# The impact of reduced muscular fitness on cardiometabolic risk factors in children aged 9-11 years 

Eva Rodríguez-Gutiérrez ${ }^{1,2} \odot$ | Ana Torres-Costoso ${ }^{1,3}$ © | Lidia Lucas-de la Cruz ${ }^{1,4} \odot$ Arthur E. Mesas ${ }^{1,5} \odot \mid$ Vicente Martínez-Vizcaíno ${ }^{1,6} \odot \mid$ Ana Díez-Fernández ${ }^{1,4} \odot$

${ }^{1}$ Health and Social Research Center, Universidad de Castilla-La Mancha, Cuenca, Spain
${ }^{2}$ Research Network on Chronicity, Primary Care and Health Promotion (RICAPPS), Cuenca, Spain
${ }^{3}$ Faculty of Physiotherapy and Nursing, Universidad de Castilla-La Mancha, Toledo, Spain
${ }^{4}$ Faculty of Nursing, Universidad de Castilla-La Mancha, Cuenca, Spain
${ }^{5}$ Postgraduate Program in Public Health, Universidade Estadual de Londrina, Londrina, Brazil
${ }^{6}$ Faculty of Health Sciences, Universidad Autónoma de Chile, Talca, Chile

## Correspondence

Lidia Lucas-de la Cruz, C/Santa Teresa Jornet s/n, Cuenca 16071, Spain.
Email: lidia.lucas@uclm.es

## Funding information

Universidad de Castilla-La Mancha, Grant/ Award Number: 2022-UNIVERS-11373; Carlos III Health Institute, Grant/Award Number: FIS PI19/01919; European Union - NextGenerationEU, Carlos III Health Institute and Ministry of Science, Innovation and Universities, Grant/Award Number: RD21/0016/0025


#### Abstract

Aim: To analyse the relationships between muscular fitness (MF), fat mass (FM), fat-free mass (FFM) and its combined ratio with cardiometabolic risk (CMR) and whether the relationship between MF and CMR is mediated by body composition in schoolchildren. Methods: A cross-sectional study was conducted on schoolchildren from Cuenca, Spain, between September and November 2017. FM and FFM were estimated using bioimpedance analysis. The CMR index was calculated from triglycerides-HDL-c ratio, arterial pressure and fasting insulin. The MF index was assessed using handgrip and standing long jump tests. Analysis of covariance models assessed CMR index differences across the MF index and the FM/FFM ratio categories. Mediation analysis examined whether the MF index and the CMR index association were mediated by FM, FFM or FM/FFM ratio. Results: The analyses involved 485 schoolchildren aged 9-11 years ( $55.4 \%$ girls). Children with a higher MF index had a lower CMR index ( $p<0.05$ ). This association did not persist after controlling for FM/FFM. FM, FFM and FM/FFM ratio mediated the relationship between the MF index and the CMR index. Conclusion: Better levels of MF are associated with better cardiometabolic profile, but a healthy body composition is determinant to improve future health.


## KEYWORDS

body composition, children, mediation, metabolic syndrome, muscular fitness

## 1 | INTRODUCTION

Cardiometabolic risk (CMR) factor levels track from infancy and adolescence to adulthood ${ }^{1}$ and predict type 2 diabetes mellitus, cardiovascular events and general mortality. ${ }^{2}$ In children, CMR has
been consistently associated with cardiorespiratory fitness and adiposity. ${ }^{3}$ Along this line, muscular fitness (MF) has been closely related to cardiovascular health in both adult and paediatric populations. ${ }^{4}$ For instance, greater muscle strength has been associated with lower blood pressure, plasma insulin, glucose and triglyceride

[^0]levels and higher high-density lipoprotein cholesterol. ${ }^{5}$ In addition, an increased MF has been inversely associated with the CMR ${ }^{6}$ and is considered a powerful marker of health during growth. ${ }^{7}$

Skeletal muscle is the most abundant insulin-sensitive tissue in the body. Insulin resistance usually begins in early puberty, with a transient increase during mid-puberty as a result of decreased glucose uptake in muscle. ${ }^{8}$ This reduction in glucose uptake, possibly due to altered mitochondrial oxidative capacity, becomes a predisposing factor for the accumulation of adipose tissue. ${ }^{9}$ In addition, a decrease in muscle mass is associated with a decrease in skeletal muscle adipokine secretion, which may counteract the metabolic influence of adipose tissue adipokines. ${ }^{10}$ Furthermore, adiposity affects muscle functionality through intramuscular fat deposition, causing a decrease in muscle mass and strength. ${ }^{11}$

Higher adiposity and lower muscle strength have been associated with higher CMR. ${ }^{12}$ Body mass index (BMI) is the most widely used tool for assessing obesity. However, BMI is a poor indicator of body composition, especially in childhood, as it has certain limitations. This is because the same absolute value of BMI can result from various combinations of fat mass (FM) and fat-free mass (FFM) without differentiating between them. ${ }^{13}$ The variability of both FM and FFM in a single index, the FM/FFM ratio, has been suggested to be an indicator of CMR in adults. ${ }^{14}$ To date, no research has provided empirical evidence on the relationship between these variables in the paediatric population. Accordingly, this study had two aims. The first was to analyse, in schoolchildren, the relationships between CMR and MF, fat mass (FM), fat-free mass (FFM) and the FM/FFM ratio. The second was to investigate whether the relationship between MF and CMR was mediated by body composition in this population.

