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ORIGINAL ARTICLE

Relationship between cardiorespiratory fitness and blood pressure in young adults: a mediation analysis of body composition

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High blood pressure levels are among the most important cardiovascular disease risk factors and are influenced by physical fitness and body composition. However, the degree to which obesity may attenuate or modify the beneficial effects of physical fitness on blood pressure levels in young adults is uncertain. Thus, the aim of this study was to analyze whether body composition is a mediator between cardiorespiratory fitness (CRF) and blood pressure levels in young adults. This work was a cross-sectional study involving first-year college students ($n=386$) at the University Campus of Cuenca (Spain). We measured weight, height, waist circumference, fat mass percentage (by densitometry), systolic and diastolic blood pressure and CRF levels (by a 20 m shuttle run test). Partial correlation coefficients were estimated to examine the relationships among adiposity variables, CRF and blood pressure variables, controlling for age and sex. ANCOVA models were conducted to explore differences in blood pressure levels across adiposity and CRF categories. Hayes's PROCESS macro was used for the simple mediation analysis. The indirect effect and Sobel test were significant ($P<0.001$), confirming that all body composition variables mediate between CRF and all of the included blood pressure variables. All body composition variables acted as mediators between CRF and blood pressure. These results highlight the importance of maintaining a healthy body composition to prevent hypertension in young adults.
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Keywords: adiposity; blood pressure; cardiorespiratory fitness; mediation analysis; young adults.

INTRODUCTION

It has been estimated that high blood pressure levels are responsible for ~12.8% of the total mortality and account for 3.7% of total disability-adjusted life years (DALYs) worldwide.[1] Moreover, high blood pressure levels have consistently been shown to be positively related to the risk of stroke and coronary heart disease.[1]

Evidence from large epidemiologic studies supports a consistent, inverse and independent relationship of physical activity and cardiorespiratory fitness (CRF) with cardiovascular and overall mortality risk.[2,3] Physically active lifestyles can mitigate age-related increases in arterial stiffness[4] (and consequently in blood pressure) through increased cardiorespiratory fitness.[5–7]

Childhood obesity is closely related to low CRF and high blood pressure levels,[8] and this relationship continues on into adolescence and adulthood.[9] The extent to which obesity may attenuate or modify the benefits of CRF in relation to blood pressure levels in young adults is uncertain.

Mediation analysis is a statistical procedure that can be used to clarify the process underlying the relationship between two variables and the extent to which this relationship can be modified, mediated or confounded by a third variable.[10]

The aim of this study was to clarify whether the relationship between CRF and different blood pressure variables in young adults is mediated by body composition.

METHODS

Study design and subjects

This study was a cross-sectional analysis of data from *The Cuenca Adults Study* (collected between 2009 and 2010), aimed at assessing changes in lifestyle and cardiovascular risk factors during university years.[11] A total of 770 first-year students of the University Campus of Cuenca ($n=963$), Spain, were invited to participate in the study, and 683 (88.7%, 504 women) accepted. The final sample included 386 (50.12%, 266 women) first-year university students with a complete set of valid data.

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The Clinical Research Ethics Committee of Virgen de la Luz Hospital in Cuenca approved the study protocol and all subjects signed informed consent forms prior to participation in the study.

Anthropometric measurements

Weight and height were measured following standardized recommendations using an electronic scale (SECA Model 861; Vogel & Halke, Hamburg, Germany, precision = 100 g, range: 0–150 kg) and a stadiometer (Type Seca 222; Vogel & Halke, precision: 0.1 cm, range: 6–230 cm). The mean of two measurements for both weight and height was used to calculate the body mass index (BMI) as the weight in kilograms divided by the square of the height in meters (kg m^{-2}). Waist circumference (WC) was determined by the average of two measurements taken with flexible tape at the waist (at the midpoint between the last rib and the iliac crest).

Diastolic and systolic blood pressure (DBP and SBP) were determined as the average of two measurements taken at an interval of 5 min, with the subject resting for at least 5 min before the first measurement. The participant was seated in a quiet and calm environment, with the right arm placed in a semi-flexed position at heart level. Blood pressure was measured by an automated procedure using the Omron M5-I monitor (Omron Healthcare Europe BV, Hoofddorp, the Netherlands). Mean arterial pressure (MAP) was calculated using the following formula: DBP+[0.333 × (SBP—DBP)].

