Contributions of Cardiorespiratory Fitness and Visceral Adiposity to Six-Year Changes in Cardiometabolic Risk Markers in Apparently Healthy Men and Women

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Context: Both excess visceral adipose tissue (VAT) and low cardiorespiratory fitness (CRF) levels are associated with a deteriorated cardiometabolic risk profile.

Objective: The aim of the study was to examine the respective contributions of changes in VAT accumulation *vs.* changes in CRF to 6-yr longitudinal changes in cardiometabolic risk markers.

Design, Settings, and Participants: We conducted a prospective, population-based study with an average follow-up of 5.9 $\pm$ 0.8 yr. We followed 132 middle-aged participants from the Quebec Family Study (mean age, 35.3 $\pm$ 13.9 yr). VAT was measured by computed tomography, whereas the level of CRF was assessed by a submaximal physical working capacity test at baseline and at follow-up. A complete cardiometabolic risk profile, including systolic and diastolic blood pressure, fasting glucose and insulin levels, C-reactive protein (n = 72), as well as a standard lipoprotein-lipid profile, was obtained at baseline and at follow-up.

Main Outcome Measures: We measured changes in CRF, VAT, and cardiometabolic risk profile over 6 yr.

Results: After adjusting for age and sex, 6-yr changes in VAT were negatively correlated with changes in CRF ($r = -0.38$; $P < 0.001$). In a multivariate model that included age, sex, changes in VAT, changes in CRF, as well as baseline levels of the above cardiometabolic risk factors, 6-yr changes in VAT were the most important predictor of the change in the metabolic syndrome score ($R^2 = 13.2\%$; $P < 0.001$). Adding 6-yr changes in CRF levels significantly improved the predictability of the model ($R^2 = 19.7\%$; $P = 0.002$).

Conclusions: Changes in both VAT and CRF levels observed over 6 yr are associated with changes in parameters of the lipoprotein-lipid profile, glucose-insulin homeostasis, and inflammatory markers. Thus, maintaining a low level of VAT and a high level of CRF are important targets for maintenance of cardiometabolic health. **(*J Clin Endocrinol Metab* 96: 1462–1468, 2011)**

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Abbreviations: CRF, Cardiorespiratory fitness; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; MetS, metabolic syndrome; PWC, physical working capacity; SBP, systolic blood pressure; VAT, visceral adipose tissue.

Although controversy exists around the added value of a clinical diagnosis of the metabolic syndrome (MetS), available evidence has clearly shown that the simultaneous presence of the features of the MetS is associated with an increased relative risk of type 2 diabetes (3- to 5-fold increase) (1, 2) and cardiovascular disease (1.5- to 2-fold increase) (3–6) compared to individuals without MetS. Metabolic abnormalities considered as features of MetS are an atherogenic dyslipidemic state [elevated triglyceride and low high-density lipoprotein (HDL) cholesterol levels], systemic hypertension, insulin resistance, low-grade inflammation, and abdominal obesity (7–10).

It has been shown that weight gain is associated with MetS incidence (11). Although the etiology of the MetS is still a matter of debate, several lines of evidence suggest that irrespective of total body weight, a preferential accumulation of adipose tissue inside the abdomen, the so-called intraabdominal or visceral adipose tissue (VAT), is closely associated with the development of the MetS, independently of body weight, total body fat, or the content of other body fat compartments such as sc adipose tissue (12–15).

Numerous prospective studies have also reported that individuals with high levels of cardiorespiratory fitness (CRF) are at reduced risk of developing MetS (16–18) and of all-cause mortality (19–24). Previous cross-sectional studies from our laboratory have shown that independent of their CRF levels, individuals carrying a certain excess of VAT were nevertheless characterized by several features of the MetS such as dyslipidemia, insulin resistance, increased blood pressure, and low-grade inflammation (25, 26). However, whether maintaining a good level of CRF could protect against the development of the MetS among individuals increasing or decreasing VAT accumulation over time remains unclear. To the best of our knowledge, no study has yet evaluated the respective contributions of specific changes in VAT accumulation and CRF over time to longitudinal changes in cardiometabolic risk markers. The objective of this 6-yr longitudinal study was to test the hypothesis that individuals who would maintain adequate levels of both CRF and VAT would be able to maintain a healthy cardiometabolic risk profile over time.

