



# Aerobic physical fitness in relation to blood lipids and fasting glycaemia in adolescents: Influence of weight status

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## KEYWORDS

Adolescence;  
Aerobic fitness;  
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Cardiovascular prevention

**Abstract** *Background and aims:* We explored the associations between aerobic physical fitness with blood lipids and a composite index of blood lipids and fasting glycaemia in adolescents, analysing possible interactions with weight status.

*Methods and results:* Body mass index and aerobic physical fitness was measured in 2090 adolescents (1034 males and 1056 females) 13–18.5 years by using the 20-m shuttle run test. Plasma glucose, total, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, triglycerides, apolipoprotein (apo) A-I, apo B-100 and lipoprotein(a) [Lp(a)] were measured in 460 of the 2090 subjects. After adjustment for confounding factors, a continuously distributed summary score for blood lipids and fasting glycaemia was significantly related to aerobic fitness in males ( $P = 0.018$ ) and females ( $P = 0.045$ , from the 2nd to the 4th quartile of aerobic fitness). After adjustment for gender, age, sexual maturation and economic status, aerobic fitness was related to the composite index of blood lipids and glycaemia in both overweight and non-overweight adolescents ( $P < 0.05$ ). However, for the same level of aerobic fitness, the composite index of blood lipids and glycaemia was significantly higher in overweight adolescents ( $P = 0.001$ ). After setting the minimal

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aerobic fitness standards to present a healthy lipid profile, about 50% of males did not reach such values.

*Conclusion:* Our data suggest that both aerobic fitness and weight management are associated with a composite index of blood lipids and glycaemia in adolescents. Our study also provides the minimal levels of aerobic physical fitness associated with a favourable lipid profile in male adolescents, a new tool which should be adopted by schools as "aerobic fitness standards".

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## Introduction

Cardiovascular disease (CVD) is the leading cause of death in developed countries. Although the clinical manifestations of CVD occur in middle adulthood, pathological data have shown that atherosclerosis begins in childhood and adolescence [1–3]. Disturbed plasma lipid profile is an important cardiovascular risk factor, capable of inducing atherosclerotic development [4,5]. This has been early shown in adults, but holds also for children and adolescents. In fact, it has been recently demonstrated that plasma low density lipoprotein (LDL) cholesterol levels measured in childhood are a consistent predictor of carotid artery intima-media thickness in young adults who are still too young to experience coronary events [6,7]. These, and other findings [8,9], suggest that a primary goal in CVD prevention should be to keep a healthy plasma lipid profile since childhood [10,11].

Fasting glycaemia also deserves some attention. In fact, fasting glucose has been proposed as a marker of loss of beta cell function and insulin response [12], and there are noticeable similarities in the cardiovascular risk factor profile in subjects with impaired fasting glycaemia and in subjects with impaired glucose tolerance [13].

Regular aerobic physical activity leads to a significant cardiovascular risk reduction, by improving the plasma lipid profile [14,15]. Along the same line, increased aerobic physical fitness (which is in part the result of regular practice of aerobic physical activity) during adolescence has been associated not only with healthier blood lipids during these years [16,17], but also later in life [18]. Therefore, it seems reasonable to initiate regular aerobic physical activity in childhood in order to prevent metabolic risk and CVD in adulthood.

The previous studies did not analyse possible associations with a metabolic composite index, but with single blood lipids. Therefore, our first aim was to explore associations between aerobic physical fitness not only with single blood lipids, but also with a composite index of blood lipids and

fasting glycaemia in adolescents. Of note, only one study [19] analysed interactions between obesity measures and aerobic physical fitness in relation to a metabolic composite index, so we also tested a similar interaction in our population. Finally, to the best of our knowledge there are no studies providing minimal criterion standards of aerobic fitness in adolescents, associated with healthy metabolic outcomes. Therefore, we secondly aimed to set minimal criterion standards of aerobic fitness associated with a favourable lipid profile in adolescents.

