Cardiorespiratory Fitness Attenuates Metabolic Risk Independent of Abdominal Subcutaneous and Visceral Fat in Men

SOJUNG LEE, MSC[1]
JENNIFER L. KUK, MSC[1]
PETER T. KATZMARZYK, PHD[1,2]
STEVEN N. BLAIR, PED[3]
TIMOTHY S. CHURCH, MD, PHD[3]
ROBERT ROSS, PHD[1,4]

OBJECTIVE — Moderate to high levels of cardiorespiratory fitness (CRF) are associated with a lower risk of the metabolic syndrome and all-cause mortality. Unknown is whether CRF attenuates health risk for a given level of abdominal visceral fat, subcutaneous fat, and/or waist circumference.

RESEARCH DESIGN AND METHODS — The sample studied comprised 297 apparently healthy men with available computed tomography or magnetic resonance imaging scans of the abdomen, metabolic data, and maximal treadmill exercise test results. Men were categorized into low-CRF (20%, $n = 56$), moderate-CRF (40%, $n = 94$), and high-CRF (40%, $n = 147$) groups based on age and exercise test results. All analyses were adjusted for age.

RESULTS — For a given level of waist circumference, visceral fat, or subcutaneous fat, the high-CRF group had lower triglyceride levels ($P < 0.05$) and higher HDL cholesterol levels than the low- or moderate-CRF groups. There was a significant group interaction ($P < 0.01$) for blood pressure, indicating that the increase in blood pressure per unit increase in visceral fat or waist circumference was greater in men in the low-CRF group compared with the high-CRF group. The relative risks of having the metabolic syndrome were 1.8 (95% CI 1.0–3.1) and 1.6 (0.9–2.7) times higher in the low- and moderate-CRF groups, respectively, compared with the high-CRF group after adjusting for age, visceral fat, and subcutaneous fat (P for trend = 0.06).

CONCLUSIONS — High levels of CRF are associated with a substantial reduction in health risk for a given level of visceral and subcutaneous fat.

Diabetes Care 28:895–901, 2005

It is well established that abdominal adiposity is a strong predictor of morbidity and mortality independent of BMI (1,2). It is also reported that high levels of cardiorespiratory fitness (CRF) are associated with lower risk of metabolic syndrome (3) and all-cause mortality (4–6). Although both abdominal fat and low CRF are significant predictors of health risk, the independent contribution of these two factors is not firmly established. Recently, Ross and Katzmarzyk (7) reported that for a given BMI, individuals with high CRF had lower abdominal skinfold thickness and waist circumference compared with individuals with lower CRF, independent of sex. Similarly, Wong et al. (8) report that for a given BMI, men with high CRF have lower total abdominal, visceral, and abdominal subcutaneous fat levels compared with men with low CRF, a finding that remains true for African-American men and women (9). Although it is clear that high CRF is associated with lower levels of abdominal adiposity, the association between CRF and measures of metabolic health for a given level of abdominal subcutaneous and/or visceral adiposity remains largely unknown.

Regular physical activity is an effective means of improving CRF and reducing waist circumference, visceral fat, and subcutaneous fat independent of a corresponding change in BMI (10,11). Furthermore, regular physical activity is also associated with favorable changes in blood lipid profiles, blood pressure, and glucose metabolism; these improvements often occur with little or no improvement in BMI (12). Recently, Nagano et al. (13) reported that high CRF is associated with a lower risk of hyperinsulinemia and increased HDL cholesterol levels after controlling for visceral fat in Japanese individuals with glucose intolerance and type 2 diabetes. In that study, the authors combined men and women in their analyses and did not simultaneously control for subcutaneous abdominal fat and/or waist circumference. Both abdominal subcutaneous fat (14) and waist circumference (15) are reported to be strong, independent correlates of metabolic risk.