Subjects and Methods

Study subjects

Study subjects were asymptomatic men and women who participated in the Québec Family Study (QFS), a longitudinal study including three phases: 1, 1980–1982; 2, 1989–1995; and 3, 1997–2001. We considered phase 2 as baseline. The mean duration of follow-up was 5.87 ± 0.84 yr. The study sample included healthy men and women with data on body composition, CRF, and plasma levels of cardiometabolic risk markers at baseline and after the follow-up. 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 Université Laval. Subjects were recruited through the media and gave their written informed consent to participate in the study. Only asymptomatic men and women, 18 to 65 yr of age, who were not under treatment for cardiovascular disease, diabetes, 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 (27). The mean of six measurements was used to calculate percentage body fat from body density using the equation of Siri (28). Fat mass was obtained by multiplying body weight by percentage body fat. Measurement of abdominal VAT areas was performed by computed tomography with a Siemens Somatom DHR scanner (Siemens, Erlanger, Germany). Briefly, participants were examined in the supine position with both arms stretched above the head. The scan was performed at the abdominal level (L4 and L5 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. Abdominal VAT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity. Abdominal sc adipose tissue area was calculated by subtracting the VAT area from the total abdominal adipose tissue area. Resting blood pressure was measured in the morning when participants were in the fasting state and in a sitting position after a 45-min rest using mercury sphygmomanometer (proper) and an appropriately sized cuff (Welch Allyn Tycos, Skaneateles Falls, NY), according to standard procedures. Participants were asked to refrain from smoking for 2 h before the procedure. Blood pressure values are the mean of two different measurements.

Biochemical analyses

After a 12-h overnight fast, blood samples were collected from an antecubital vein into Vacutainer tubes containing EDTA (Miles Pharmaceuticals, Rexdale, Ontario, Canada) 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, Tarrytown, NY), and enzymatic reagents were obtained from Randox Laboratories Ltd. (Crumlin, UK). Plasma very low-density lipoproteins (LDLs) (density < 1.006 g/ml) were isolated by ultracentrifugation (29), and the HDL fraction was obtained after precipitation of LDLs in the infranatant (density > 1.006 g/ml) with heparin and $MnCl_2$ (30). The cholesterol content of the infranatant fraction was measured before and after the precipitation step, allowing the calculation of LDL-cholesterol. ELISAs were used to measure plasma adiponectin (B-Bridge International, Inc., San Jose, CA), IL-6, and TNF-α (R&D Systems Inc., Minneapolis, MN). Plasma C-reactive protein (CRP) levels were measured with a highly sensitive immunoassay that used a monoclonal antibody coated with polystyrene particles (high-sensitivity CRP); the assay was per-

formed with a Behring BN-100 nephelometer (Dade Behring, Deerfield, IL). Participants with plasma levels of CRP above 10 mg/dl were excluded from the analyses on inflammatory markers. Frozen plasma samples for the measurement of inflammatory markers before and after the follow-up were only available for 72 subjects. Plasma glucose was measured enzymatically, whereas plasma insulin was measured by RIA with polyethylene glycol separation (31). The homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated as previously described for each participant (32).

Assessment of CRF

CRF of each participant was assessed by a progressive submaximal physical working capacity (PWC) test performed on a modified Monark cycle ergometer (Stockholm, Sweden). Heart rate was measured through one electrocardiogram derivation and recorded during three consecutive 6-min workloads, each separated by a 1-min rest. The test was designed to exceed a heart rate of 150 beats per minute at the end of the last workload. PWC_{150}, which is the power output at 150 beats per minute, was then calculated from the linear relationship between heart rate and power output. To take into account the individual differences in body weight, PWC_{150} was expressed by kilograms of body weight and was specifically used as the marker of CRF in the present study.