## Methods

### Study population and design

This research was part of the AVENA study (Análisis y Valoración del Estado Nutricional en Adolescentes españoles [Assessment of Nutritional Status in Spanish Adolescents]), a population-based cross-sectional multicentric study of the aetiology and pathogenesis of obesity and related metabolic disorders during adolescence. The general methodology of the study, as well as the sample inclusion criteria, has been published elsewhere [20,21]. Briefly, 2851 Spanish adolescents (1354 males and 1497 females) aged 13–18.5 years were selected by means of a multiple-step, simple random sampling, taking into account the location (Madrid, Murcia, Granada, Santander and Zaragoza) and random assignment of the schools within each city. The inclusion criteria were: (1) not to be a consumer of alcohol, drugs or steroids, (2) not to have familial hypercholesterolaemia, (3) no history of CVD, (4) to be free of disease and medication at the time of the study, and (5) not to be pregnant. Socioeconomic status was assessed by examining paternal educational level and occupation. The subjects were accordingly classified into five categories: low, medium-low, medium, medium-high and high socioeconomic status.

Parents or supervisors were informed by letter about the nature and purpose of the study and they gave their written informed consent. The

study protocol was performed in accordance with the ethical standards laid down in the 1975 Declaration of Helsinki, and approved by the Review Committee for Research Involving Human Subjects of the Hospital Universitario Marqués de Valdecilla (Santander, Spain).

### Aerobic physical fitness assessment

Aerobic fitness was measured by the progressive 20-m shuttle run test [22]. This test was validated for use in children about 20 years ago [23,24]. Since then, it has been used in schools worldwide to assess aerobic physical fitness in children and adolescents. Two thousand ninety adolescents (1034 males and 1056 females) completed satisfactorily the test (characteristics of the study population are shown in Table 1). This test required subjects to run back and forth between two lines set 20 m apart. Running pace was determined by audio signals, emitted from a pre-recorded cassette tape, the initial velocity being 8.5 km/h, and increasing by 0.5 km/h every minute (step). The tape used was calibrated over 1 min duration and the tape machine was checked for accuracy prior to each test. Subjects were instructed to run in a straight line, to pivot upon completing a shuttle and to pace themselves in accordance with the time intervals. The test was finished when the subject failed to reach the end lines concurrent with the audio signals on two

consecutive occasions. The final score was computed as the number of steps completed (precision of 0.5 steps). A constant level of encouragement was given to participants throughout the test. Subjects were instructed to abstain from strenuous exercise in the 48 h preceding the test.

### Anthropometric assessment

For anthropometric measurements, subjects were barefoot and in their underwear. Weight was measured with a Seca scale (precision of 50 g), and height with incorporated stadiometer to the scale (precision of 1 mm). Trained interviewers asked the adolescents to classify themselves in one of the five Tanner stages of pubertal maturity. This standard staging describes breast and pubic hair development in girls and genital and pubic hair development in boys. The first Tanner stage corresponds to the prepubertal state; subjects classified in Tanner stage 5 are completely mature. Harmonization and standardization of anthropometric measurements used to assess body composition within the AVENA multicentre study were strictly controlled and have been previously published elsewhere [21,25]. To establish the overweight (including obesity) and non-overweight categories, we used the gender- and age-adjusted cut-off points provided by the International Obesity Task Force [26].

### Laboratory methods

#### Blood sampling

Blood was collected in 581 subjects 5 days before the 20-m shuttle run test. Four hundred and sixty (248 males and 212 females) out of the initial 581 subjects completed satisfactorily the aerobic fitness test. Blood collection was carried out between 8:00 and 9:00 a.m., and after an 8-h overnight fast. The subjects were selected randomly (according to age, gender, geographical location, and economic status) and were instructed to abstain from alcoholic beverages for at least 2 weeks before sampling, and to refrain from vigorous exercise during the 48 h preceding blood collection. Within 1 hour after collection, blood was centrifuged and aliquots of sera were sent refrigerated to a central laboratory (Clinical Biochemistry Service, Granada University Hospital), where all the clinical chemistry tests were performed within 24 h after collection.