## 2 | METHODS

## 2.1 | Study design and participants

A cross-sectional analysis was conducted on baseline measurements of a cluster randomised controlled trial involving schoolchildren in the 4 th and 5 th grades from the province of Cuenca, Spain. The baseline measurements were taken between September 1 and November 31, 2017. The trial is referred to as The MOVI-daFit! Project 15, with the ClinicalTrials.gov identifier NCT03236337. Recruitment, measurements and data collection have been described elsewhere. ${ }^{15}$ The following inclusion criteria were met by all schoolchildren. First, not having any Spanish learning disability. Second, not having any physical or mental disorder or any chronic disorder impeding his/her participation in the activities of the program. This includes conditions such as attention deficit hyperactivity disorder, autism or any physical disability that would impede normal physical activity.

The development of this project was supported by the Department of Education and Science of the regional government of Castilla-La Mancha, Spain, which sent information to each school that agreed to participate in the study. Before the study started, the

## Key notes

- Understanding the interplay between muscular fitness, fat mass/fat-free mass and cardiometabolic risk in schoolchildren is important for designing early intervention strategies.
- This study revealed a negative association between muscular fitness and cardiometabolic risk, mediated by body composition variables, in 485 schoolchildren aged 9-11 years.
- These findings underscore the importance of not only promoting muscular fitness, but also maintaining a healthy body composition for optimal cardiometabolic health in children.
researchers provided information about the objectives and procedures of the trial to the head teacher, the school board and the physical education teachers at the schools.


## 2.2 | Anthropometric measurements

Weight and height were measured twice, and their average was considered for the analyses. We used a scale and a wall stadiometer, specifically the Seca 861 and Seca 222 models (Vogel \& Halke, Hamburg, Germany). BMI was calculated as weight in $\mathrm{kg} / \mathrm{height}$ squared in $\mathrm{m}^{2}$. Body FM and FFM were estimated before breakfast and after urination using an eight-electrode Tanita Segmental-418 bioimpedance analysis system (Tanita Corp., Tokyo, Japan). FM was divided by FFM to determine the FM/FFM ratio.

Diastolic and systolic blood pressure were determined twice at 5 min intervals after 5 min resting period. Blood pressure was measured automatically using the OMRON M5-I monitor (Omron Healthcare Europe BV, Hoofddorp, Netherlands). The mean arterial pressure (MAP) was calculated using the following formula: diastolic blood pressure $+(0.333 \times$ (systolic blood pressure - diastolic blood pressure)).

## 2.3 | Health dietary score index

The Children's Eating Habits Questionnaire ${ }^{16}$ was used to estimate food consumption and the health dietary score index. Higher scores indicate a better quality of diet.

## 2.4 | Biochemical assessments

Blood samples were obtained under standardised conditions by puncturing the cubital vein. These were taken between 8.15 and
9.00 am after at least 12 h of fasting. One aliquot of each sample was frozen to determine biochemical variables.

Lipid profiles including triglyceride and high-density lipoprotein cholesterol (HDL-c) levels were determined over a 48-h period using a Roche Cobas c701 automatic analyser (Roche Diagnostics, Mannheim, Germany). Insulin levels were assessed using an Immulite 2000 double-system platform (Siemens Healthineers, Forchheim, Germany).

The CMR index was calculated as the sum of the age-sex standardised scores of triglycerides-to-HDL-c ratio, MAP and fasting insulin. The validity of this index has been previously tested using confirmatory factor analysis. ${ }^{17}$

## 2.5 | Muscular fitness assessment

We assessed upper and lower body MF using handgrip and standing long jump tests. Handgrip strength (maximum handgrip strength assessment) was measured using a TKK 5401 Grip-D dynamometer (Takeya, Tokyo, Japan). The weight range was from 5 to 100 kg , with a precision of 0.1 kg . The test was performed twice with each hand and the maximum score for each hand was recorded in kilograms. The average of the maximum scores for both hands was used in the analyses. For the standing long jump (lower body explosive strength assessment), the child jumped horizontally to achieve the maximum distance and the best of three attempts was recorded in centimetres. These tests have been validated and are reliable for measuring musculoskeletal fitness. ${ }^{18}$ These tests are included in the PREFIT battery, ${ }^{19}$ which assess physical fitness in preschool children.

To avoid the potential biasing effect of body weight on the estimation of MF, handgrip strength and standing long jump were adjusted by the allometric normalisation method proposed by Jaric et al. ${ }^{20}$ In addition, a sex- and age-specific MF index was constructed from the sum of standardised $z$-scores on the handgrip/weight ${ }^{0.67}$ and standing long jump/weight ${ }^{0.67}$ tests.

To identify the minimum sufficient adjustment set for the total effect of the MF index on the CMR index, we constructed a theoretical causal diagram based on previous knowledge available in the scientific literature. We used the online tool DAGitty (Johannes Textor, Nijmegen, The Netherlands) to construct a directed acyclic graph. The covariates sex, age and health dietary score index were identified as the minimum sufficient adjustment set.

