44.8–72.1) | 59.3 ± 6.7 | 3.5 to 7.3 |
| Maximum HR (bpm) | 202 ± 8 (177–221) | 200 ±8 (180–216) | 201 ± 8 | −0.3 to 4.4 |
| Maximum RER | 1.11 ± 0.08 (0.94–1.36) | 1.13 ± 0.07 (0.95–1.30) | 1.12 ± 0.07 | −0.04 to 0.01 |

CI, confidence interval, BMI, body mass index. Values are means ± SD. For gender: * $P < 0.01$; ** $P < 0.001$.

that $\dot{V}O_{2max}$-BM and $\dot{V}O_{2max}$-FFM were significantly and inversely associated with waist circumference, systolic blood pressure, and triglycerides, and that there were positive associations between $\dot{V}O_{2max}$–BM and $\dot{V}O_{2max}$-FFM and HDL (Table 2).

**Cardiovascular fitness and the metabolic syndrome.** Figure 1A illustrates the means for $\dot{V}O_{2max}$-A (adjusted for gender, age, total fat mass, and FFM) in children grouped by the number of features of the metabolic syndrome. No overall effect of fitness was found across groups. In comparison, $\dot{V}O_{2max}$-BM and $\dot{V}O_{2max}$-FFM both decreased as the number of features of the metabolic syndrome increased ($P < 0.001$ and $P < 0.002$, overall $P$ values for the metabolic syndrome, respectively). For $\dot{V}O_{2max}$-BM, pairwise comparisons revealed that children with no features of the metabolic syndrome had significantly higher $\dot{V}O_{2max}$-BM than those with one, two, or three or more features ($P < 0.05$, $P < 0.001$, and $P < 0.001$, respectively). Additionally, participants with one feature were more fit than those with either two or three features ($P < 0.05$ and $P < 0.01$, respectively); no significant difference was found between those with either two or three features (Fig. 1B). For $\dot{V}O_{2max}$-FFM, pairwise comparisons revealed that children with no features of the metabolic syndrome had significantly higher $\dot{V}O_{2max}$-FFM than those with two or three or more features ($P < 0.05$ and $P < 0.01$, respectively) (Fig. 1C).

## DISCUSSION

Despite mounting evidence in the adult population demonstrating an inverse relationship between cardiovascular fitness and the metabolic syndrome, little is known regarding these associations in children. To our knowledge, this is the first study to investigate the relationship between a direct measure of $\dot{V}O_{2max}$ and the metabolic syndrome in children. We found that after adjusting for gender, age, total fat mass, and FFM, $\dot{V}O_{2max}$ was not independently correlated with any feature of the metabolic syndrome. Moreover, no fitness differences were found across children with zero, one, two, or three or more features.

It appears that in our population, the association between cardiovascular fitness and metabolic health is a function of body composition. We have recently reported, in a smaller sample of the same cohort, that $\dot{V}O_{2max}$ expressed relative to total body mass ($\dot{V}O_{2max}$-BM) is positively related to insulin sensitivity measured via the frequently sampled intravenous glucose tolerance test. However, once body composition was statistically accounted for, the two were no longer

TABLE 2. Pearson partial correlations and simple Pearson correlations (partial analysis adjusted for gender, age, total fat mass, and total FFM).

| | Partial Correlation Log $\dot{V}O_{2max}$-A ($L \cdot min^{-1}$) | Simple Correlation Log $\dot{V}O_{2max}$-BM ($mL \cdot kg^{-1} \cdot min^{-1}$) | Simple Correlation $\dot{V}O_{2max}$-FFM ($mL \cdot kg \cdot FFM^{-1} \cdot min^{-1}$) |
|---|---|---|---|
| Log waist circumference | 0.05, $P = 0.576$ | **−0.53, $P < 0.001$** | **−0.42, $P < 0.001$** |
| Log fasting glucose | 0.05, $P = 0.518$ | 0.07, $P = 0.348$ | 0.12, $P = 0.129$ |
| 2-h glucose | −0.04, $P = 0.585$ | −0.07, $P = 0.403$ | −0.07, $P = 0.415$ |
| Log systolic blood pressure | −0.11, $P = 0.152$ | **−0.33, $P < 0.001$** | **−0.29, $P < 0.001$** |
| Log diastolic blood pressure | −0.08, $P = 0.351$ | −0.12, $P = 0.136$ | −0.07, $P = 0.398$ |
| Log HDL | 0.07, $P = 0.351$ | **0.33, $P = 0.001$** | **0.25, $P = 0.001$** |
| Log triglycerides | −0.07, $P = 0.360$ | **−0.17, $P = 0.027$** | **−0.19, $P = 0.014$** |

Significant values in bold. $\dot{V}O_{2max}$-A, $\dot{V}O_{2max}$ statistically adjusted for gender, age, and fat-free mass, and total fat mass; $\dot{V}O_{2max}$-TBM, $\dot{V}O_{2max}$ divided by total body mass in kilograms; $\dot{V}O_{2max}$-FFM, $\dot{V}O_{2max}$ divided by total fat-free mass in kilograms.