#### Lipids, lipoproteins, and Lp(a)

Plasma glucose, total cholesterol, triglycerides and high density lipoprotein (HDL) cholesterol were

**Table 1** Physical characteristics and lipid profile of the study population

	Boys (n = 1034)	Girls (n = 1056)	P
Age (years)	15.4 (1.3)	15.4 (1.3)	NS
Weight (kg)	63.8 (12.9)	56.3 (9.6)	<0.001
Height (cm)	171.2 (8.5)	161.9 (6.2)	<0.001
BMI (kg/m <sup>2</sup> )	21.7 (3.5)	21.5 (3.3)	NS
Total cholesterol (mg/dl)	155.8 (26.0)	168.5 (26.4)	<0.001
Glucose (mg/dl)	96.4 (10.9)	92.0 (8.7)	<0.001
LDL cholesterol (mg/dl)	89.9 (23.4)	96.3 (23.8)	<0.01
HDL cholesterol (mg/dl)	51.5 (9.5)	59.2 (11.5)	<0.001
Triglycerides (mg/dl)	72.4 (31.9)	64.7 (26.9)	<0.01
Apo A-I (mg/dl)	116.8 (20.0)	126.4 (25.3)	<0.001
Apo B-100 (mg/dl)	67.4 (14.8)	70.8 (14.7)	<0.05
Lp(a) (mg/dl)	30.5 (36.3)	31.1 (39.6)	NS

Results expressed as mean (SD). Lipid and glucose data are from 460 subjects (248 males and 212 females). P values are from either Student's *t*-test (parametric variables) or Mann-Whitney *U*-test (non-parametric variables). Apo, apolipoprotein; BMI, body mass index; Lp(a), lipoprotein(a).

measured by enzymatic assay using a Hitachi 911 Analyzer (Roche Diagnostics, Indianapolis, USA). For the HDL cholesterol assay, precipitation was done using reagents provided by Boehringer (Ingelheim, Germany). LDL cholesterol was calculated with the Friedewald formula [27] adjusted for plasma triglycerides levels [28]. Apolipoprotein (apo) A-I, apo B-100 and lipoprotein(a) [Lp(a)] were measured using an immunonephelometric assay on Array 306 system (Beckman GMI, Inc., Albertville, MN, USA). Quality control of the assays was assured by the Regional Health Authority, as it is compulsory for all hospital clinical laboratories in Spain.

### Determination of a composite index of blood lipids and fasting glycaemia

To investigate whether a metabolic composite index was related to aerobic fitness, we decided to compute a continuous score from the following four measurements: triglycerides, HDL cholesterol, LDL cholesterol, and fasting glucose. For each of these variables, a Z score was computed as the number of SD units from the sample mean after normalization of the variables, i.e.,  $Z = ([\text{value} - \text{mean}] / \text{SD})$ . The HDL cholesterol Z score was multiplied by  $-1$  to indicate higher cardiovascular risk with increasing value. The composite index of blood lipids and fasting glycaemia was the sum of the four Z scores. The mean of this continuously distributed metabolic composite index was therefore zero by definition.

### Determination of aerobic fitness standards associated with a favourable lipid profile

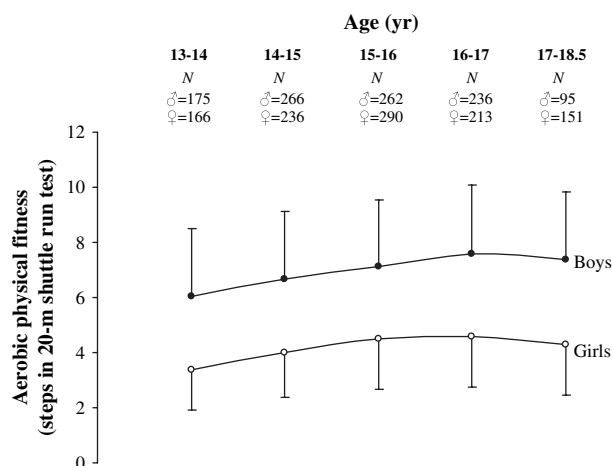
For aerobic fitness assessment, it was necessary to calculate a normalized score of aerobic fitness (score in the 20-m shuttle run test).