Statistical analyses

Data are presented as mean ± SD or median (interquartile range) in Tables 1 and 2 and as mean ± SEM in Fig. 1. Baseline anthropometric and metabolic characteristics of participants are presented in men and women separately. Paired *t* tests were performed to compare baseline and follow-up levels of cardiometabolic risk markers and anthropometric parameters. Based on the changes in cardiometabolic risk markers over the follow-up period [systolic blood pressure (SBP), diastolic blood pressure (DBP), HOMA-IR index, as well as triglyceride and HDL cholesterol levels], a "metabolic syndrome score" was developed. Participants were allowed one point when a change in one of the above risk markers was equal to or above the 75th percentile of the distribution of changes observed over 6-yr in the whole cohort (equal to or below the 25th percentile for HDL cholesterol). Over the 6-yr follow-up period, the 75th percentile of changes corresponded to an increase in SBP of 6.0 mm Hg, an increase in DBP of 4.0 mm Hg, an increase in the HOMA-IR index of 1.26 U, and an increase in triglyceride levels of 0.23 mmol/liter; and finally, the 25th percentile of HDL cholesterol changes corresponded to a decrease in HDL cholesterol levels of −0.13 mmol/liter. Mean changes in cardiometabolic risk markers and in the MetS score were also obtained in participants classified on the basis of median changes in VAT and CRF ($<$ or $\geq$ 11.83 cm^2 for VAT; and $<$ or $\geq$ 1.0 kilopond per minute/kg for CRF). Because there was no important difference between either VAT or CRF variations over time in men and women, pooled analyses were conducted. Because plasma levels were available in a smaller proportion of the study sample, we did not include changes in inflammatory markers. Multiple regression analyses were also performed to quantify the respective contributions of changes in VAT and CRF to the variance in cardiometabolic risk variables over time. A P value <0.05 was considered to be statistically significant. All statistical analyses were performed with the SAS package (SAS Institute, Cary, NC).

Results

A complete cardiometabolic risk profile was available for 132 participants at baseline and after a mean follow-up of 6 yr. Characteristics of the study participants before and after the follow-up period are presented in Table 1. During that timeframe, most men and women gained weight, and all body fatness indices were significantly increased at follow-up. CRF levels were higher after 6 yr than at the beginning of the study. Among the parameters of the lipoprotein-lipid profile, total and LDL cholesterol levels, as well as the total to HDL cholesterol ratio decreased. However, there were no changes in fasting triglycerides and HDL cholesterol levels, indicating that the change in the total to HDL cholesterol ratio is largely attributable to the decrease in non-HDL cholesterol levels. Most of the parameters of the glucose-insulin homeostasis were higher after the study follow-up. Although significant decreases were observed in plasma levels of adiponectin, changes in inflammatory markers were mostly inconsistent.

Based on the changes in cardiometabolic risk markers over the follow-up (SBP, DBP, insulin resistance, as well as triglyceride and HDL cholesterol levels), a MetS score was developed (see *Statistical analyses*). MetS score represents the change in the severity indices of our cardiometabolic risk variables as a function of changes in VAT and CRF.

Table 2 presents the results of multivariate regression analyses that considered the contributions of changes in VAT, changes in CRF, age, sex, and baseline levels of cardiometabolic risk markers to the variance in the response of the cardiometabolic risk markers and MetS score over time. Changes in VAT were associated with changes in SBP (R^2 = 16.0%; $P < 0.001$), DBP (R^2 = 10.9%; $P < 0.001$), HOMA-IR index (R^2 = 7.3%; $P < 0.05$), and CRP (R^2 = 17.9%; $P = 0.005$). Changes in CRF were associated with changes in HDL cholesterol (R^2 = 7.3%; $P < 0.05$). Changes in both VAT and CRF were associated with changes in the MetS score (R^2 = 13.2%, $P < 0.001$; and R^2 = 19.7%, $P = 0.002$, respectively).

Although changes in CRF and VAT were negatively correlated ($r = -0.38$; $P < 0.001$ after adjusting for age and sex), the correlation was of moderate magnitude. This moderate association suggests that several participants increased VAT over the follow-up period without concomitant changes in CRF, whereas other subjects decreased CRF without concomitant changes in VAT. Figure 1 illustrates mean changes in MetS score in participants classified on the basis of changes in VAT (below or equal or above median) and changes in CRF levels (below or equal or above median). Fig. 1 shows that individuals who increased their VAT and decreased their CRF had the most detrimental changes in indices of severity of MetS score