Measurements were performed by nurses trained for the purpose of the project in order to minimize inter-observer variability at the university.

Body composition: dual-energy X-ray absorptiometry (DXA)

The total body fat percentage (%FM) was measured by a whole-body DXA scanner, using the total body scan mode: Lunar iDXA (GE Medical Systems Lunar, Madison, WI, USA). The analyses were performed using enCore 2008 software version 12.30.008 (GE Medical Systems Lunar, Madison, WI, USA). The machine's calibration was checked and passed on a daily basis before each scanning session, using the GE Lunar calibration phantom (GE Medical Systems Lunar). Participants were instructed to wear clothing containing no metal. They were asked to lie down on the scanning table within the scanning area and relax and stay still until the full scan was finished. Their feet were loosely fastened together to keep the lower body in a stable position. The scan time for a total body scan was ~6 min. An X-ray technician performed all DXA scans.

Cardiorespiratory fitness

CRF was assessed by the 20 m shuttle run test.[12] Participants were required to run between two lines 20 m apart, while keeping pace with audio signals emitted from a pre-recorded compact disc. The initial speed was 8.5 km h^{-1}, which was increased by 0.5 km h^{-1} every minute. Participants were encouraged to keep running for as long as possible throughout the course of the test. We recorded the last half stage completed as an indicator of CRF. Estimations of submaximal oxygen consumption (VO_2max) were obtained using Leger's formulae.

Statistical analyses

Both statistical (Kolmogorov-Smirnov test) and graphical methods (normal probability plots) were used to examine the fit to a normal distribution for each continuous variable. The descriptive data were assessed by the *t*-test, and the participants' characteristics were described as the mean ± standard deviation (s.d.).

Partial correlation coefficients were estimated to examine the relationships among adiposity variables (BMI, WC and %FM), CRF and blood pressure variables (DBP, SBP and MAP), controlling for age and sex.

The %FM, WC and CRF were categorized as low (first quartile), medium (second and third quartiles) or high (fourth quartile). Participants were classified as normal weight, overweight or obese according to WHO cutoffs.[13] ANCOVA models were used to assess differences in blood pressure levels across the different adiposity and CRF categories, controlling for age and sex (model 1), with further adjustment for %FM, WC, BMI or CRF, depending on the fixed factor (models 2–4). Pairwise post *hoc* hypotheses were tested using the Bonferroni correction for multiple comparisons.

Mediation analysis was conducted to examine whether the association between CRF and blood pressure variables was mediated by body composition variables using the PROCESS macro for SPSS (SPSS, Chicago, IL, USA).[14] The goal of this model was to investigate the total (c) and direct effects (a, b, c'), reflected by the unstandardized regression coefficient and significance between the independent and dependent variables in each model. The model also investigated the indirect effect (IE) obtained from the product of coefficients (a × b), which indicates the change in the blood pressure variable for every unit change in CRF level that is mediated by the proposed mediator.

This macro used bootstrapping methods recommended by Preacher and Hayes[15] for testing mediation hypotheses, using a resampling procedure of 10 000 bootstrap samples. Point estimates and confidence intervals (95%) were estimated for the IE. The point estimate was considered significant when the confidence interval did not contain zero. We also assessed mediation using the following steps outlined by Sobel:[16] first, we estimated the IE, and then we divided it by its standard error and performed a Z test of the null hypothesis: that the IE is equal to zero.

Statistical analyses were performed using SPSS-IBM (Software, v.19.0 SPSS), and the level of significance was set at $P \leqslant 0.05$.

RESULTS

Table 1 describes the characteristics of the study sample. The means of the CRF, body composition indicators and blood pressure parameters were higher in men than in women except for %FM, which had higher levels in women ($P<0.001$).

Table 2 shows partial correlation coefficients between adiposity variables, CRF and blood pressure variables, controlling for age

Table 1 Characteristics of the study sample

	Total (n = *386*)	*Men* (n = *120*)	*Women* (n = *266*)	P-*value*
Age (year)	20.1 ± 4.1	19.9 ± 2.9	20.1 ± 4.5	0.611
BMI (kg m^{-2})	22.6 ± 3.6	23.7 ± 3.4	22.2 ± 3.6	< **0.001**
Waist circumference (cm)	80.8 ± 8.9	84.4 ± 8.7	79.6 ± 8.6	< **0.001**
Fat mass percentage	30.3 ± 7.3	22.3 ± 6.1	32.8 ± 5.6	< **0.001**
CRF (ml kg^{-1} min^{-1})	36.2 ± 7.2	44.5 ± 6.0	32.5 ± 3.7	< **0.001**
DBP (mm Hg)	69.2 ± 7.1	70.9 ± 7.2	68.6 ± 7.0	**0.001**
SBP (mm Hg)	113.1 ± 12.7	127.3 ± 11.4	108.9 ± 9.3	< **0.001**
MAP (mmHg)	83.9 ± 8.0	89.7 ± 7.5	82.0 ± 7.2	< **0.001**

Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; MAP, mean arterial pressure (DBP+(0.333 × (SBP – DBP))); SBP, systolic blood pressure.
The data are presented by mean ± s.d.
CRF indicates VO_2max values obtained with Leger's formulae. Boldface type indicates statistical significance $P<0.05$.

Table 2 Pearson correlation coefficients (*r*) between adiposity variables with CRF and blood pressure variables, controlling for age and sex

	WC	*%FM*	*CRF*	*DBP*	*SBP*	*MAP*
BMI	0.89**	0.68**	−0.32**	0.34**	0.35**	0.38**
WC		0.71**	−0.58**	0.29**	0.31**	0.33**
%FM			−0.58**	0.25**	0.21**	0.26**
CRF				−0.07	−0.01	−0.05
DBP					0.63**	0.93**
SBP						0.87**
MAP						

Abbreviations: BMI, body mass index; CRF, Cardiorespiratory fitness; DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure; WC, waist circumference; %FM, fat mass percentage.
**$P<0.001$.

Table 3 Mean differences in blood pressure variables by fat mass and cardiorespiratory fitness categories

	Model 1				Model 2			
	Low	Medium	High	P-value	Low	Medium	High	P-value
Fat mass categories								
SBP	111.3±1.0$^{L\text{-}H}$	112.7±0.6	117.6±0.9	<**0.001**	111.4±1.3	114.7±0.7	119.8±1.2	<**0.001**
DBP	67.1±0.8$^{L\text{-}H}$	68.7±0.4	72.6±0.7	<**0.001**	67.0±0.9$^{L\text{-}H}$	69.4±0.5	72.6±0.8	<**0.001**
MAP	81.7±0.8$^{L\text{-}H}$	83.4±0.4	87.6±0.6	<**0.001**	81.8±0.9	84.5±0.5	88.3±0.9	<**0.001**
Cardiorespiratory fitness categories								
SBP	115.8±1.2$^{L\text{-}H}$	114.2±0.7$^{M\text{-}H}$	115.2±1.4	0.465	113.5±1.2$^{L\text{-}H}$	114.0±0.7$^{M\text{-}H}$	118.7±1.5	**0.030**
DBP	70.6±0.8$^{L\text{-}H}$	69.7±0.5	67.1±0.9	**0.031**	69.1±0.9$^{L\text{-}H}$	69.8±0.5$^{M\text{-}H}$	69.2±1.1	0.701
MAP	85.6±0.8$^{L\text{-}H}$	84.6±0.5$^{M\text{-}H}$	83.1±0.9	0.202	83.9±0.9$^{L\text{-}H}$	84.5±0.5$^{M\text{-}H}$	85.3±1.1	0.542

Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; L-H, low-high; M, Medium-High; SBP, systolic blood pressure; MAP, mean arterial pressure (DBP+(0.333×(SBP−DBP))).
The data are presented by marginal estimated mean±s.e.
Model 1: controlling for age and sex. Model 2: controlling for age, sex and cardiorespiratory fitness level (in fat mass categories) or fat mass (in cardiorespiratory fitness categories).
CRF indicates VO_2max values obtained with Leger's formulae. *P*-value in bold indicates $P<0.05$. Pairwise mean comparisons using Bonferroni post *hoc* test were statistically significant except for superscript letters (L-H, Low-High; M, Medium-High; $P>0.05$).

and sex. BMI, WC and %FM were positively associated with all BP variables ($P<0.001$). Correlation coefficients between CRF and adiposity variables were negative and significant ($P<0.001$), but we did not observe any association between CRF and BP variables ($P>0.05$).

Table 3 presents the mean differences in BP variables by the categories %FM and CRF, controlling for age and sex (model 1). The levels of all BP variables were significantly higher in young adults with higher adiposity ($P<0.001$), and only DBP was significantly lower in individuals with a higher CRF ($P=0.031$).