## 2.6 | Statistical analysis

The distribution of continuous variables was checked for normality before further analysis. Fasting insulin and triglycerides/HDL-c data were normalised with a natural logarithm transformation. Descriptive data were assessed with the $t$-test, and participants' characteristics were described as means and standard deviations. Pearson correlation coefficients were estimated to examine the
relationship between CMR factors, the FM/FFM ratio and MF in the total sample and by sex. Partial correlation coefficients were estimated between the MF index and FFM, controlling for the percentage of FM.

The MF index and the FM/FFM ratio were categorised as low (first quartile), medium (second and third quartiles) or high (fourth quartile). Analysis of covariance models was used to assess differences in the CMR factors across the MF index and the FM/FFM ratio categories. It was specified in each model which covariable was included (age, diet index quality, MF index or FM/FFM ratio), stratified by sex. Pairwise post hoc hypotheses were tested using the Bonferroni correction for multiple comparisons.

A simple mediation analysis was conducted to examine whether the association between the MF index and the CMR index was mediated by FM, FFM or the FM/FFM ratio. The analysis followed the checklist A Guideline for Reporting Mediation Analyses (Table S1) and used the PROCESS macro for SPSS (Andrew F. Hayes, Calgary, Canada). The goal of this model is to explore the total (c) and direct effects ( $a, b$ and $c^{\prime}$ ) that indicate the unstandardised regression coefficient and significance between the independent and dependent variables in each model. The analysis included assessing the indirect effect, indicating the change in the CMR index for every unit change in the MF index, mediated by the proposed mediator. The variable waist circumference was removed from the original CMR index for these mediation models to avoid multicollinearity.

Additional mediation analysis models were conducted between the MF index and each component of the CMR index, including log triglycerides/HDL-c, log insulin and MAP. The analysis considered both boys and girls, including age and diet index quality as covariates. Covariates were determined based on the minimum sufficient adjustment set identified through the directed acyclic graph. Figure S1 shows that when controlling for the minimum sufficient adjustment set of covariates, bias pathways were closed, leaving only the causal pathways open, both direct and indirect through mediators.

We used bootstrapping methods for testing mediation hypotheses (using a resampling procedure of 10000 bootstrap samples). ${ }^{21}$ Point estimates and confidence intervals (95\%) were estimated for the indirect effect. The point estimate was considered to be significant when the confidence interval did not contain zero.

All the statistical analyses were performed using SPSS Software, version 22.0 (IBM Corp, New York, USA) and the level of significance was set at $p \leq 0.05$.

## 2.7 | Ethics

This research was conducted according to the guidelines established by the Declaration of Helsinki, and the study protocol was approved by the Clinical Research Ethics Committee of the Virgen de la Luz Hospital in Cuenca (REG: 2016/PIO21). In addition, the children's parents were asked to sign an informed consent form allowing their children to participate. After the data were gathered, the parents were informed by letter of their children's results.

## 3 | RESULTS

This study involved 485 schoolchildren with full data (55.4\% girls). Table 1 summarises the participants' characteristics by sex. Girls had higher FM/FFM ratio values than boys ( $0.35 \pm 0.1 \mathrm{vs} .0 .30 \pm 0.1$, respectively, $p<0.001$ ). Boys scored significantly better than girls in terms of physical fitness variables, as indicated by the absolute handgrip strength ( $12.8 \pm 3.8$ vs. $12.0 \pm 3.2$, respectively, $p=0.043$ ), standing long jump ( $121.4 \pm 21.6$ vs. $112.2 \pm 19.0$, respectively, $p<0.001$ ) and MF index ( $0.24 \pm 1.8$ vs. $-0.23 \pm 1.5$, respectively, $p=0.001$ ).

Partial correlations between FM, FFM, the FM/FFM ratio, Log Insulin, Log triglycerides/HDL-c, MAP, CMR, the MF index and diet index quality are shown in Table 2. All the correlations were statistically significant ( $p<0.05$ ) in the total sample and by sex. An
exception was found for girls and the total sample for FFM and MF index, after controlling for the percentage of FM. In addition, the diet quality index was not correlated with body composition variables, the MF index and some CMRi components. The MF index was negatively correlated with all CMR factors and the FM/FFM ratio.

Analysis of covariance models testing mean differences in the CMR index across FM/FFM ratio categories including different covariates (age, diet index quality and MF index) in boys (a) and girls (b) are shown in Figure 1. Including age (model one) and age plus diet index quality (model two) and age plus MF (model three) as covariables, the CMR index was significantly higher in those with higher levels of FM/FFM ratio. Pairwise mean comparisons using the Bonferroni post hoc tests were statistically significant ( $p<0.001$ ) (low < medium < high), except between the low and medium categories for most models.

TABLE 1 Characteristics of the study sample.

