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# Low Cardiorespiratory Fitness Levels and Elevated Blood Pressure

## What Is the Contribution of Visceral Adiposity?

Caroline Rhéaume, Benoit J. Arsenault, Stéphane Bélanger, Louis Pérusse, Angelo Tremblay, Claude Bouchard, Paul Poirier, Jean-Pierre Després

**Abstract**—Individuals with poor cardiorespiratory fitness have higher blood pressure than fit individuals. Individuals with low fitness levels also tend to be characterized by higher visceral adiposity compared with physically fit individuals. We tested the hypothesis that the relationship between low fitness and elevated blood pressure could be related, at least in part, to the higher level of visceral adipose tissue often found among unfit individuals. This study included 407 asymptomatic, nondiabetic participants. Visceral adipose tissue was assessed by computed tomography, and fitness was measured by a progressive submaximal physical working capacity test. Participants in the highest visceral adipose tissue tertile showed the highest systolic and diastolic blood pressures, whereas participants in the highest fitness tertile had the lowest blood pressure values ( $P < 0.001$ ). When participants were classified into fitness tertiles and then subdivided on the basis of visceral adipose tissue (high versus low), participants with a high visceral adipose tissue had higher systolic and diastolic blood pressure values ( $P = 0.01$ ), independent of their fitness category. Linear regression analyses showed that age and visceral adipose tissue, but not fitness, predicted systolic blood pressure ( $r^2 = 0.11$  [ $P < 0.001$ ],  $0.12$  [ $P < 0.001$ ], and  $0.01$  [ $P$  value nonsignificant], for age, visceral adipose tissue, and fitness, respectively) and diastolic blood pressure ( $r^2 = 0.17$  [ $P < 0.001$ ],  $0.14$  [ $P < 0.001$ ], and  $0.01$  [ $P$  value nonsignificant], for age, visceral adipose tissue, and fitness, respectively). Individuals with high visceral adipose tissue levels have higher blood pressure, independent of their fitness. Visceral adipose tissue may represent an important clinical target in the management of elevated blood pressure. (*Hypertension*. 2009;54:91-97.)

**Key Words:** cardiorespiratory fitness ■ systolic and diastolic blood pressures  
■ visceral adipose tissue ■ body mass index

Over the past 20 years, several studies have shown that individuals with low levels of cardiorespiratory fitness (unfit individuals) have higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) at rest than fit individuals, thereby increasing cardiovascular disease (CVD) risk.<sup>1-3</sup> The association between cardiorespiratory fitness (CRF) and blood pressure has been found to be independent of body mass index (BMI) and other adiposity indices.<sup>4,5</sup> However, even with a BMI in the normal range, individuals with high levels of visceral adipose tissue (VAT) are often characterized by an altered lipoprotein-lipid profile, insulin resistance, and a proinflammatory and prothrombotic profile, which are likely to increase CVD risk.<sup>6,7</sup> A previous report from our laboratory has shown that even after controlling for BMI, men with low CRF had higher ( $\approx 30\%$ ) VAT than men with high CRF levels. Incidentally, these men were also characterized by an increased prevalence of specific features of the metabolic syndrome.<sup>8</sup>

Although investigations have reported that individuals with abdominal obesity are at risk for future hypertension,<sup>9-12</sup> whether individuals with high CRF and high VAT levels would also have elevated blood pressure remained to be investigated. Therefore, the purpose of the present study was to test the hypothesis that the relationship between low CRF levels and high resting SBP and DBP could be related to the high VAT level found frequently among unfit individuals.

## Methods

### Study Population

Study participants were apparently healthy men and women without diabetes mellitus who participated in the Québec Family Study (QFS). The study sample was composed of participants for whom we obtained data on body composition, CRF, and plasma levels of cardiometabolic risk markers. Briefly, the QFS is a population-based study of French-Canadian families living in and around the Québec city area. The QFS was approved by the medical ethics committee of

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Université Laval. Participants were recruited through the media and gave their written informed consent to participate in the study. Only healthy men and women, 18 to 65 years of age (prevalence of smokers was 21%), who were not under a drug regimen for CVD, diabetes mellitus, hypertension, dyslipidemias, or endocrine disorders were considered for the present analyses.