The primary purpose of this study was, therefore, to determine whether higher levels of CRF are associated with lower levels of selected metabolic risk factors for a given level of abdominal subcutaneous fat, visceral fat, and waist circumference. To examine this question, we studied a sample of Caucasian men

From the [1]School of Physical and Health Education, Queen's University, Kingston, Ontario, Canada; the [2]Department of Community Health and Epidemiology, Queen's University, Kingston, Ontario, Canada; the [3]Centers for Integrated Health Research, The Cooper Institute, Dallas, Texas; and the [4]Division of Endocrinology and Metabolism, Department of Medicine; Queen's University, Kingston, Ontario, Canada.
Address correspondence and reprint requests to Robert Ross, PhD, School of Physical and Health Education, Queen's University, Kingston, Ontario, Canada, K7L 3N6. E-mail: rossr@post.queensu.ca.
Received for publication 8 September 2004 and accepted in revised form 2 January 2005.
Abbreviations: CRF, cardiorespiratory fitness.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

varying widely in abdominal adiposity and CRF.

RESEARCH DESIGN AND METHODS

— At Queen's University (Kingston, Canada), subjects comprised 95 men who had participated in body composition studies and were recruited via the general media. At the Cooper Clinic (Dallas, TX), subjects comprised 202 white men who voluntarily received a comprehensive medical examination including computed tomography, maximal exercise test, and clinical examination. Inclusion criteria required that the subjects were white, were nonsmokers, and were not taking medications known to affect the primary outcome variables. Exclusion criteria were a history of diabetes, cardiovascular disease, or cancer. All participants gave informed consent in accordance with the ethical guidelines of the respective institutional review boards.

Venous blood samples were obtained from the antecubital vein after a 12-h overnight fast. Measurements included total cholesterol, HDL cholesterol, triglyceride, and glucose levels using standard analytical techniques. Blood pressure was measured with a mercury sphygmomanometer using auscultatory methods. Body mass was measured on a balance scale with the subjects dressed in standard T-shirts and shorts. Barefoot standing height was measured to the nearest 0.1 cm using a stadiometer. Waist circumference was obtained at the level of the umbilicus. Metabolic syndrome was defined according to the criteria established by Adult Treatment Panel III (16). Participants were classified as having the metabolic syndrome if they had three or more of the following risk factors: *1*) high blood pressure (≥130 mmHg systolic); 2) central obesity (waist circumference >102 cm); *3*) high triglyceride level (≥150 mg/ml); *4*) low HDL cholesterol level (<40 mg/ml); and *5*) high fasting plasma glucose level (≥110 mg/ml).

Measurement of visceral and subcutaneous fat

A single axial image of the abdomen (L4–L5) was obtained using a 1.5-Tesla magnetic resonance imaging scanner (General Electric, Milwaukee, WI) at Queen's University, and with an electron beam computed tomography scanner (Imatron; General Electric, Milwaukee, WI) at the Cooper Clinic using established protocols (17,18). For magnetic resonance imaging, images were obtained using a T1-weighted, spin-echo sequence (TR = 210 ms, TE = 17 ms) with a 480-mm field of view and a 256-squared matrix. For computed tomography, images (L4–L5) were obtained using 130 kV and 630 mA with a 480-mm field of view and a 512 × 512 matrix.

Maximal treadmill test

At Queen's University, CRF was determined by $V\text{O}_{2\text{max}}$ using a graded maximal treadmill test. For all subjects, the treadmill speed, predetermined during a practice session, was held constant. The initial grade was set at 0% for the 1st and 2nd min, was 2% for the 3rd min, and was increased by 1% every 2 min thereafter. All tests used standard open-circuit spirometry techniques (SensorMedics, Yorba Linda, CA). $V\text{O}_{2\text{max}}$ was attained when at least two of the following three criteria were achieved: no increase in $V\text{O}_{2\text{max}}$ despite further increases in treadmill grade, a heart rate at or above age-predicted maximum (220 − age), and/or a respiratory exchange ratio in excess of 1.0. At the Cooper Clinic, CRF was evaluated with a maximal exercise test performed on a treadmill according to a modified Balke procedure (19). Initial treadmill speed was 88 m/min. The grade was 0% for the 1st min, was 2% for the 2nd min, and then was increased by 1% every minute until 25 min. For participants able to continue beyond 25 min, the grade remained constant, and the speed was increased 5.4 m/min each minute until test termination. Total treadmill endurance time with this protocol has been shown to highly correlate with $V\text{O}_{2\text{max}}$ ($r = 0.94$) (20). Total treadmill time was converted to $V\text{O}_{2\text{max}}$ using a standard prediction equation (20).