|  | Total ( $n=485$ ) | Boys ( $n=233$ ) | Girls ( $\mathrm{n}=252$ ) | $p$-Value |
| :---: | :---: | :---: | :---: | :---: |
| Age (year) | $9.6 \pm 0.7$ | $9.6 \pm 0.7$ | $9.6 \pm 0.7$ | 0.252 |
| Tanner stage ${ }^{\text {a }}$ | $1.62 \pm 0.76$ | $1.60 \pm 0.65$ | $1.64 \pm 0.84$ | 0.300 |
| Tanner stage (I-II/III-V) (\%) ${ }^{\text {a }}$ | 86.5/13.5 | 91.9/8.1 | 81.9/18.1 | 0.005 |
| Height (cm) | $140.9 \pm 7.3$ | $141.0 \pm 7.1$ | $140.8 \pm 7.6$ | 0.766 |
| Weight (kg) | $36.6 \pm 10.0$ | $36.8 \pm 10.2$ | $36.5 \pm 9.8$ | 0.692 |
| FM\% | $24.0 \pm 6.9$ | $22.5 \pm 7.3$ | $25.3 \pm 6.3$ | <0.001 |
| FM (kg) | $9.4 \pm 5.5$ | $8.9 \pm 5.8$ | $9.8 \pm 5.2$ | 0.080 |
| FFM (kg) | $27.3 \pm 5.1$ | $27.9 \pm 5.0$ | $26.8 \pm 5.2$ | 0.009 |
| Ratio FM/FFM | $0.33 \pm 0.14$ | $0.30 \pm 0.1$ | $0.35 \pm 0.1$ | <0.001 |
| MAP (mmHg) | $75.4 \pm 6.7$ | $75.8 \pm 6.8$ | $75.0 \pm 6.6$ | 0.204 |
| Triglycerides (mg/dL) | $71.1 \pm 33.9$ | $67.0 \pm 35.7$ | $75.0 \pm 31.8$ | 0.009 |
| HDL-c (mg/dL) | $59.6 \pm 13.4$ | $61.1 \pm 14.1$ | $58.2 \pm 12.7$ | 0.018 |
| Log triglycerides/HDL-c (mg/dL) | $0.12 \pm 0.6$ | $0.02 \pm 0.6$ | $0.2 \pm 0.5$ | <0.001 |
| Fasting Insulin (mg/dL) | $8.2 \pm 6.4$ | $7.8 \pm 6.5$ | $8.7 \pm 6.2$ | 0.105 |
| Log Fasting Insulin (mg/dL) | $1.93 \pm 0.6$ | $1.85 \pm 0.6$ | $2.00 \pm 0.2$ | 0.003 |
| Cardiometabolic risk index | $0.04 \pm 2.9$ | $-0.12 \pm 3.0$ | $0.18 \pm 2.7$ | 0.258 |
| Participants at risk (n (\%) ${ }^{\text {b }}$ | 42 (8.7\%) | 22 (9.4\%) | 20 (7.5\%) | 0.556 |
| Health dietary score index ${ }^{\text {c }}$ | $65.5 \pm 7.1$ | $65.7 \pm 7.4$ | $65.3 \pm 6.8$ | 0.566 |
| Dynamometry (kg) | $12.4 \pm 3.5$ | $12.8 \pm 3.8$ | $12.0 \pm 3.2$ | 0.008 |
| Dynamometry/weight ${ }^{0.67}$ | $1.12 \pm 0.3$ | $1.16 \pm 0.3$ | $1.09 \pm 0.2$ | 0.005 |
| Standing long jump | $116.6 \pm 20.8$ | $121.4 \pm 21.6$ | $112.2 \pm 19.0$ | <0.001 |
| Standing long jump/weight ${ }^{0.67}$ | $10.9 \pm 2.9$ | $11.3 \pm 3.0$ | $10.5 \pm 2.8$ | 0.001 |
| Muscular fitness index ${ }^{\text {d }}$ | $-0.0056 \pm 1.7$ | $0.24 \pm 1.8$ | $-0.23 \pm 1.5$ | 0.001 |

[^1]TABLE 2 Pearson correlation coefficients ${ }^{\text {a }}$ between body composition, cardiometabolic risk index and its components and muscular fitness variables.

|  |  | FFM | FM/FFM ratio | Log insulin | Log triglycerides/ HDL-c | MAP | CMR <br> index | MF <br> index | Diet index quality |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| FM | Total | 0.78 | 0.96 | 0.56 | 0.48 | 0.34 | 0.57 | -0.44 | -0.04* |
|  | Boys | 0.80 | 0.97 | 0.57 | 0.49 | 0.44 | 0.62 | -0.63 | -0.09* |
|  | Girls | 0.79 | 0.95 | 0.55 | 0.46 | 0.24 | 0.51 | -0.65 | 0.02* |
| FFM | Total |  | 0.61 | 0.47 | 0.33 | 0.32 | 0.43 | 0.06* | 0.02* |
|  | Boys |  | 0.69 | 0.46 | 0.39 | 0.39 | 0.48 | 0.14 | -0.17* |
|  | Girls |  | 0.60 | 0.53 | 0.33 | 0.24 | 0.43 | -0.01* | 0.06* |
| Ratio FM/FFM | Total |  |  | 0.54 | 0.48 | 0.30 | 0.56 | -0.69 | -0.06* |
|  | Boys |  |  | 0.57 | 0.48 | 0.41 | 0.62 | -0.68 | -0.10* |
|  | Girls |  |  | 0.49 | 0.45 | 0.21 | 0.48 | -0.69 | 0.01* |
| Log Insulin | Total |  |  |  | 0.55 | 0.26 | 0.77 | -0.41 | -0.16* |
|  | Boys |  |  |  | 0.53 | 0.33 | 0.78 | -0.45 | -0.23 |
|  | Girls |  |  |  | 0.54 | 0.22 | 0.75 | -0.34 | -0.06* |
| Log triglycerides /HDL-c | Total |  |  |  |  | 0.27 | 0.78 | -0.34 | -0.20 |
|  | Boys |  |  |  |  | 0.31 | 0.78 | -0.33 | -0.23 |
|  | Girls |  |  |  |  | 0.25 | 0.77 | -0.32 | -0.15* |
| MAP | Total |  |  |  |  |  | 0.66 | -0.17 | -0.15 |
|  | Boys |  |  |  |  |  | 0.69 | -0.22 | -0.14* |
|  | Girls |  |  |  |  |  | 0.65 | -0.14 | -0.17 |
| CMR index | Total |  |  |  |  |  |  | -0.42 | -0.22 |
|  | Boys |  |  |  |  |  |  | -0.44 | -0.25 |
|  | Girls |  |  |  |  |  |  | -0.37 | -0.17 |
| MF index | Total |  |  |  |  |  |  |  | 0.003* |
|  | Boys |  |  |  |  |  |  |  | 0.002* |
|  | Girls |  |  |  |  |  |  |  | 0.003* |