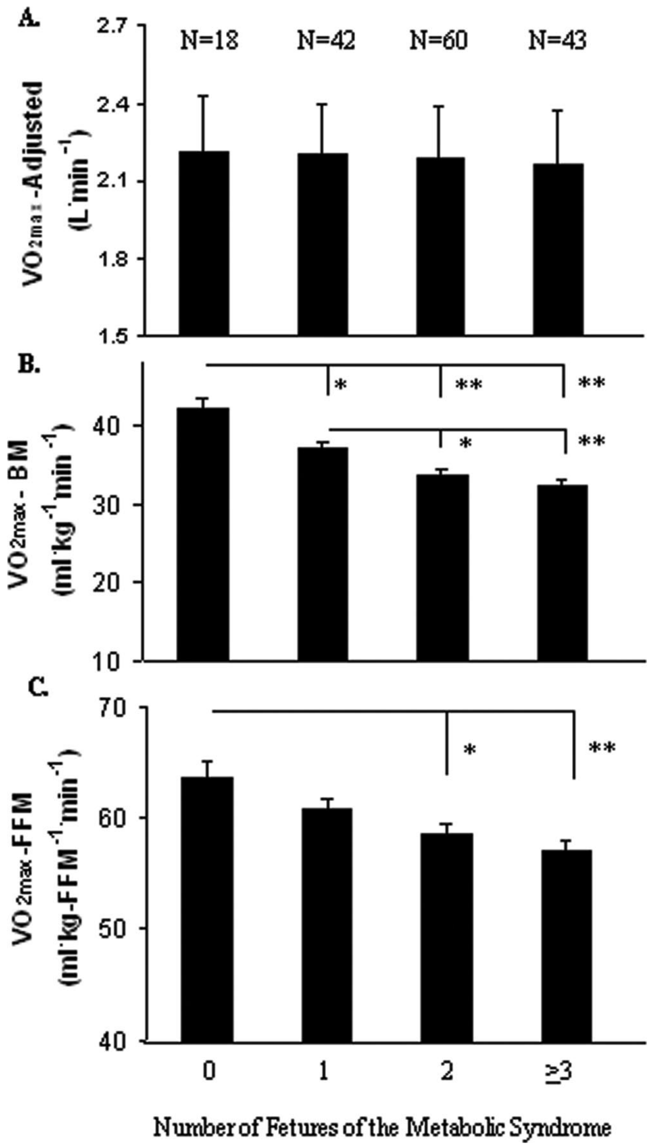


**FIGURE 1—Fitness and the number of features of the metabolic syndrome. A. Adjusted least square means ± SEM of $\dot{V}O_{2max}$-A (adjusted for gender, age, total fat mass, and fat-free mass). B. Mean ± SEM of $\dot{V}O_{2max}$-BM (divided by total body mass). C. Mean ± SEM of $\dot{V}O_{2max}$-FFM (divided by fat-free mass). * $P < 0.05$, ** $P < 0.01$.**

significantly correlated (4). This suggests that the relationship between cardiovascular fitness and metabolic health is not independent of, but rather mediated through, body composition, that is, body fat.

In adults, higher fitness levels are associated with reduced risk of cardiovascular disease (9), Type 2 diabetes (29), the metabolic syndrome (22), and all-cause mortality (5). Moreover, these associations appear to be independent of adiposity (30). One explanation of the different findings in children is that physical fitness in adults is a modifiable construct that, when improved, leads to positive health outcomes; the same has yet to be confirmed in children (24). In adults, aerobic exercise training results in specific physiologic adaptations in skeletal muscle that in turn lead to improvements in $\dot{V}O_{2max}$. These physiologic adaptations, which are thought to provide the protective mechanism between exercise training and metabolic health, include increased mitochondrial volume and density, increased substrate use, and increased capillarization (16), as well as adaptations that do not directly improve fitness, such as enhanced insulin sensitivity (19). Although children can improve cardiovascular fitness levels, albeit to a lesser degree than adults, the exercise-induced health-promoting adaptations may not be comparable. Consequently, factors other than fitness such as body composition (10) and insulin sensitivity (8) may be the primary determinants of physiologic health in the pediatric population.