Statistical analyses

Participants were categorized as low CRF (lowest, 20%), moderate CRF (middle, 40%), or high CRF (highest, 40%) based on age-specific $V\text{O}_{2\text{max}}$ cutoff points derived from the Aerobics Center Longitudinal Study cohort (6). A one-way ANOVA was used to examine differences in subject characteristics across fitness groups. When the ANOVA result was significant ($P < 0.05$), a Tukey's post hoc comparison test was used to identify specific between-group differences. General linear models were used to determine the influence of CRF on the relationship between abdominal obesity and metabolic risk. CRF and abdominal measures (waist circumference, visceral fat, and subcutaneous fat) were the independent variables and metabolic risk factors were the dependent variables. Both abdominal measures and metabolic risk factors were entered as continuous variables, whereas CRF groups were entered as categorical variables in the general linear models. Both the main effects for CRF group and interaction effects (e.g., visceral fat × CRF group) were included in each of the models to test for the equality of slopes. If the interaction effects were not significant (e.g., the slopes were not different), the analyses for main effects were repeated excluding the interaction term. All analyses were adjusted for age.

All general linear models were tested for institutional differences in the relationships between waist circumference, visceral fat, and subcutaneous fat and metabolic risk. An institution term was added to the models to examine the influence of institutions on the relationships between all the independent variables. Because no institutional interactions were found in any model, subjects from the two institutions were pooled for all analyses. To facilitate comparisons, all figures were standardized to a 40-year-old individual.

Proc GENMOD was used to determine the relative risk (RR) and 95% CI estimates for the metabolic syndrome between the CRF groups. For these analyses, tertiles of age, visceral fat, and abdominal subcutaneous fat were used as the independent variables in the models. The presence of the metabolic syndrome was coded as a categorical variable and was used as the dependent variable in the models. The high-CRF group was used as the reference category (RR 1.0). All analyses were performed using SAS software and procedures (version 8; SAS Institute, Cary, NC).

RESULTS

— The subject characteristics in Table 1 show that the subjects varied widely in age, all measures of abdominal adiposity, and CRF.

Relationship between waist circumference, visceral fat, and metabolic risk

For a given level of waist circumference (Fig. 1*A*) or visceral fat (Fig. 2*A*), men with high CRF had lower triglyceride lev-