Note: All $p$-values $\leq 0.005$, except for those marked with *.
Abbreviations: CMR index, cardiometabolic risk index (sum of standardised z score of its components: log insulin, MAP and log TG/HDL-c); FFM, Fatfree mass; FM, Fat mass; Log Insulin, logarithm of fasting insulin; Log TG/HDL-c, logarithm of triglyceride to high-density lipoprotein cholesterol ratio; MAP, mean arterial pressure; MF index, Muscular fitness index (sum of standardised z score of dynamometry/weight ${ }^{0.67}$ and standing long jump/ weight ${ }^{0.67}$, according to allometric parameters defined by Jaric).
${ }^{\text {a Correlation coefficients between muscular fitness index and FFM are partial correlation coefficients controlling for } \% \text { FM. }}$

Figure 2 includes mean differences in the CMR index across the MF index categories including different covariates (age, diet index quality and FM/FFM ratio) in boys (a) and girls (b). All the models were statistically significant ( $p<0.001$ ) (low $>$ medium $>$ high), showing that participants with higher MF index had lower CMR index values. Only after controlling for age and FM/FFM ratio (model three), comparisons using the Bonferroni post hoc were non-significant in both boys and girls ( $p>0.05$ ).

The mediation analysis models are depicted in Figure 3. The MF index was negatively and significantly related to the FM/FFM ratio and there was a positive relationship between the FM/FFM ratio and the CMR index. The relationship between the MF index and the CMR index was mediated by the FM/FFM ratio as the direct effect lost the significance. After testing the mediation hypotheses using the bootstrapping method, the indirect effect was significant
( $-0.366,95 \% \mathrm{Cl}=-0.477 /-0.259$ ). Thus, the relationship between the MF index and the CMR index is mediated by the FM/FFM ratio.

Similar results were found when FM and FFM acted as individual mediators. The influence of FFM on the relationship between the MF index and the CMR index was lower (indirect effect $=-0.155$, $95 \% \mathrm{Cl}=-0.226 /-0.092$ ) than FM (indirect effect $=-0.365,95 \%$ $\mathrm{Cl}=-0.474 /-0.263)$, but both were significant.

When analysing the CMR factors and the general index in both boys and girls, the results were similar. FM, FFM and the FM/FFM ratio acted as mediators of the relationships between the MF index and the CMR index, log triglycerides/HDL-c, log insulin and MAP (Figures S2-S4 for boys and Figures S5-S7 for girls). Notably, the FM/FFM ratio did not act as a mediator between the MF index and MAP, as no statistically significant relationship was observed (Figure S3).

FIGURE 1 Mean differences (95\% confidence intervals) in the cardiometabolic risk index according to fat mass-to-fat mass ratio. Marginal estimated means and upper and lower Cl . All the pairwise mean comparison using Bonferroni post hoc test were statistically significant ( $p<0.001$ ), except for the comparisons marked with * ( $p>0.05$ ). White refers to low quartile, grey to middle quartile and black to upper quartile.

(B) Girls

## 4 | DISCUSSION

We believe that this was the first study to investigate the role of the FM/FFM ratio in CMR in schoolchildren. The present study analysed the relationship between MF and the FM/FFM ratio with CMR and explored the potential mediating role of the FM/FFM ratio in the relationship between MF and CMR in this population. The main findings indicated the protective effect of MF on CMR and its components and highlighted the mediating role of the FM/FFM ratio in that relationship in schoolchildren of both sexes.

Nutritional status can influence muscle quality and muscle strength. Muscle deconditioning is related to a higher inflammatory status ${ }^{22}$ and the development of fatty infiltration, which can increase FM. ${ }^{11} \mathrm{BMI}$ is not an optimal indicator of the influence of obesity. ${ }^{13}$ However, most studies have used it to analyse the association between MF and body composition, which varies according to whether the population is underweight, has a normal weight or
is overweight. ${ }^{13}$ Replacing the use of BMI with a combined index of FM and FFM might help to disentangle the role of MF according to weight status categories. ${ }^{14}$ In this sense, our results using a FM/ FFM ratio were similar to previous studies, ${ }^{23}$ in which greater muscle strength was associated with a lower FM/FFM ratio.