#### Normalization of the aerobic fitness score

Scores in steps of the 20-m shuttle run test ( $n = 2090$ ) were classified for age (13–14, 14–15, 15–16, 16–17, and 17–18.5 years) and gender (male or female). Because the aerobic physical fitness varies according to age and gender, we standardized the value for age and gender with the use of conversion to a Z score. Z normalized values (mean 0; SD 1) were obtained for each age group and gender. Z normalized value =  $(\text{value} - \text{mean}) / \text{SD}$ .

#### Determination of the presence/absence of healthy lipid profile

In accordance with the American Heart Association [29], based on the NCEP Expert Panel on Blood Cholesterol in Children and Adolescents [30], and



**Figure 1** Aerobic fitness scores by gender and age. Data are expressed as mean  $\pm$  SD.

based on other studies [31,32], we set undesirable serum total cholesterol, LDL cholesterol and Lp(a) levels higher than 240 mg/dl, 130 mg/dl, and 32 mg/dl, respectively, and HDL cholesterol lower than 35 mg/dl as indicators of lipid cardiovascular risk factors in children and adolescents. We considered the presence of a healthy lipid profile when healthy values were obtained in all of the indicated lipids. Absence of a healthy lipid profile was considered when at least one of the indicated lipid cardiovascular risk factors was detected.

#### Calculation of aerobic fitness standards to present a healthy lipid profile

After the dichotomised classification of the lipid profile (presence/absence of healthy lipid profile), receiver operating characteristic (ROC) analysis was performed in order to summarize the potential of age- and gender- normalized aerobic fitness to discriminate between presence or absence of healthy lipid profile [33]. The aerobic fitness standards for presenting a healthy lipid profile were settled defining the best tradeoff between true-positive and false-positive rates [34].

#### Statistical analysis

Inter-groups differences among gender were assessed by either Student's *t*-test (parametric variables) or Mann–Whitney *U*-test (non-parametric variables). General linear modelling was used to test associations between aerobic fitness, blood lipids, and glycaemia, after adjustment for confounding factors. ROC analysis was used to summarize the potential diagnostic accuracy of aerobic fitness (see above) to discriminate between the presence/absence of a favourable lipid profile.

**Table 2** General linear model analysis showing associations between blood lipids and aerobic fitness in adolescents

	Aerobic fitness (quartiles)								
	Boys (n = 248)				Girls (n = 212)				
	1	2	3	4	1	2	3	4	
Total cholesterol (mg/dl)	157.6 (33.8)	156.4 (23.5)	155.9 (20.9)	154.4 (23.7)	166.0 (29.6)	168.6 (29.5)	169.1 (22.3)	169.6 (26.5)	0.903
Triglycerides (mg/dl)	76.1 (37.4)	83.0 (36.4)	65.0 (21.7)	65.3 (27.5)	69.2 (35.6)	67.4 (23.7)	59.8 (17.7)	60.3 (20.0)	0.191
LDL cholesterol (mg/dl)	94.8 (30.2)	89.2 (20.9)	91.0 (20.8)	84.9 (20.1)	97.9 (24.4)	102.5 (25.6)	98.1 (19.4)	94.3 (23.7)	0.415
HDL cholesterol (mg/dl)	49.0 (9.1)	50.6 (9.5)	52.7 (9.8)	53.9 (9.3)	57.2 (10.6)	58.8 (11.4)	60.4 (9.9)	63.4 (14.0)	0.045
Glucose (mg/dl)	96.9 (8.2)	96.1 (8.4)	97.2 (17.8)	95.3 (8.1)	90.7 (9.1)	95.0 (7.0)	92.7 (7.3)	92.4 (9.7)	0.430
Apo A-I (mg/dl)	111.2 (14.7)	116.4 (18.9)	117.2 (24.5)	121.8 (20.2)	120.6 (15.3)	120.3 (25.7)	119.2 (22.8)	129.8 (28.4)	0.173
Apo B-100 (mg/dl)	67.0 (17.8)	68.3 (13.4)	68.7 (13.1)	66.5 (14.2)	71.3 (16.0)	74.6 (16.4)	72.5 (12.4)	68.6 (13.6)	0.261
Lp(a) (mg/dl)	32.9 (38.6)	30.7 (41.3)	31.3 (36.1)	26.2 (28.6)	29.4 (36.6)	31.0 (40.7)	39.1 (51.4)	26.3 (29.0)	0.573