### Anthropometric, Body Composition, and Hemodynamic Measurements

Height, body weight, and waist circumference were measured following standardized procedures. Body density was measured by the hydrostatic weighing technique.<sup>13</sup> Measurement of abdominal adipose tissue areas was performed by computed tomography with a Siemens Somatom scanner. Briefly, participants were examined in the supine position with both arms stretched above the head. The scan was performed at the abdominal level (L<sub>4</sub> and L<sub>5</sub> vertebrae) using an abdominal scout radiograph to standardize the position of the scan to the nearest millimeter. Total adipose tissue area was calculated by delineating the abdominal scan with a graph pen and then by computing the total abdominal adipose tissue area with an attenuation range of -190 to -30 Hounsfield units. The abdominal VAT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. The abdominal subcutaneous adipose tissue area was calculated by subtracting the VAT area from the total abdominal adipose tissue area. Resting blood pressure was taken by the same trained person, in the morning in the fasting state, in a sitting position after a 45-minute rest using a mercury sphygmomanometer (Propper) and an appropriately sized cuff (Welch Allyn Tyco), according to standard procedures. Participants were asked to refrain from smoking for 2 hours before the procedure. Blood pressure values were means of 2 different measurements.

### Biochemical Analyses

After a 12-hour overnight fast, blood samples were collected from an antecubital vein into Vacutainer tubes (Miles Pharmaceuticals, Rexdale) for the measurement of plasma lipid and lipoprotein levels. Plasma cholesterol and triglyceride concentrations were determined in plasma and lipoprotein fractions using a Technicon RA-500 analyzer (Bayer Corporation), and enzymatic reagents were obtained from Randox (Randox Laboratories Ltd). Plasma very low-density lipoproteins (<1.006 g/mL) were isolated by ultracentrifugation,<sup>14</sup> and the high-density lipoprotein fraction was obtained after precipitation of low-density lipoprotein in the infranantant (density: >1.006 g/mL) with heparin and MnCl<sub>2</sub>.<sup>15</sup> The cholesterol content of the infranantant fraction was measured before and after the precipitation step, allowing the calculation of low-density lipoprotein cholesterol. Plasma C-reactive protein levels were measured with a highly sensitive immunoassay that used a monoclonal antibody coated with polystyrene particles; the assay was performed with a Behring BN-100 nephelometer (Dade Behring). Plasma glucose was measured enzymatically, whereas plasma insulin was measured by radioimmunoassay with polyethylene glycol separation.<sup>16</sup>

### Cardiorespiratory Fitness

CRF was assessed by a progressive submaximal physical working capacity (PWC) test performed on a modified Monark cycle ergometer. Heart rate was measured through 1 ECG derivation and recorded during 3 consecutive 6-minute workloads, each separated by a 1-minute rest. The test was designed to exceed a heart rate of 150 bpm at the end of the last workload. PWC<sub>150</sub>, which is the power output at 150 bpm, was then calculated from the linear relationship between heart rate and power output. To take into account individual differences in body weight, PWC<sub>150</sub> was expressed by kilogram of body weight (PWC<sub>150/kg</sub>).

### Statistical Analysis

Data are presented as mean±SD or medians (interquartile range) in the tables and as means±SEM in the figures. Baseline anthropometric and metabolic characteristics of participants are presented separately in men and women. Multiple regression analyses were