Excess weight deteriorates the CMR profile in schoolchildren, ${ }^{24}$ but FM and FFM play different roles in CMR. The adverse effects of high FM may be offset by the protective effects of high FFM as in adults, where a higher FM/FFM ratio has been related to a worse CMR profile. ${ }^{25}$ Nevertheless, our results showed a positive association between FFM and the CMR index. This may be supported because insulin is an important anabolic stimulus for muscle proteins, but its dysregulation may contribute to insulin resistance and metabolic disturbances. ${ }^{26}$ Our results support previous findings in adults, ${ }^{27}$ indicating that children with a higher FM/FFM ratio had higher CMR than their peers with a lower ratio, even after controlling for MF. Therefore, it seems reasonable that the positive effect of MF
(A) Boys


## (B) Girls



FIGURE 2 Mean differences (95\% confidence intervals) in the cardiometabolic risk index according to the category of muscular fitness index. Marginal estimated means and upper and lower Cl . All the pairwise mean comparison using Bonferroni posthoc test were statistically significant ( $p<0.001$ ), except for the comparisons marked with * ( $p>0.05$ ). White refers to low quartile, Grey to middle quartile and black to upper quartile.
on CMR could be due to the influence of MF on both body composition compartments.

The changes in insulin levels described at puberty ${ }^{8}$ may play a role in adipose tissue. However, most children included in our study were prepubertal, which makes it difficult to assume that sexual maturation played a role in these associations. Nevertheless, before sexual maturation occurs, the first secretions of oestrogen and progesterone appear, leading to changes in adiposity, a phenomenon known as adiposity rebound. ${ }^{28}$

Children with higher levels of MF have a better cardiometabolic profile in adulthood. ${ }^{6}$ Our findings suggested that maintaining a good MF during childhood might play a protective role in the development of CMR through the indirect effect of MF on the FM/FFM ratio. Thus, our data, according to previous evidence using BMI as a measure of body composition, ${ }^{29}$ revealed a mediating role of the FM/FFM ratio in the relationship between MF and CMR. However, the main difference from this previous finding is that our data made it clear that this was due to the influence of FM and FFM on body composition. It is important to note that two individuals with the same BMI may have different CMRs depending on their FM/FFM ratio.

Some limitations of our study should be recognised. First, the main limitation was the cross-sectional design, which does not allow us to establish causal relationships. Therefore, the reported results should be confirmed prospectively. Second, body composition was measured with bioelectrical impedance analysis, rather than dualenergy X-ray absorptiometry, which is considered the gold standard test. However, bioelectrical impedance analysis is a simpler technique and does not emit radiation to the study participant. ${ }^{30}$ Third, the sample used in this study involved relatively healthy children, which could hamper the sensitivity in detecting associations. However, it is important to prevent unhealthy body composition from an early age and to emphasise the importance of muscle strength to improve the cardiometabolic profile. Finally, the generalisability of these results should be considered cautiously because of the complex impact on the cardiometabolic profile in children. This impact is influenced by several factors, including regional variability in CMR prevalence, genetics, environmental influences and sexual maturity, among others. However, the validity of our results was supported by the population-based sample size with a narrow age range and the representativeness of the sample.

$\mathrm{IE}=\mathbf{- 0 . 3 6 6}(\mathbf{9 5 \% C I}=-\mathbf{0 . 4 7 7 / - 0 . 2 5 9})$

$I E=-0.365(95 \% C I=-0.474 /-0.263)$


$$
\mathrm{IE}=-0.155(95 \% \mathrm{CI}=-0.226 /-0.092)
$$

FIGURE 3 Body composition mediation models of the relationship between the muscular fitness index and the cardiometabolic risk indexes. Abbreviations: FM, Fat mass; FFM, Fat free mass; IE, Indirect effect; a, b, c, total effects; c', direct effect; Cl , confidence interval. Muscular fitness index was calculated by the sum of standardized z score of dynamometry/ weight ${ }^{0.67}$ and standing long jump/weight ${ }^{0.67}$ ). Cardiometabolic risk index was calculated by sum of standardized z score of its components: log insulin, MAP, and log triglycerides/HDL-c). Covariables: age and dietary index. $\mathrm{n}=320$.

## 5 | CONCLUSION

Our data were relevant from a clinical perspective because they supported, in schoolchildren, that both MF and the FM/FFM ratio were associated with CMR. Moreover, they suggested that interventions aimed at increasing MF such as resistance training could indirectly result in benefits in terms of CMR through an improvement in body composition. Therefore, promoting interventions designed to motivate schoolchildren to lead strengthening exercises may help to reduce the CMR by improving body composition measured as the FM/FFM ratio.

## AUTHOR CONTRIBUTIONS

Lidia Lucas-de la Cruz: Investigation; methodology; visualization; supervision. Eva Rodríguez-Gutiérrez: Conceptualization; methodology; writing - review and editing; writing - original draft. Ana Torres-Costoso: Validation; data curation; supervision. Arthur E. Mesas: Visualization; formal analysis; software; project administration. Vicente Martínez-Vizcaíno: Visualization; conceptualization; resources; supervision; funding acquisition. Ana Díez-Fernández: Investigation; writing - original draft; formal analysis.

## FUNDING INFORMATION

This study was funded by the Ministry of Economy and Competitiveness Carlos III Health Institute and FEDER funds (FIS PI19/01919), Health Outcomes-Oriented Cooperative Research Networks (RD21/0016/0025) co-funded with European UnionNextGenerationEU funds, Carlos III Health Institute and Ministry of Science, Innovation and Universities, and by the Universidad de Castilla-La Mancha (2022-UNIVERS-11373).