TABLE 1. Characteristics of men and women before and after the study follow-up

	Men (n = 68)				Women (n = 64)			
	Baseline	6-yr follow-up	% change	*P* value	Baseline	6-yr follow-up	% change	*P* value
Age (yr)	36.9 ± 14.7	42.7 ± 14.7			33.7 ± 13.0	39.6 ± 12.9		
PWC (kpm/kg)	11.0 ± 3.3	12.2 ± 3.3	10.9	<0.001	7.3 ± 2.4	8.4 ± 2.9	15.1	<0.001
Body mass index (kg/m^2)	25.7 ± 4.3	26.5 ± 4.5	3.1	0.001	24.2 ± 4.5	25.3 ± 4.5	4.5	<0.001
Waist circumference (cm)	88.6 ± 12.2	91.2 ± 12.8	2.9	<0.001	75.5 ± 11.5	78.4 ± 12	3.8	<0.001
AT accumulation (cm^2)								
Total	305.0 ± 184.3	329.6 ± 187.5	8.1	0.002	328.0 ± 162.7	371.5 ± 171.2	13.3	<0.001
Visceral	105.0 ± 61.5	119.2 ± 74.7	13.5	<0.001	69.9 ± 49.4	81.1 ± 51.4	16.0	<0.001
Subcutaneous	200.0 ± 133.3	210.4 ± 126.5	5.2	0.04	258.1 ± 128.1	290.4 ± 132.3	12.5	<0.001
SBP (mm Hg)	117 ± 11	116 ± 14	−0.8	0.40	112 ± 12	113 ± 19	0.9	0.50
DBP (mm Hg)	73 ± 10	72 ± 12	−1.4	0.22	69 ± 9	70 ± 13	1.4	0.68
Total cholesterol (mmol/liter)	4.85 ± 0.95	4.70 ± 0.91	−3.1	0.04	4.78 ± 0.91	4.46 ± 0.96	−6.7	<0.001
LDL cholesterol (mmol/liter)	3.07 ± 0.77	2.92 ± 0.74	−4.9	0.03	2.90 ± 0.78	2.58 ± 0.80	−11.0	<0.001
HDL cholesterol (mmol/liter)	1.15 ± 0.25	1.15 ± 0.24	0.0	0.98	1.36 ± 0.33	1.38 ± 0.32	1.5	0.60
Total cholesterol/HDL cholesterol	4.41 ± 1.28	4.27 ± 1.19	−3.2	0.10	3.67 ± 0.98	3.43 ± 1.03	6.5	<0.001
Triglycerides (mmol/liter)	1.26 (0.90–1.71)	1.31 (0.95–1.63)	4.0	0.48	1.11 (0.86–1.38)	0.99 (0.68–1.47)	−10.8	0.20
Glucose (mmol/liter)	5.28 ± 0.73	5.72 ± 1.5	8.3	<0.001	4.86 ± 0.42	5.10 ± 0.49	4.9	<0.001
Insulin (pmol/liter)	46.5 (34.0–71.5)	62.0 (44.5–85.5)	33.3	0.06	47.5 (29.5–64.5)	57.0 (31.5–71.5)	20.0	0.05
HOMA-IR	1.85 (1.31–2.81)	2.38 (1.70–3.58)	28.6	0.01	1.71 (1.11–2.24)	2.05 (1.21–2.75)	19.9	0.006
CRP (mg/liter)[a]	0.74 (0.36–2.00)	0.74 (0.27–1.22)	0.0	0.08	1.56 (0.56–3.46)	2.05 (0.57–3.24)	31.4	0.65
Adiponectin ($\mu g/ml$)[a]	5.06 (3.57–6.98)	4.37 (3.53–5.06)	−13.6	0.04	7.76 (5.32–9.88)	5.60 (4.57–7.10)	−27.8	<0.001
IL-6 (pg/ml)[a]	1.24 (0.93–1.62)	1.12 (0.72–1.93)	−9.7	0.17	1.35 (1.00–2.26)	1.25 (0.87–2.26)	−7.4	0.34
TNF-α (pg/ml)[a]	1.65 (1.35–2.02)	1.58 (1.35–1.74)	−4.2	0.13	1.63 (1.39–1.89)	1.44 (1.21–1.65)	−11.7	0.02

Data are presented as mean ± SD or median (interquartile range). AT, Adipose tissue.