**Table 1. Baseline Anthropometric and Metabolic Characteristics of the 184 Men and 223 Women of the Study**

Parameter	Men	Women	P
No. of participants	184	223	
Age, y	37.6±14.3	36.1±12.9	0.28
PWC, kpm/kg	11.1±3.3	7.2±2.5	<0.0001
BMI, kg/m <sup>2</sup>	25.8±4.5	26.4±6.5	0.3
Waist circumference, cm	89±13	81±15	<0.0001
AT accumulation, total, cm <sup>2</sup>	309.2±183.2	396.9±212.7	<0.0001
Visceral	108.7±69.4	82.8±52.4	<0.0001
Subcutaneous	200.5±129.2	314.1±173.4	<0.0001
SBP, mm Hg	114±12	112±13	0.09
DBP, mm Hg	71±9	69±9	0.01
Total cholesterol, mmol/L	4.9±1.0	4.8±1.2	0.22
LDL cholesterol, mmol/L	3.1±0.9	2.8±0.8	0.0007
HDL cholesterol, mmol/L	1.1±0.3	1.3±0.3	<0.0001
Total cholesterol:HDL cholesterol ratio	4.6±1.4	3.9±2.8	0.0008
Triglycerides, mmol/L	1.3 (0.9 to 1.9)	1.1 (0.9 to 1.5)	0.006*
Glucose, mmol/L	5.3±0.6	5.0±0.5	<0.0001
Insulin, pmol/L	51.5 (35.0 to 70.5)	51.0 (39.0 to 74.0)	0.55*

PWC indicates physical working capacity at 150 bpm; AT, adipose tissue; LDL, low-density lipoprotein; HDL, high-density lipoprotein; kpm, kilo/pound/meter. Data are presented as mean±SD or medians (interquartile range), unless otherwise specified. P values are for differences between men and women.

\*Data show log-transformed values.

computed to quantify the contributions of cardiometabolic risk markers to the variance in SBP and DBP in the total sample and then in men and women separately. The sex-specific relationships between cardiometabolic risk factors and SBP and DBP were assessed by adjusted and unadjusted Spearman rank correlations. SBP and DBP were compared between participants classified on the basis of VAT levels (<130 cm<sup>2</sup> or ≥130 cm<sup>2</sup> for men and <100 cm<sup>2</sup> or ≥100 cm<sup>2</sup> for women), as suggested previously,<sup>17</sup> and sex-specific tertiles of CRF. Differences among groups were compared with 1-way ANOVA. A P<0.05 was considered to be statistically significant. All of the statistical analyses were performed with the SAS package 9.1 (SAS Institute).

### Results

A total of 184 healthy men and 223 healthy women were evaluated in the present cross-sectional analyses. Mean age was 36.7±13.6 years, and mean BMI was 26.1±5.7 kg/m<sup>2</sup>. Mean waist circumference values were 89.0±12.7 cm in men and 80.6±15.0 cm in women. In our study sample, 290 participants had normal BP, 100 participants were prehypertensive, and 17 had hypertension according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.<sup>18</sup> Table 1 presents anthropometric characteristics, SBP and DBP, and PWC<sub>150/kg</sub> values in men and women separately. Lipoprotein-lipid profile and glucose-insulin homeostasis variables are also shown.

**Table 2. Multivariate Regression Analyses Show the Contributions of VAT Accumulation, Age, BMI, Fasting Insulin Levels, and CRF Levels to the Variance of SBP and DBP**

Dependent Variables	Independent Variables	Total $R^2$ , %	$P$
<b>Total</b>			
SBP	VAT	11.7	<0.0001
	+Age	15.4	<0.0001
	+BMI	16.2	0.06
	+Fasting insulin		
	+CRF		
DBP	Age	16.7	<0.0001
	+BMI	21.2	<0.0001
	+VAT	21.8	0.09
	+Fasting insulin		
	+CRF		
<b>Men</b>			
SBP	Age	5.7	0.001
	+CRF	7.4	0.07
	+VAT		
	+BMI		
	+Fasting insulin		
DBP	Age	14.1	<0.0001
	+BMI	16.0	0.04
	+VAT		
	+Fasting insulin		
	+CRF		
<b>Women</b>			
SBP	VAT	21.2	<0.0001
	+Age	25.9	0.0002
	+CRF	26.7	0.14
	+BMI		
	+Fasting insulin		
DBP	VAT	22.0	<0.0001
	+Age	27.5	<0.0001
	+CRF	28.4	0.10
	+BMI		
	+Fasting insulin		

Variables included in the multivariate model were SBP, DBP, VAT, age, BMI, CRF, and fasting insulin.