In addition to physiologic differences between children and adults, study differences in data expression and interpretation may partially explain our findings. Reports in the adult population have either used indirect measures of $\dot{V}O_{2max}$ (20,31) or have inappropriately controlled for body composition in their analysis (20–22). Several investigations have expressed cardiovascular fitness relative to total body mass while simultaneously adjusting for BMI (a global measure of adiposity) in their statistical procedures. Although conceptually acceptable, statistically this approach is problematic in that kilograms of body mass is used to determine both the dependent variable $\dot{V}O_{2max}$ (mL·kg$^{-1}$·min$^{-1}$) as well as the controlling variable BMI (kg·m$^{-2}$). When this analysis is implemented in our data set, the decline in fitness with the increased clustering of features of the metabolic syndrome observed in Figure 1B approaches significance ($P = 0.08$ for main effect of the metabolic syndrome on fitness). Although our data set is smaller in number and younger, the relationship between fitness and the metabolic syndrome may represent an artifact of data expression and analysis rather than an independent relationship.

Further support for a lack of association between fitness and disease risk during childhood are studies that have longitudinally examined the effects of specific exercise interventions on risk factors related to the metabolic syndrome in the pediatric population. Gutin and colleagues (12) found that 8 months of physical training and lifestyle education in 13–16-yr-old boys and girls significantly reduced visceral adipose tissue (VAT), a correlate of waist circumference, compared with those who engaged in lifestyle education alone. Although simple correlations between change in fitness (measured as $\dot{V}O_2$ relative to total body mass at a HR of 170 bpm) and change in VAT as a result of the intervention were inversely related, this may have been a reflection of a decrease in overall adiposity rather than an independent effect of fitness on VAT. In follow-up analyses from the same cohort, Kang et al. (17) found that participants who engaged in high-intensity physical training had greater improvements in cardiovascular disease risk markers compared with those who received only lifestyle education. These included significant decreases in diastolic blood pressure and triglycerides, both of which are components of the metabolic syndrome. However, unlike the previous analysis, these changes in scores were not significantly related to changes in fitness. The authors postulated that improvements in blood pressure as a result of physical training might be mediated by exercise-induced reductions in adiposity. Based on the current findings and those from other reports (13,14), it appears that cardiovascular fitness does not wield a unique role on the features associated with the metabolic syndrome.

The strengths of our study include a direct measure of $\dot{V}O_{2max}$, a large sample size, objective definitions and cutoffs for the metabolic syndrome based on current population-specific guidelines, and accurate estimates of body composition by DEXA. We acknowledge several limitations that may hinder the generalizability of our findings. First, our population consisted of overweight Latino youths with a positive family history of Type 2 diabetes only. Clearly, this group is at increased risk of early cardiovascular disease and Type 2 diabetes, as is evident by the large proportion with the metabolic syndrome (8) as well as other risk factors including hypertension (25). The relationship between fitness and the metabolic syndrome in youths from different ethnicities and/or a wider range of body composition has yet to be determined. It is known, however, that nonoverweight children do not share similar patterns of the metabolic syndrome as their overweight peers (7), thus limiting any potential relationship with fitness. Second, given that $\dot{V}O_{2max}$ has both a strong genetic and familial component (6), a potential lack of variance due to homogeneity (Latino, overweight, and positive family history of diabetes) in our population compared with that in the general population may limit the amount of individual difference within our sample. Third, in the present analysis, only children who reached objective criteria for $\dot{V}O_{2max}$ were included. It has been argued that because a substantial proportion of youths fail to meet objective criteria, those studies that use maximal criteria for data analysis may bias the population in favor of lighter youths (12). Approximately 16% of our population did not achieve maximal criteria, yet no differences were found in metabolic measures when they were compared with children who were able to reach maximum (data not shown). Given that $\dot{V}O_{2max}$ is considered the single best physiologic indicator of oxygen transport and use and represents the functional limits of the oxygen delivery chain, we chose to employ this measure of fitness rather than use a less accurate estimation from a submaximal test. Last, incorporating complementary measures of overall fitness such as strength or power could provide a more comprehensive understanding of the relationship between fitness and metabolic health in our population.

In summary, these data suggest that after statistically accounting for differences in body composition, $\dot{V}O_{2max}$ is not independently associated with any feature of the metabolic syndrome in overweight Latino youths with a family history of Type 2 diabetes. Furthermore, after adjusting for confounding variables, $\dot{V}O_{2max}$ is not lower in children with a clustering of features compared with those with no features. Longitudinal and intervention studies are necessary to determine whether alterations in cardiovascular fitness (independent of changes in body composition) over time mediate the relationship between adiposity and disease risk in this population.

The authors are grateful to the project coordinator, Quintilia Avila, and to the nurses and nutrition staff at the USC-GCRC. Additionally, they express their gratitude to the children and their families for making this study possible. This work was supported by National Institutes of Health grant R01 DK 59211 and by GCRC, National Center for Research Resources, grant M01 RR 00043.

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