[a] n = 72 (participants with CRP levels above 10 mg/ml at baseline or at follow-up were excluded).

compared with the other subgroups. Supplemental Fig. 1A (published on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org) shows that although the relationship did not reach statistical significance, individuals who improved their CRF over the study follow-up appeared to have lowered their SBP, whereas those who decreased their CRF increased in their SBP, independently of their changes in VAT. Participants who had the lowest increase in VAT and the smallest decrease in CRF were the only subgroup who showed a decrease in DBP over the 6-yr follow-up (Supplemental Fig. 1B). As for the HOMA-IR index, only participants who had simultaneous increases in VAT and decreases in CRF levels showed an increase in the HOMA-IR index over the follow-up period (Supplemental Fig. 1C). Participants who did not increase their VAT showed no change in triglyceride levels, whereas those who increased their VAT experienced a small increase in their triglyceride levels, but only in the presence of a simultaneous decrease in CRF (Supplemental Fig. 1D). Finally, individuals who had the smallest increase of VAT combined with an increase in CRF levels significantly increased their HDL cholesterol levels, with no changes observed in the other subgroups (Supplemental Fig. 1E).

Discussion

In this 6-yr longitudinal study conducted in a population of asymptomatic men and women, we found that changes in VAT were associated with changes in SBP, DBP, HOMA-IR index, and CRP. On the other hand, only

TABLE 2. Multivariate regression analyses showing the contributions of changes in VAT, CRF, age, sex, and baseline levels of cardiometabolic risk markers to the variance of the cardiometabolic risk markers and MetS score

Changes	Independent variables	Total R^2 (%)	*P* value
SBP	Age at baseline	16.0	<0.0001
	+ Changes in VAT	20.7	0.006
	+ Triglycerides at baseline	20.1	0.05
DBP	DBP at baseline	10.9	<0.0001
	+ Changes in VAT	16.8	0.003
	+ Age at baseline	19.5	0.04
HOMA-IR index	Changes in VAT	7.3	0.002
	+ Age at baseline	12.0	0.01
	+ HOMA-IR at baseline	15.0	0.04
Triglycerides	Triglycerides at baseline	22.4	<0.0001
	+ Age at baseline	32.9	<0.0001
	+ Sex	34.3	0.10
HDL cholesterol	HDL cholesterol at baseline	12.6	<0.0001
	+ Changes in CRF	17.9	0.005
	+ Sex	20.5	0.04
	+ SBP at baseline	22.8	0.05
MetS score	Changes in VAT	13.2	<0.0001
	+ Changes in CRF	19.7	0.002
	+ HDL cholesterol at baseline	22.6	0.03
	+ Age at baseline	25.7	0.02
	+ DBP at baseline	27.3	0.09
CRP[a]	Changes in VAT	17.3	0.0003
	+ Sex	19.8	0.14
Adiponectin[a]	HOMA-IR at baseline	5.4	0.05
IL-6[a]	SBP at baseline	5.3	0.05
TNF-α[a]	Sex	7.6	0.02
	+ SBP at baseline	10.8	0.12

Variables included in the model were changes in VAT, CRF, sex, age, HOMA-IR index, SBP, DBP, triglycerides, and HDL cholesterol levels at baseline as well as baseline levels of VAT and CRF.

[a] n = 72 (participants with CRP levels above 10 mg/ml at baseline or at follow-up were excluded). +, Variables added in the model.

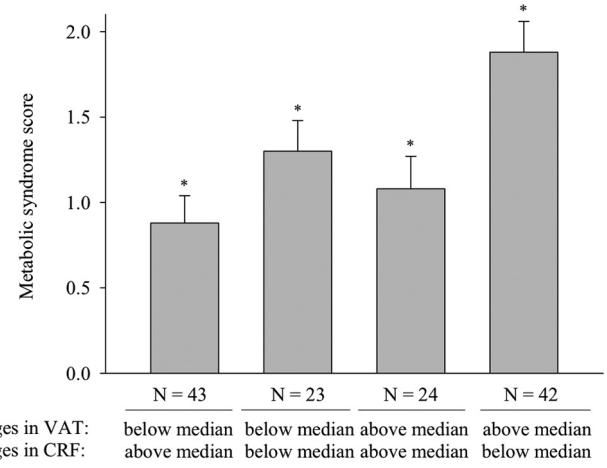

FIG. 1. Mean changes in indices of severity of MetS score in participants classified on the basis of changes in VAT accumulation (low = below median; high = above or equal to median) and changes in CRF levels (low = above or equal to median; high = below median). *, $P < 0.05$. See Supplemental Fig. 1 for changes in SBP (A), DBP (B), HOMA-IR index (C), plasma triglyceride levels (D) and plasma HDL cholesterol levels (E). §, $P < 0.10$ and >0.05 in Supplemental Fig. 1D.

changes in CRF were independently associated with changes in HDL cholesterol levels. Changes in both VAT and CRF were associated with changes in the MetS score. We also found that individuals who increased their VAT and who decreased their CRF over time experienced the most detrimental changes in their cardiometabolic risk profile. Taken together, these observations provide for the first time longitudinal data suggesting that maintaining low levels of VAT and high levels of CRF are both important targets for the maintenance of a healthy cardiometabolic risk profile in asymptomatic individuals.