Table 1—*Subject characteristics*

	Low-CRF group	Moderate-CRF group	High-CRF group
n	56	94	147
Age (years)	45.4 ± 8.5 (25–62)*	49.4 ± 8.2 (30–69)	51.4 ± 7.5 (27–73)
Body mass (kg)†	101.3 ± 13.6 (72–137)	91.7 ± 11.9 (61–124)	86.3 ± 11.6 (60–126)
BMI (kg/m^2)†	32.1 ± 3.5 (23.5–40.8)	29.1 ± 3.4 (20.8–35.8)	26.9 ± 3.2 (21.2–38.3)
Waist circumference (cm)†	111.0 ± 9.4 (92–133)	103.4 ± 9.2 (80–121)	94.9 ± 10.1 (70–129)
Vo_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)†	29.7 ± 3.7 (20.5–36.2)	36.2 ± 3.7 (26.4–43.2)	44.3 ± 4.6 (35.2–58.3)
Visceral fat (cm^2)	170.0 ± 55.7 (71–293)	162.7 ± 51.1 (63–280)	130 ± 55 (29.9–284.2)‡
Subcutaneous fat (cm^2)†	326.8 ± 97.3 (165–607)	267.3 ± 82.7 (115–487)	214.2 ± 79.7 (35–484)
Total cholesterol (mg/dl)	201.8 ± 35.2 (135–310)	203.6 ± 35.2 (135–299)	204.9 ± 40.0 (109–308)
Triglycerides (mg/dl)	207.8 ± 130.4 (80–628)	174.9 ± 99.3 (47–602)	129.1 ± 64.7 (37–380)‡
HDL cholesterol (mg/dl)	35.7 ± 9.0 (13–55)*	43.3 ± 13.4 (9–98)	47.2 ± 10.2 (25–73)§
Fasting glucose (mg/dl)	100.8 ± 15.5 (73–148)	99.5 ± 10.3 (73–131)	99.9 ± 9.1 (76–124)
Systolic blood pressure (mmHg)‖	124.4 ± 15.3 (100–160)	122.9 ± 12.0 (100–150)	122.2 ± 10.8 (90–144)
Metabolic syndrome (%)	60	33.3	12.2

Data are means ± SD (range) unless otherwise indicated. *$P < 0.01$, different from moderate- and high-CRF groups; †$P < 0.01$, all groups are significantly different from each other; ‡$P < 0.01$, different from low- and moderate-CRF groups; §$P = 0.025$, different from moderate-CRF group; ‖obtained from $n = 31$, $n = 87$, and $n = 139$ in the low-, moderate-, and high-CRF groups, respectively.

els (main effect, $P < 0.05$) than men with low or moderate CRF. However, the low- and moderate-CRF groups were not different ($P > 0.05$). For a given level of waist circumference (Fig. 1*B*) or visceral fat (Fig. 2*B*), men with moderate or high CRF had a higher HDL cholesterol level (main effect, $P < 0.05$ for each) than men with low CRF. No significant difference was observed between men with moderate and high CRF ($P > 0.05$). No significant waist circumference or visceral fat × CRF group interactions for triglyceride or HDL cholesterol levels were observed, indicating that the slopes were not different between the groups ($P > 0.05$).

There was a significant group interaction ($P < 0.05$) for systolic blood pressure, indicating that the slope of the relationship between systolic blood pressure and waist circumference (Fig. 1*C*) or visceral fat (Fig. 2*C*) was significantly higher ($P < 0.01$) in the low-CRF group compared with the high-CRF group.

No group differences were observed in fasting glucose for a given level of waist circumference (Fig. 1*D*) or visceral fat (Fig. 2*D*).

Relationship between subcutaneous fat and metabolic risk

For a given level of subcutaneous fat, men with high CRF had lower triglyceride levels (main effect, $P < 0.05$) than men with low and moderate CRF (data not shown). No significant differences were observed between the low- and moderate-CRF groups ($P > 0.05$). Men with moderate and high CRF had a higher HDL cholesterol level (main effect, $P < 0.05$) than men with low CRF. No significant difference between the moderate- and high-CRF groups was observed ($P > 0.05$). No significant subcutaneous fat × CRF group interactions for triglyceride or HDL cholesterol levels were found, indicating that the slopes were not different between the groups ($P > 0.05$).

No CRF group differences were observed for systolic blood pressure or fasting glucose for a given level of subcutaneous fat (data not shown).

CRF and RRs for the metabolic syndrome

As depicted in Fig. 3, after adjustment for age, the RRs of having the metabolic syndrome were 4.6 (95% CI 2.7–7.8) and 2.7 (1.5−4.6) times higher in the low- and moderate-CRF groups, respectively, compared with the high-CRF group (*P* for trend <0.001). After adjustment for age and visceral fat, the RRs of having the metabolic syndrome were 2.5 (1.4–4.4) and 1.8 (1.0–3.1) times higher in the low- and moderate-CRF groups, respectively, than in the high-CRF group (*P* for trend <0.001). Similarly, after adjusting for age and subcutaneous fat, the RRs of having the metabolic syndrome were 2.7 (1.6–4.6) and 1.8 (1.1–31) times higher in the low- and moderate-CRF groups, respectively, by comparison with the high-CRF group (*P* for trend <0.001). After adjustment for age, visceral fat, and subcutaneous fat, the RRs of having the metabolic syndrome were 1.8 (1.0–3.1) and 1.6 (0.9–2.7) times higher in the low- and moderate-CRF groups compared with the high-CRF group (*P* for trend = 0.06).