Table 2 presents the independent contributors to the variations in SBP and DBP. In men and women combined, VAT and age were found to be the best predictors of both SBP and DBP. In men, age was the most important contributor to variation in DBP, whereas in women both VAT and age predicted the variance in SBP and DBP. Our studied cardiometabolic risk markers predicted 26.7% and 28.4% of the variation in SBP and DBP, respectively, in women. However, cardiometabolic risk markers predicted only 7.4% and 16.0% of the variations in SBP and DBP in men. We repeated these analyses excluding participants with hypertension and found no differences in the main findings (data not shown).

Spearman correlation coefficients among age, BMI, VAT, and plasma levels of fasting insulin and C-reactive protein, as

well as CRF and circulating levels of inflammatory markers, are presented in Table 3 before and after adjustment for either CRF or VAT accumulation. In men and women, VAT showed the highest association with both SBP and DBP, even after adjustment for CRF. In fact, all of the cardiometabolic risk markers were found to be significantly associated with SBP and DBP before and after adjustment for CRF but not after adjustment for VAT in men. In women, only age appeared to be associated with SBP and DBP after adjusting for VAT levels. Interestingly, we found that the relationship between waist circumference and blood pressure was no longer existent after adjustment for visceral adiposity, whereas, after adjustment for waist circumference, the relationship between visceral adiposity and blood pressure remained statistically significant (results not shown). These observations suggest that the relationship between waist circumference and blood pressure appears to be explained by visceral adiposity.

To examine whether a high VAT level is associated with higher SBP and DBP, we classified men and women according to BMI ( $<25 \text{ kg/m}^2$  or  $\geq 25 \text{ kg/m}^2$ ) and then further classified overweight/obese subjects according to VAT level ( $<130 \text{ cm}^2$  or  $\geq 130 \text{ cm}^2$  in men and  $<100 \text{ cm}^2$  or  $\geq 100 \text{ cm}^2$  in women).<sup>17</sup> Figure 1 shows that overweight/obese participants with a low VAT accumulation had similar SBP (Figure 1A) and DBP (Figure 1B) than normal-weight participants. However, overweight/obese subjects with an elevated VAT level were characterized by significantly higher SBP and DBP compared with the 2 other subgroups.

Figure 2 presents mean values of SBP and DBP in men and women classified into sex-specific tertiles of CRF and then further subdivided into 2 groups by VAT level ( $<130 \text{ cm}^2$  or  $\geq 130 \text{ cm}^2$  for men and  $<100 \text{ cm}^2$  or  $\geq 100 \text{ cm}^2$  for women).<sup>17</sup> In participants with a low VAT level, those in the lowest fitness subgroups were characterized by higher mean SBP and DBP compared with subjects with low VAT and high CRF. However, among participants with high VAT levels, both mean SBP and DBP values were higher than those of participants with low VAT, irrespective of fitness levels.

## Discussion

Results of the present study show that individuals characterized by a high level of CRF have lower SBP and DBP than those with low fitness. However, our study also shows for the first time that such benefits of a high level of CRF are limited to individuals with low VAT levels. Indeed, irrespective of their fitness level, individuals with high VAT had systematically higher SBP ( $\approx 7$  to  $15 \text{ mm Hg}$ ) and DBP ( $\approx 4$  to  $8 \text{ mm Hg}$ ) than subjects with low levels of VAT. VAT was the best correlate of SBP and DBP, and the relationship between fitness and blood pressure was no longer significant after adjustment for VAT. We also observed that, irrespective of BMI, individuals with high VAT had the most detrimental blood pressure indices. Based on these results, it is reasonable to suggest that the relationship between poor fitness and high blood pressure might be related to the fact that unfit individuals are most likely to be characterized by high VAT levels rather than to their low fitness levels, per se.