Similar results were obtained when CRF was included in the ANCOVA model as a covariate with %FM categories as the fixed factor (model 2). However, when %FM was added to the ANCOVA model as a covariate with CRF categories as the fixed factor, the effect of CRF changed, remaining significant only in the SBP variable, where the participants with higher CRF levels had a significantly higher SBP ($P=0.030$).

When the fixed factors were the BMI or WC categories, the results remained the same in models 1 and 2, but there was no significant difference in BP variables across CRF categories when WC (model 3) or BMI (model 4) was included as a covariate (Supplementary Table 1).

Mediation analysis diagrams are depicted in Figure 1. Overall, body composition variables (BMI, %FM and WC) mediated the relationship between CRF and blood pressure variables. In the first regression step (path a), CRF was negatively related to the adiposity component (BMI, %FM or WC) ($P<0.001$). In the second step (path c), the regression coefficient of CRF on the independent variable (DBP, SBP or MAP) was not significant ($P>0.05$). In the last regression model, the mediator variable was positively related to the dependent variable (path b) ($P<0.001$), but when both CRF and the adiposity variable were included in the model (path c'), the regression coefficient became positive. Finally, both the IE and the Sobel test were significant, confirming the mediation role of all adiposity variables in these models.

DISCUSSION

Our results show that adiposity mediates the association between CRF and blood pressure in young adults. To our knowledge, this study is the first to examine this relationship using mediation analysis.

Obesity causes functional and structural changes in the microcirculation (including altered endothelial function) that impair microvascular function.[17] It has been suggested that obesity-related microvascular dysfunction might increase peripheral vascular resistance and consequently contribute to the development of hypertension.[17,18] Microvascular dysfunction has also been shown to be involved in the development of obesity-related insulin resistance, which precedes type 2 diabetes.[19]

The mechanisms involved in obesity-related microvascular dysfunction are multifactorial. Obesity-related microvascular dysfunction may be caused by an imbalance between the vasodilator effects of nitric oxide and the vasoconstrictor effects of endothelin-1.[19] Furthermore, adipokines secreted by visceral adipocytes have been linked to diminished insulin-mediated vasodilation and increased BP.[19] In addition, a proinflammatory and/or anti-inflammatory adipokine effect has also been found to be involved in the initiation of microvascular dysfunction.[19]

Previous studies have shown a positive relationship between adiposity parameters and BP in children, adolescents and adults.[20,21] Our findings in young adults were consistent with these past results as we found higher BP levels in participants in the higher adiposity categories. However, we observed that differences in BP levels among adiposity categories (model 2) persisted after including CRF as a covariate in the ANCOVA models. This result suggests that CRF might not counteract the harmful effects of adiposity on BP.

The beneficial effects of CRF on health are well known. In particular, CRF improves cardiovascular health, contributes to the attenuation of the age-related progressive increase in BP and prevents hypertension.[3,11] However, CRF does not completely eliminate the increased mortality associated with higher adiposity in adults.[2] The mechanisms that explain the beneficial effects of CRF on BP levels are based on decreased vascular peripheral resistance together with reduced sympathetic nervous system activity,[18] neuro-hormonal changes (reducing circulating noradrenaline, angiotensin II and insulin resistance among others) and vascular remodeling in vessels, (increasing lumen diameter and length), muscle and adipocytes.[22,23] Therefore, the effects of CRF on the BP levels in the vascular and endocrine functions are similar, but act in the opposite direction to obesity.