Comparison with other studies

VAT is closely associated with the development of the MetS, independently of the other body fat compartments such as sc adipose tissue and specific measures of insulin resistance (12–15). Additionally, numerous prospective studies have reported that high levels of CRF are associated with lower risk of MetS (16–18, 33) and all-cause mortality (19–24, 34). Previous cross-sectional studies from our laboratory have confirmed the notion that independent of CRF, individuals carrying a certain excess of VAT were simultaneously characterized by several features of the MetS such as dyslipidemia, insulin resistance, high blood pressure, and low-grade inflammation (26, 35). The present longitudinal study provides evidence that individuals with the largest increment of CRF and decrement in VAT had the most substantial improvements in their cardiometabolic risk factors/markers over a 6-yr follow-up period. In a previous cross-sectional study, we have suggested that the relationship between poor CRF and high blood pressure might be related to the fact that unfit individuals were most likely characterized by high VAT levels (26). We have also reported similar findings regarding other features of the MetS and plasma biomarkers of low-grade inflammation (25). We believe that this prospective study further reinforces the notion that apparently healthy individuals should be encouraged to maintain low levels of VAT and adequate levels of CRF to prevent them from the development of atherogenic and diabetogenic metabolic abnormalities.

Pathophysiological consequences of high VAT and low CRF levels

Several pathophysiological mechanisms may contribute to explaining our observations that both VAT and CRF were associated with changes in the cardiometabolic risk profile. For instance, VAT secretes several adipokines that may impact numerous biological systems such as

plasma glucose-insulin homeostasis, lipoprotein-lipid metabolism, immune response, thrombosis, as well as regulation of blood pressure. This has led several investigators to suggest that adipose tissue, and especially VAT, is at the center of an important cross-talk among several other organs such as liver, skeletal muscle, heart, pancreas, and brain. It is also reasonable to believe that because most individuals with poor CRF levels concomitantly show elevated VAT levels, such an accumulation of VAT may represent an important biological mediator in the relationship between low CRF levels and a deteriorated cardiometabolic risk profile. However, our results suggest that the relationship between changes in CRF levels and specific cardiometabolic risk markers may well be partly independent of VAT. For instance, several studies have shown that increasing physical activity/CRF levels have beneficial HDL-raising effects (16, 36). Similar observations were also found for the relationship between CRF and blood pressure (37–39).

Study strengths and limitations

An important strength of our study is that an extensive cardiometabolic risk profile was measured both at baseline and after the 6-yr follow-up period. Moreover, we have directly measured body fat distribution by computed tomography. However, it must be kept in mind that our study sample is of limited size and it only includes middle-aged Caucasians in whom the prevalence of MetS was somewhat low. This may limit our ability to translate our findings to other populations and ethnic groups with broader age ranges (40).

Clinical implications

In primary care facilities, VAT is not routinely assessed by computed tomography. As an alternative, we believe that the measurement of waist circumference, a crude marker of visceral adiposity, could be used by primary care physicians to identify patients who are at high-risk for hypertension and/or MetS (41). In this regard, we also found that changes in SBP, triglyceride, HDL, insulin resistance, adiponectin, IL-6, and TNF-α were all significantly associated with 6-yr changes in waist circumference (data not shown). It is important to point out that the objective of our study was to investigate the "natural" evolution of the cardiometabolic risk profile associated with changes in VAT and CRF over time. We believe that intervention studies with specific measurements of fitness and visceral adiposity are required to properly investigate their association with the cardiometabolic risk profile. Additionally, because our results show that both VAT and CRF have a strong impact on the cardiometabolic risk profile, we believe that further studies are warranted to investigate whether or not CRF and VAT both contribute to predicting cardiovascular endpoints and/or type 2 diabetes incidence.

In conclusion, our results suggest that VAT and CRF have additive and independent contributions to the variation in cardiometabolic risk factors over time. Therefore, targeting both VAT and CRF should be considered for the maintenance of a healthy cardiometabolic risk profile in primary care.

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