## CONFLICT OF INTEREST STATEMENT

None declared

## ETHICS STATEMENT

The Clinical Research Ethics Committee of the Virgen de la Luz Hospital in Cuenca approved the study protocol (REG: 2016/PI021).

## ORCID

Eva Rodríguez-Gutiérrez © https://orcid.org/0000-0001-6907-7872
Ana Torres-Costoso (D) https://orcid.org/0000-0001-8961-3169
Lidia Lucas-de la Cruz (D) https://orcid.org/0000-0002-3411-9830
Arthur E. Mesas (D) https://orcid.org/0000-0002-0088-8607
Vicente Martínez-Vizcaíno (D) https://orcid.
org/0000-0001-6121-7893
Ana Díez-Fernández (D) https://orcid.org/0000-0002-7673-986X

## REFERENCES

1. Weiss R, Bremer AA, Lustig RH. What is metabolic syndrome, and why are children getting it? Ann N Y Acad Sci. 2013;1281(1):12340. doi:10.1111/NYAS. 12030
2. Wilson PWF, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation. 2005;112(20):3066-72. doi:10.1161/CIRCULATIONAHA.105.539528
3. Brand C, Dias AF, Fochesatto CF, et al. The role of body fat in the relationship of cardiorespiratory fitness with cardiovascular risk factors in Brazilian children. Motriz: Revista de Educação Física. 2018;24(4):101811. doi:10.1590/S1980-6574201800040015
4. Smith JJ, Eather N, Morgan PJ, Plotnikoff RC, Faigenbaum AD, Lubans DR. The health benefits of muscular fitness for children and adolescents: a systematic review and meta-analysis. Sports Med. 2014;44(9):1209-23. doi:10.1007/S40279-014-0196-4
5. Chong H, Choi YE, Kong JY, et al. Association of Hand Grip Strength and Cardiometabolic Markers in Korean adult population: the Korea National Health and nutrition examination survey 2015-2016. Korean J Fam Med. 2020;41(5):291-8. doi:10.4082/KJFM.18.0129
6. de Lima TR, Martins PC, Torre GL, Mannocci A, Silva KS, Silva DAS. Association between muscle strength and risk factors for metabolic syndrome in children and adolescents: a systematic review. J Pediatr Endocrinol Metab. 2020;34(1):1-12. doi:10.1515/ JPEM-2020-0135
7. Ortega FB, Ruiz JR, Castillo MJ, Sjöström M. Physical fitness in childhood and adolescence: a powerful marker of health. Int J Obes. 2008;32(1):1-11. doi:10.1038/SJ.IJO.0803774
8. HannonTS, Janosky J, ArslanianSA. Longitudinalstudy of physiologic insulin resistance and metabolic changes of puberty. Pediatr Res. 2006;60(6):759-63. doi:10.1203/01.PDR.0000246097.73031.27
9. Fleischman A, Kron M, Systrom DM, Hrovat M, Grinspoon SK. Mitochondrial function and insulin resistance in overweight and normal-weight children. J Clin Endocrinol Metab. 2009;94(12):492330. doi:10.1210/JC.2009-1590
10. Petersen KF, Dufour S, Savage DB, et al. The role of skeletal muscle insulin resistance in the pathogenesis of the metabolic syndrome Proc Natl Acad Sci USA. 2007;104(31):12587-94. doi:10.1073/ PNAS. 0705408104
11. Pagano AF, Brioche T, Arc-Chagnaud C, Demangel R, Chopard A, Py G. Short-term disuse promotes fatty acid infiltration into skeletal muscle. J Cachexia Sarcopenia Muscle. 2018;9(2):335-47 doi:10.1002/JCSM. 12259
12. Lopez-Lopez JP, Cohen DD, Ney-Salazar D, et al. The prediction of metabolic syndrome alterations is improved by combining waist circumference and handgrip strength measurements compared to either alone. Cardiovasc Diabetol. 2021;20(1):68. doi:10.1186/ S12933-021-01256-Z
13. Freedman DS, Wang J, Maynard LM, et al. Relation of BMI to fat and fat-free mass among children and adolescents. Int J Obes. 2005;29(1):1-8. doi:10.1038/SJ.IJO.0802735
14. Xiao J, Purcell SA, Prado CM, Gonzalez MC. Fat mass to fat-free mass ratio reference values from NHANES III using bioelectrical impedance analysis. Clin Nutr. 2018;37(6):2284-7. doi:10.1016/j clnu.2017.09.021
15. Martínez-Vizcaíno V, Álvarez-Bueno C, Cavero-Redondo I, et al. MOVI-daFIT! Intervention: rationale and design of a cluster randomized controlled trial testing the effects on improving adiposity, cognition, and subclinical atherosclerosis by increasing cardiorespiratory fitness in children. Medicine. 2019;98(9):e14737 doi:10.1097/MD.0000000000014737
16. Lanfer A, Hebestreit A, Ahrens W, et al. Reproducibility of food consumption frequencies derived from the Children's eating habits questionnaire used in the IDEFICS study. Int J Obes. 2011;35(Suppl 1):S61-S68. doi:10.1038/IJO.2011.36
17. Martínez-Vizcaíno V, Martínez MS, Aguilar FS, et al. Validity of a single-factor model underlying the metabolic syndrome in children a confirmatory factor analysis. Diabetes Care. 2010;33(6):1370-2 doi:10.2337/DC09-2049
18. Artero EG, Espaa-Romero V, Castro-Piero J, et al. Reliability of field-based fitness tests in youth. Int J Sports Med. 2011;32(3):159 69. doi:10.1055/S-0030-1268488
19. Cadenas-Sanchez C, Martinez-Tellez B, Sanchez-Delgado G, et al. Assessing physical fitness in preschool children: feasibility, reliability and practical recommendations for the PREFIT battery. J Sci Med Sport. 2016;19(11):910-5. doi:10.1016/J.JSAMS.2016.02.003
20. Jaric S, Mirkov D, Markovic G. Normalizing physical performance tests for body size: a proposal for standardization. J Strength Cond Res. 2005;19(2):467-74. doi:10.1519/R-15064.1
21. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav Res Methods. 2008;40(3):879-91. doi:10.3758/ BRM.40.3.879
22. Artero EG, España-Romero V, Jiménez-Pavón D, et al. Muscular fitness, fatness and inflammatory biomarkers in adolescents. Pediatr Obes. 2014;9(5):391-400. doi:10.1111/J.2047-6310.2013. 00186.X
23. Merchant RA, Seetharaman S, Au L, et al. Relationship of fat mass index and fat free mass index with body mass index and association with function, cognition and sarcopenia in pre-frail older adults. Front Endocrinol (Lausanne). 2021;12:765415. doi:10.3389/ FENDO.2021.765415
24. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and metaanalysis. BMJ. 2012;345(7876):e4759. doi:10.1136/BMJ.E4759
25. Fan Z, Shi Y, Huang G, Hou D, Liu J. Long-term changes in body composition and their relationships with cardiometabolic risk factors: a population-based cohort study. PLoS One. 2021;16(5):e0251486. doi:10.1371/JOURNAL.PONE. 0251486
26. Fujita S, Rasmussen BB, Cadenas JG, Grady JJ, Volpi E. Effect of insulin on human skeletal muscle protein synthesis is modulated by insulin-induced changes in muscle blood flow and amino acid availability. Am J Physiol Endocrinol Metab. 2006;291(4):E745-E754. doi:10.1152/AJPENDO.00271.2005
27. Calcaterra V, Verduci E, de Silvestri A, et al. Predictive ability of the estimate of fat mass to detect early-onset metabolic syndrome in prepubertal children with obesity. Children (Basel). 2021;8(11):966. doi:10.3390/CHILDREN8110966
28. Hughes AR, Sherriff A, Ness AR, Reilly JJ. Timing of adiposity rebound and adiposity in adolescence. Pediatrics. 2014;134(5):e1354e1361. doi:10.1542/PEDS.2014-1908
29. Díez-Fernández A, Sánchez-López M, Gulías-González R, et al. BMI as a mediator of the relationship between muscular fitness and cardiometabolic risk in children: a mediation analysis. PLoS One. 2015;10(1):e0116506. doi:10.1371/JOURNAL.PONE. 0116506
30. Marra M, Sammarco R, De Lorenzo A, et al. Assessment of body composition in health and disease using bioelectrical impedance analysis (BIA) and dual energy X-ray absorptiometry (DXA): a critical overview. Contrast Media Mol Imaging. 2019;2019:1-9. doi:10.1155/2019/3548284