CONCLUSIONS

— The primary finding of this study was that for given levels of abdominal subcutaneous fat, visceral fat, or waist circumference, men with higher levels of CRF had substantially lower metabolic risk compared with men with low CRF. Furthermore, we observed a dose-response relationship between CRF and the prevalence of metabolic syndrome, even after controlling for age, visceral fat, and subcutaneous fat. These findings suggest that higher levels of CRF are associated with a substantially reduced metabolic risk for a given level of abdominal obesity.

Katzmarzyk et al. (21) reported that moderate and high levels of CRF attenuated the risk of all-cause and cardiovascular disease mortality in men associated with the metabolic syndrome. Furthermore, in men with the metabolic syndrome, there was a significant negative dose-response relationship with mortality across CRF tertiles. Similarly, Blair et al. (6) reported that an improvement in CRF is associated with a 44% lower all-cause mortality independent of changes in BMI. Therefore, our observations are consistent with previous observations suggesting that CRF protects against health risk in men.

It is noteworthy that we observed a stepwise dose-response relationship be-

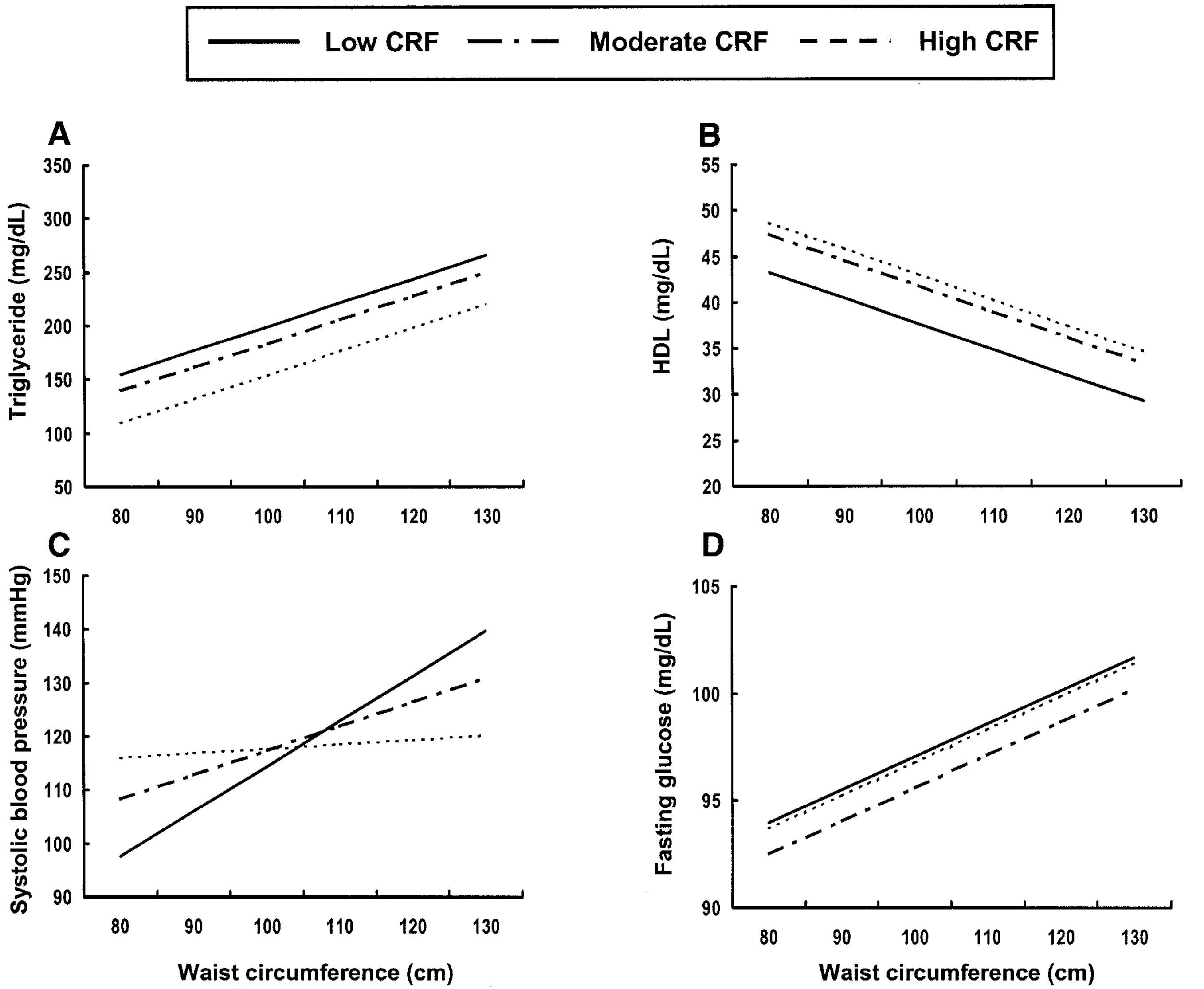

Figure 1—*Relationship between waist circumference (WC) and metabolic risk, standardized to 40 years of age.* A: *Low CRF,* y = −14.60 − 0.17 *(age)* + 2.20 *(WC); moderate CRF,* y = −29.81 − 0.17 *(age)* + 2.20 *(WC); high CRF,* y = −59.79 − 0.17 *(age)* + 2.20 *(WC).* B: *Low CRF,* y = 57.26 + 0.21 *(age)* − 0.28 *(WC); moderate CRF,* y = 61.43 + 0.21 *(age)* − 0.28 *(WC); high CRF,* y = 62.64 + 0.21 *(age)* − 0.28 *(WC).* C: *Low CRF,* y = 13.67 + 0.42 *(age)* + 0.84 *(WC); moderate CRF,* y = 55.49 + 0.42 *(age)* + 0.45 *(WC); high CRF,* y = 93.03 + 0.42 *(age)* + 0.08 *(WC).* D: *No group or group × WC effect.*