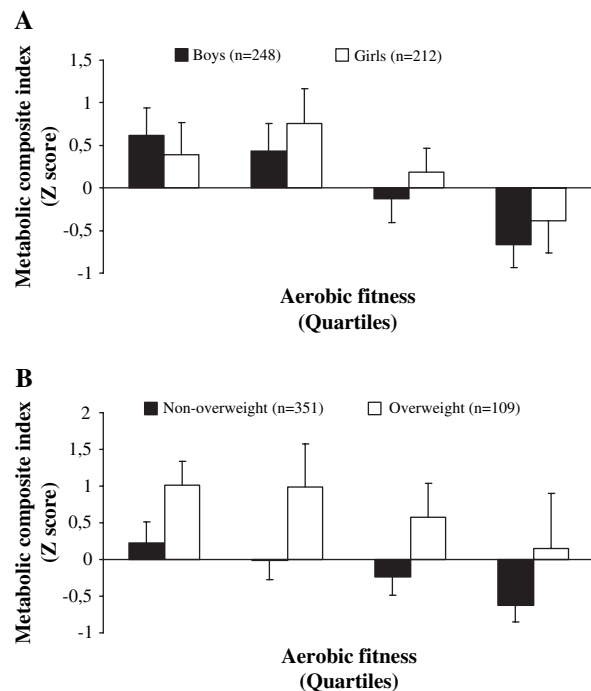
Results expressed as mean (SD). P for trend was calculated after adjustment for age, sexual maturation, and economic status. LDL refers to low density lipoprotein; HDL, high density lipoprotein; Apo, apolipoprotein; Lp(a), lipoprotein(a).

The level of significance for all analyses was set at  $P < 0.05$ .

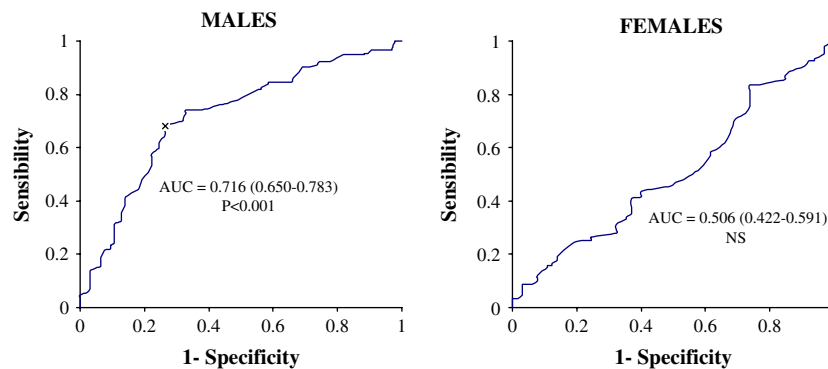
## Results

As expected, aerobic physical fitness was significantly higher in males compared with females for all ages ( $P < 0.001$ ) (Fig. 1).

After general linear model analysis adjusted for age, sexual maturation and economic status, aerobic physical fitness was related to triglycerides ( $P = 0.004$ ), HDL cholesterol ( $P = 0.013$ ), and Apo A-I ( $P = 0.028$ ) in male adolescents (Table 2). In females, aerobic fitness was only significantly related to HDL cholesterol ( $P = 0.045$ ) (Table 2).