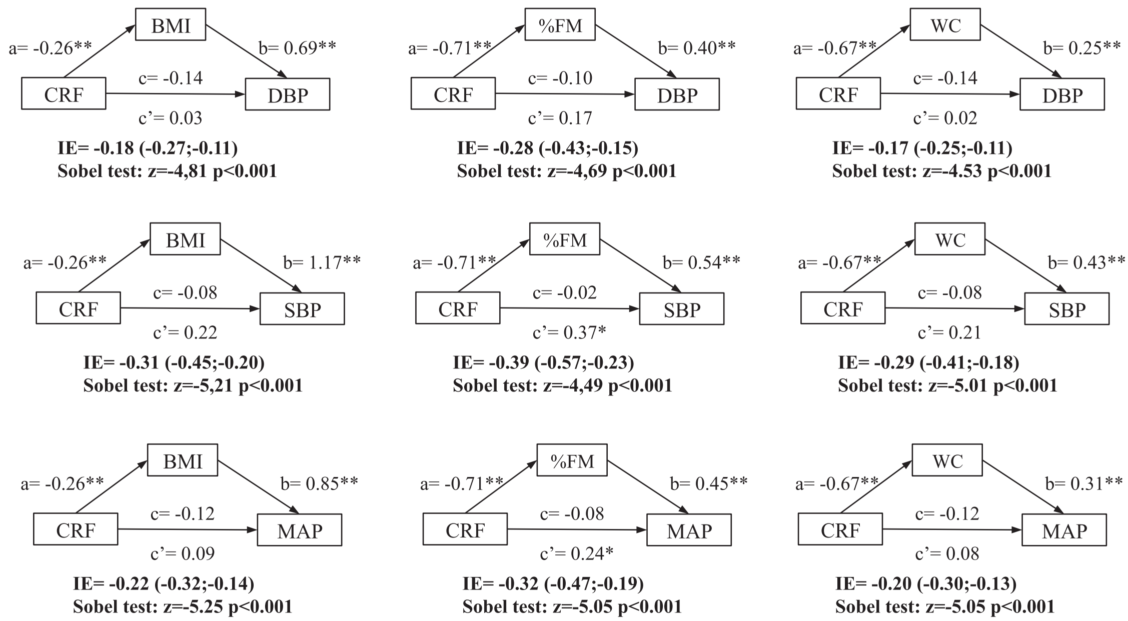

Figure 1 Body composition mediation models of the relationships between cardiorespiratory fitness and blood pressure variables, controlling for age and sex. CRF indicate VO_2max values obtained with Leger's formulae. a, b, c and c' are expressed as the unstandardized regression coefficient, as suggested by Hayes[14]. $*P<0.05$; $**P<0.001$. BMI, body mass index; CRF, cardiorespiratory fitness; DBP, diastolic blood pressure; IE, Indirect effect; MAP, mean arterial pressure; SBP, systolic blood pressure; WC, Waist circumference.

Our mediation analysis offers new insight into understanding the relationship between adiposity, CRF and BP, suggesting that adiposity mediates the relationship between CRF and BP. We found that the effect of CRF on BP levels is minimized by the negative effect of body adiposity. Rhéaume *et al.*[24] studied the relationship among these factors by assessing visceral adipose tissue using computed tomography. Through linear regression analysis, they found that age and visceral adipose tissue, but not fitness, predicted both systolic and diastolic blood pressure, highlighting visceral adipose tissue as a target for controlling BP.

These results lead to uncertainty regarding the effectiveness of strategies for diminishing BP levels by improving CRF in metabolically normal obese subjects while maintaining an unhealthy body composition. Moreover, they support the idea that high-level fitness counteracts the harmful effects of an unhealthy body composition.

It is widely known that improving CRF from a low-to-moderate or high level is associated with better cardiovascular status and overall survival.[25] In accordance with this association, our study shows that CRF is positively correlated with SBP in young adults when total body fat percentage is included as a covariate. However, a J-curve pattern has also been reported with these parameters. In fact, a very high level CRF was associated, to some extent, with a loss of cardiovascular health benefits.[26–28] Chronic, intense and sustained exercise greatly exceeding general recommendations for physical activity in healthy adults,[29,30] might be associated with increased cardiovascular risk; myocardial fibrosis, particularly in the atria, interventricular septum and right ventricle; coronary artery calcification; diastolic dysfunction; and large-artery wall stiffening.[26]

Limitations

Our study has several limitations that should be acknowledged. First, the cross-sectional design prevented us from making cause and effect inferences. Second, our findings were obtained from a sample of young adults, aged 18–30 years; thus, caution is necessary when making inferences about other age ranges. Third, CRF levels in university students might be lower than expected, as shown in a previous study using this sample,[31] and therefore fail to show the full range of benefits of fitness for BP and adiposity. Finally, we did not consider potential behavior-related confounders, moderators or mediators, such as dietary habits or alcohol consumption, in this study. Complex models, including more than one mediator, moderation-mediation models or the longitudinal data would be useful in future research to confirm our findings.

CONCLUSION

Our study highlights the importance of maintaining a healthy body composition for preventing hypertension and achieving satisfactory CRF levels from early adulthood. This approach has important implications (clinical and public health) for preventing cardiovascular events, especially those related to high BP levels.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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