**Table 3. Correlation Coefficients Between CVD Risk Factors/Markers and SBP and DBP Before and After Adjustment for Either CRF or VAT Accumulation**

Variable	SBP			DBP		
	Unadjusted	Adjusted for CRF	Adjusted for VAT	Unadjusted	Adjusted for CRF	Adjusted for VAT
<b>Men</b>						
Age	0.17*	0.16†	0.01	0.35*	0.32*	0.12
BMI	0.24*	0.21*	0.00	0.29*	0.31*	0.00
VAT	0.26*	0.24*		0.37*	0.41*	
Fasting insulin	0.17*	0.16†	0.07	0.13†	0.21*	-0.01
C-reactive protein (n=143)	0.17*	0.12	0.00	0.30*	0.27*	0.09
CRF	-0.18*		-0.11	-0.17*		0.00
<b>Women</b>						
Age	0.37*	0.35*	0.14†	0.43*	0.42*	0.19*
BMI	0.32*	0.31*	0.07	0.33*	0.34*	0.07
VAT	0.46*	0.44*		0.51*	0.48*	
Fasting insulin	0.12†	0.08	-0.01	0.10	0.06	-0.04
C-reactive protein (n=180)	0.30*	0.24*	0.08	0.29*	0.22*	0.03
CRF	-0.28*		-0.05	-0.30*		-0.07

\* $P < 0.05$ .† $P < 0.10$  and  $> 0.05$ .

Other studies have shown that individuals with high levels of CRF had lower SBP and DBP than those with low fitness.<sup>2,5</sup> In this regard, Carnethon et al<sup>3</sup> have shown that poor fitness in young adulthood is associated with the development of several CVD risk factors, including high blood pressure. It has also been suggested that moderate improvements in CRF achieved by moderate-intensity physical activity can improve hemodynamics and cardiac performance in prehypertensive individuals and reduce the work of the left ventricle, ultimately resulting in lower left ventricular mass.<sup>19,20</sup>

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure indicated that, for individuals aged 40 to 70 years, each increment of 20 mm Hg in SBP or 10 mm Hg in DBP doubles the risk of CVD across the entire BP range from 115/75 to 185/115 mm Hg.<sup>21</sup> We showed that, among men with high fitness levels, SBP was  $\approx 109$  mm Hg in men with low VAT and  $\approx 124$  mm Hg in men with high VAT ( $\approx 15$ -mm Hg difference). In the same subgroups, DBP was  $\approx 67$  mm Hg compared with 75 mm Hg in fit men with low and high VAT, respectively ( $\approx 8$ -mm Hg difference). Therefore, the results of our study may suggest that increased blood pressure might represent another potential link between VAT accumulation and CVD risk.

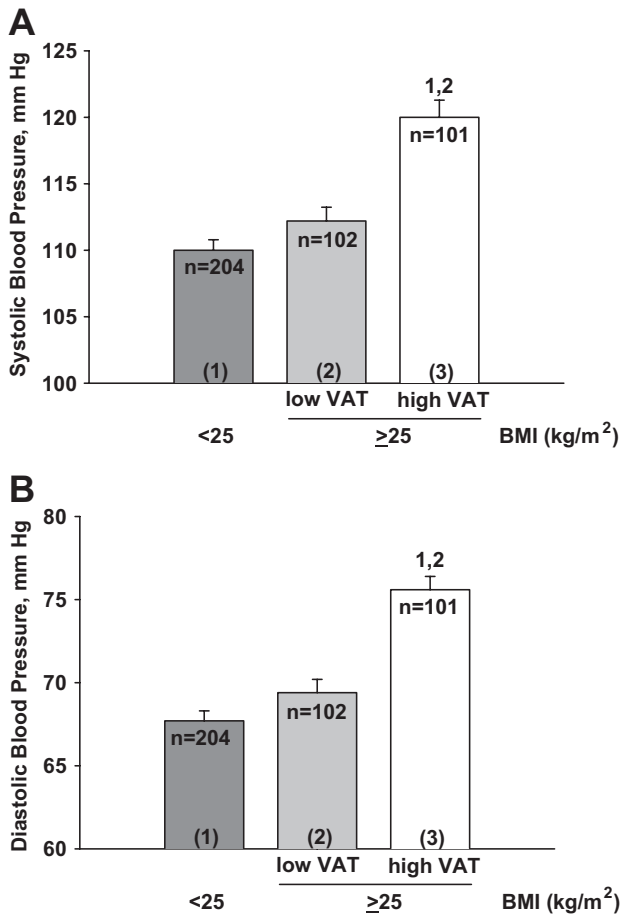
In contrast to our results, a previous study performed in men found that the relationship between VAT and SBP was somewhat strong in men with low CRF levels, whereas it was almost nonexistent in men with elevated CRF levels, suggesting that, independent of VAT, fit men had lower SBP.<sup>22</sup> Men included in the latter study were older and the prevalence of obesity was higher in that study sample.<sup>22</sup> The results of our study should not be seen as evidence against the importance of maintaining an adequate level of CRF.<sup>23</sup> In fact, our results