**Figure 2** (A) General linear modelling showing associations between a composite index of blood lipids and fasting glycaemia and aerobic fitness in adolescents, after adjustment for age, sexual maturation, and economic status. In males there was a significant association ( $P = 0.018$ ); in females a significant association was found from the 2nd quartile to the 4th quartile of aerobic fitness ( $P = 0.045$ ). Data are expressed as mean  $\pm$  SEM. (B) Metabolic composite index of blood lipids and fasting glycaemia according to quartiles of aerobic fitness and weight categories, after adjustment for gender, age, sexual maturation, and economic status. The metabolic composite index was significantly higher in overweight adolescents ( $P = 0.001$ ). In both overweight and non-overweight categories, the metabolic composite index was related to aerobic fitness ( $P < 0.05$ ). Data are expressed as mean  $\pm$  SEM.



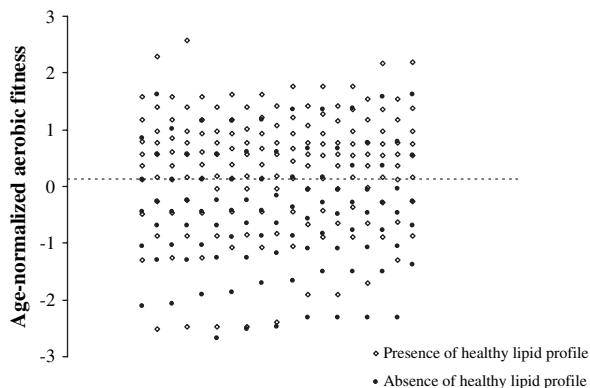
**Figure 3** Receiver operating characteristic (ROC) curve summarizing the potential of aerobic fitness to discriminate between the absence/presence of healthy plasma lipid profile in males ( $n = 248$ ) and females ( $n = 212$ ). The cross denotes the best cut-off point to discriminate the absence or presence of healthy plasma lipid profile in males, with a specificity of 0.734. Such a cut-off point was 0.1411 (age-normalized aerobic fitness). AUC, area under the curve.

A composite index of blood lipids and fasting glycaemia was significantly related to aerobic fitness in males ( $P = 0.018$ ), after adjustment for age, sexual maturation and economic status (Fig. 2A). In females, a significant trend was found from the 2nd quartile to the 4th quartile of aerobic fitness ( $P = 0.045$ ) (Fig. 2A). Although the same pattern remained in overweight (including obesity) and non-overweight adolescents after adjustment for gender, age, sexual maturation and economic status ( $P < 0.05$ , Fig. 2B), the metabolic composite index was significantly higher in overweight (including obesity) adolescents ( $P = 0.001$ ).

ROC analysis showed a significant diagnostic accuracy of age-normalized aerobic fitness to

discriminate the presence/absence of healthy plasma lipid profile in males (AUC = 0.716,  $P < 0.001$ ) but not in females (AUC = 0.506,  $P = 0.88$ ) (Fig. 3). The best age-normalized aerobic fitness value capable of discriminating the presence/absence of healthy lipid profile in males was 0.1411 (the cross in Fig. 3 and the dotted line in Fig. 4). Males with age-normalized aerobic fitness values above such a cut-off point presented increased odds (odds ratio 5.91, 95% confidence interval 3.35–10.45,  $P < 0.01$ ) of having a healthy lipid profile than those with aerobic fitness values below 0.1411 (Fig. 4).

Table 3 shows, according to age, the male aerobic fitness needed to present a healthy lipid profile. About 50% of the male study population did not reach such values.



**Figure 4** Distribution of the absence or presence of healthy lipid profile in males according to the age-normalized aerobic fitness ( $n = 248$ ). The dotted line represents the best age-normalized aerobic fitness (0.1411) for discriminating the absence/presence of healthy lipid profile. 73.4% of subjects without a healthy lipid profile were below such aerobic standard. The age-normalized aerobic fitness standard for presenting a healthy lipid profile was settled defining the best tradeoff between true-positive and false-positive rates [34].

## Discussion

Previous studies in children [16,17,35,36] have shown associations between aerobic physical fitness and blood lipids. We also show here associations between aerobic fitness and single blood lipids, mainly in males. The only association found in girls in our study was to HDL cholesterol levels, but even the first quartile of aerobic physical fitness had mean HDL cholesterol levels of  $57.2 \pm 10.6$  mg/dl, quite acceptable. This discrepancy is also noted by Boreham et al. [17], who revealed significant relationships between three cardiovascular risk factors and fitness in 12 year old boys, whereas only one cardiovascular risk factor and fitness in 12 year old girls.