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article

How to cite this article: Rodríguez-Gutiérrez E, Torres-
Costoso A, Lucas-de la Cruz L, Mesas AE, Martínez-Vizcaíno V, Díez-Fernández A. The impact of reduced muscular fitness on cardiometabolic risk factors in children aged 9-11 years. Acta Paediatr. 2024;113:1364-1372. https://doi.org/10.1111/ apa. 17178


[^0]:    Abbreviations: BMI, body mass index; CMR, cardiometabolic risk; FFM, fat-free mass; FM, fat mass; HDL-c, high-density lipoprotein cholesterol; MAP, mean arterial pressure; MF, muscular fitness.

[^1]:    Note: Data are presented by mean $\pm$ standard deviation and number (percentage). Cardiometabolic risk index was calculated as the sum of standardised $z$ score of its components: log fasting insulin, waist circumference, mean arterial blood pressure and log TG/HDL-c. $p$-values $<0.05$ were marked in bold.

    Abbreviations: DBP, diastolic blood pressure; FFM, Fat-free mass; FM, Fat mass; HDL-c, high-density lipoprotein cholesterol; Log fasting insulin, logarithm of fasting insulin; Log triglycerides/HDL-c, logarithm of triglyceride to high-density lipoprotein cholesterol ratio; MAP, mean arterial pressure $(\mathrm{DBP}+\{0.333 \times(\mathrm{SBP}-\mathrm{DBP})\})$; SBP, systolic blood pressure.
    ${ }^{\text {a }}$ Tanner stage was available only in 371 participants ( 172 boys and 199 girls).
    ${ }^{\text {b }}$ Cardiometabolic risk index score $\geq 4.2$ according to Martinez-Vizcaíno et al. ${ }^{17}$
    ${ }^{\mathrm{c}}$ Higher scores indicate a better quality of diet.
    ${ }^{d}$ Sum of the standardised $z$ score of handgrip dynamometry/weight ${ }^{0.67}$ and standing long jump/weight ${ }^{0.67}$.