suggest that fit individuals had lower SBP and DBP because they had a healthier body composition and low levels of VAT.<sup>8</sup>

Several pathophysiological mechanisms may contribute to the higher blood pressure values observed in viscerally obese individuals. First, sympathetic activation associated with obesity and molecules released by hypertrophied fat cells may promote the formation of angiotensin and aldosterone, which have direct vasopressor and antinatriuretic effects, thereby increasing blood pressure.<sup>24</sup> Second, a local renin-angiotensinogen system was identified in human adipose tissue, where it may act independently from the plasma renin-angiotensinogen system.<sup>25,26</sup> Third, obesity, particularly abdominal obesity,<sup>27</sup> is characterized by an abnormal production of proinflammatory cytokines, arising from expanded abdominal fat<sup>28,29</sup> and related perivascular tissues,<sup>30,31</sup> which may have an influence on endothelial cells and vascular modulation. Obesity-associated insulin resistance has also been related to hypertension and related metabolic abnormalities. Of interest here is that individuals with insulin resistance and elevated fasting insulin levels are generally characterized by central obesity.<sup>10,32</sup>

Age was an important predictor of the variation in resting SBP and especially DBP in men of the present study. The relationship between blood pressure and age was highlighted recently in a systematic review.<sup>33</sup> Several studies have already shown that aging is associated with increased VAT accumulation<sup>34,35</sup> and that age-associated metabolic complications could be a consequence of VAT accumulation.<sup>36-38</sup> Therefore, studies are warranted to investigate whether the increased blood pressure associated with aging could be attributable to age-dependent VAT increases.

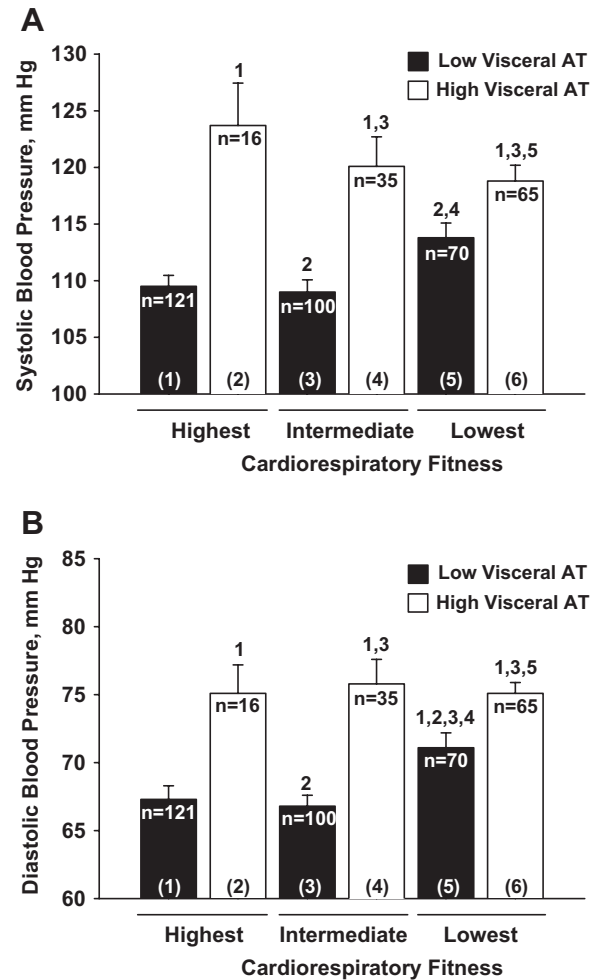
In women, VAT and age were the strongest predictors of SBP and DBP compared with men. It is well documented that