With respect to the lipid profile and fasting glucose as a whole, we also show here associations between increased aerobic physical fitness and

**Table 3** Aerobic fitness standards required to present a healthy lipid cardiovascular profile in males

	Age (years)					True positive rate (%)	False negative rate (%)
	13–14	14–15	15–16	16–17	17–18.5		
Aerobic fitness standard	6.4	7.0	7.5	7.8	7.8	73.4	26.6
Percentage of population above the standard	49.7	51.9	49.2	52.1	51.6		

Aerobic fitness standard values are expressed in steps scored in the 20-m shuttle run test. The aerobic fitness standards for presenting a healthy lipid profile were settled defining the best tradeoff between true-positive and false-positive rates [34].

lower composite index of blood lipids and fasting glycaemia in adolescents, in both overweight and non-overweight adolescents. However, overweight (including obesity) adolescents with high aerobic fitness presented a higher composite index than their non-overweight counterparts with the same aerobic fitness level. This suggests the necessity to improve both aerobic fitness level and weight status in adolescents in order to prevent an unhealthy metabolic profile. This is biologically plausible. Firstly, some studies in children [16,17,35,36] have shown associations between aerobic physical fitness and blood lipids. Secondly, other studies have shown abdominal subcutaneous fat [37,38] and visceral adipose tissue [39,40] as determinants of metabolic atherogenesis risk factors in youth. Finally, we [41] have shown previously that overweight and obesity may induce a chronic low-grade inflammatory state in adolescents, which points out the importance of maintaining an appropriate body weight to avoid obesity-related diseases during adolescence.

Thus, our data suggest that both the promotion of physical activity and the reduction of excessive weight during adolescence may reduce exposure to metabolic risk factors in adolescents, which is in agreement with recent data [42]. According to several longitudinal studies [18,43,44], such a protection during adolescence could be expanded later in life.

In this study we also intended to provide, by using ROC analysis, the minimal values of aerobic physical fitness needed to present a healthy lipid profile in adolescents. Because the association between aerobic physical fitness and blood lipids was weaker in females compared to males, we were able to get the minimal values of aerobic fitness only in males. About 50% of male adolescents did not reach such required aerobic fitness values. Thus, the present aerobic fitness in adolescents seems to be less than acceptable. In this regard, some studies documented a progressive decrease in aerobic fitness among children over the last decades [45,46]. In fact, while in the 1980s

children aged 12–14 years had mean of the 20-m shuttle run score of  $8.0 \pm 1.7$  and  $6.4 \pm 1.5$  steps for boys and girls respectively [23], we report updated mean scores of  $6.0 \pm 2.4$  and  $3.4 \pm 1.5$  steps for boys and girls aged 13–14 years. Although aerobic fitness has a strong genetic component [47], and a part of the variability in health-related fitness is not accounted for by physical activity [18,48], such a decrease is probably mediated by a diminution in physical activity among adolescents over recent years.

According to the American Heart Association [29], the decrease in aerobic fitness may be due to a variety of reasons: (1) children tend to walk less and increasingly rely on cars for transportation; (2) sedentary entertainment has increased among adolescents; (3) participation in organized athletics diminishes greatly after middle school. Since physical fitness is very predictable from early years [49], and physical activity during childhood and adolescence is related to adult physical activity [50,51] and may influence the development of cardiovascular risk later in life [44,50], it is of interest to promote physical activity from childhood. In this respect, schools are in a uniquely favourable position to increase aerobic physical activity among their students.

In conclusion, our data suggest that both aerobic fitness and weight management may be necessary for the prevention of metabolic risk in adolescents. In addition, we add the minimal criterion standards of aerobic fitness to present a healthy plasma lipid profile in male adolescents. This is a new tool which should be adopted by schools as "aerobic fitness standards" in order to keep a healthy plasma lipid profile and, thus, to prevent metabolic and CVD risk during adolescence and later in life.

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