**Figure 1.** Mean SBP (A) and DBP (B) in men and women classified according to BMI (<25 kg/m<sup>2</sup> or ≥25 kg/m<sup>2</sup>) and further classified on the basis of VAT accumulation (<130 cm<sup>2</sup> or ≥130 cm<sup>2</sup> in men and <100 cm<sup>2</sup> or ≥100 cm<sup>2</sup> in women). 1, 2 significantly different from corresponding subgroup. *P*<0.05.

women (before menopause) have much less VAT than men. Accordingly, we have reported previously that this lower accumulation of VAT in women was an important factor to explain their more favorable CVD risk profile compared with men.<sup>39</sup> However, we have also reported previously that this gender difference in the CVD risk profile was largely attenuated when women and men with the same excess of VAT were compared. Thus, as found in the present article, these results suggest that visceral obesity (which is less common in women than in men) has a greater relative impact on their CVD risk factor profile compared with men.

An important strength of this study is that we directly quantified VAT level by computed tomography. In fact, VAT appeared to be more closely associated with blood pressure than waist circumference, a crude anthropometric measurement of abdominal adipose tissue accumulation. This observation, along with the above-mentioned biological mechanisms linking VAT and blood pressure, may suggest that, on top of estimating abdominal adiposity by anthropometry, careful attention should be given to approaches providing better estimates of visceral adiposity. Moreover, because our results show that fitness is moderately associated with blood pressure, maintaining an adequate level of fitness might help



**Figure 2.** SBP (A) and DBP (B) in men and women classified into sex-specific tertiles of cardiorespiratory fitness with either low or high VAT accumulation (<130 cm<sup>2</sup> or ≥130 cm<sup>2</sup> in men and <100 cm<sup>2</sup> or ≥100 cm<sup>2</sup> in women). 1, 2, 3, 4, 5: significantly different from corresponding subgroup. *P*<0.05.

in keeping blood pressure within the normal range. It must be kept in mind that our study population was limited to middle-aged white subjects in whom the prevalence of systemic hypertension was somewhat low. This may limit the generalizability of our findings to other populations with various ethnicities and with broader age ranges.<sup>40</sup>

It is also relevant to point out that our study sample was composed of participants with a certain degree of relatedness. We have, therefore, repeated some of the analyses presented in the article in unrelated children and in unrelated parents separately. Although a lack of statistical power did not allow us to always reach statistical significance, we found that the correlation coefficients (Table 3) were very similar to those observed in the overall sample. Thus, as for other CVD risk variables that we studied in the past,<sup>41</sup> we concluded that the familial structure of this database had no influence on the associations reported.

Based on our findings, we believe that longitudinal and/or intervention studies with specific measurements of fitness and visceral adiposity are required to properly investigate the risk factors for systemic hypertension. Although it might be

reasonable to believe that both fitness and visceral adiposity might be 2 important risk factors that independently contribute to the development of systemic hypertension, longitudinal and intervention studies are required to investigate the extent to which the relationship between fitness and systemic hypertension is explained by visceral adiposity. Moreover, because several studies have suggested that increasing physical activity and/or CRF levels are associated with decreased VAT accumulation,<sup>42,43</sup> further intervention studies will be needed to investigate whether increasing fitness levels and decreasing VAT accumulation will lead to improvements in blood pressure indices and, consequently, CVD risk. Identifying the risk factors for systemic hypertension and the extent to which these risk factors contribute to blood pressure are the keys in the development of successful blood pressure managing strategies.

### Perspectives

Results of the present study suggest that, independent of fitness levels, individuals with high VAT levels have an increased blood pressure. These results also suggest that VAT should be considered as an important target in the management of elevated blood pressure. In this regard, intervention and longitudinal studies are needed to evaluate the effectiveness of exercise program and other lifestyle interventions on VAT and in the management of systemic hypertension.

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### Disclosures

None.

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