tween CRF and the metabolic syndrome after controlling for age, visceral fat, and subcutaneous fat. This finding extends a previous observation by Nagano et al. (13), who recently reported that the prevalence of hyperinsulinemia and a low HDL cholesterol level is significantly lower in high-fit Japanese men and women compared with the low-fit group after controlling for age and visceral fat in insulin-resistant individuals. The fact that we did not observe a beneficial effect of CRF on fasting glucose is consistent with our previous exercise intervention studies, which failed to demonstrate improvements in fasting glucose in obese men (10) and women (11) despite significant reductions in abdominal fat and insulin sensitivity (10). In this way, insulin data would have been useful because, consistent with the findings of Nagano et al. (13), it is more likely that insulin values would be lower in those with high CRF compared with low CRF for a given glucose level.

Because CRF is a strong correlate of physical activity (22), one might expect that physical activity, like CRF, would be related to health risk independent of abdominal obesity. However, in contrast to this notion, Hunter et al. (23,24) reported that visceral fat remains associated with cardiovascular disease risk factors after controlling for physical activity, whereas physical activity is not associated with cardiovascular disease risk factors after controlling for visceral fat in both men (24) and women (23). The disparate findings may be due to the use of self-report measures of physical activity compared with maximal exercise testing. Self-report physical activity questionnaires are inaccurate, and the inaccuracy increases with the respondent's weight (25). Use of maximal exercise tests to quantify CRF pro-

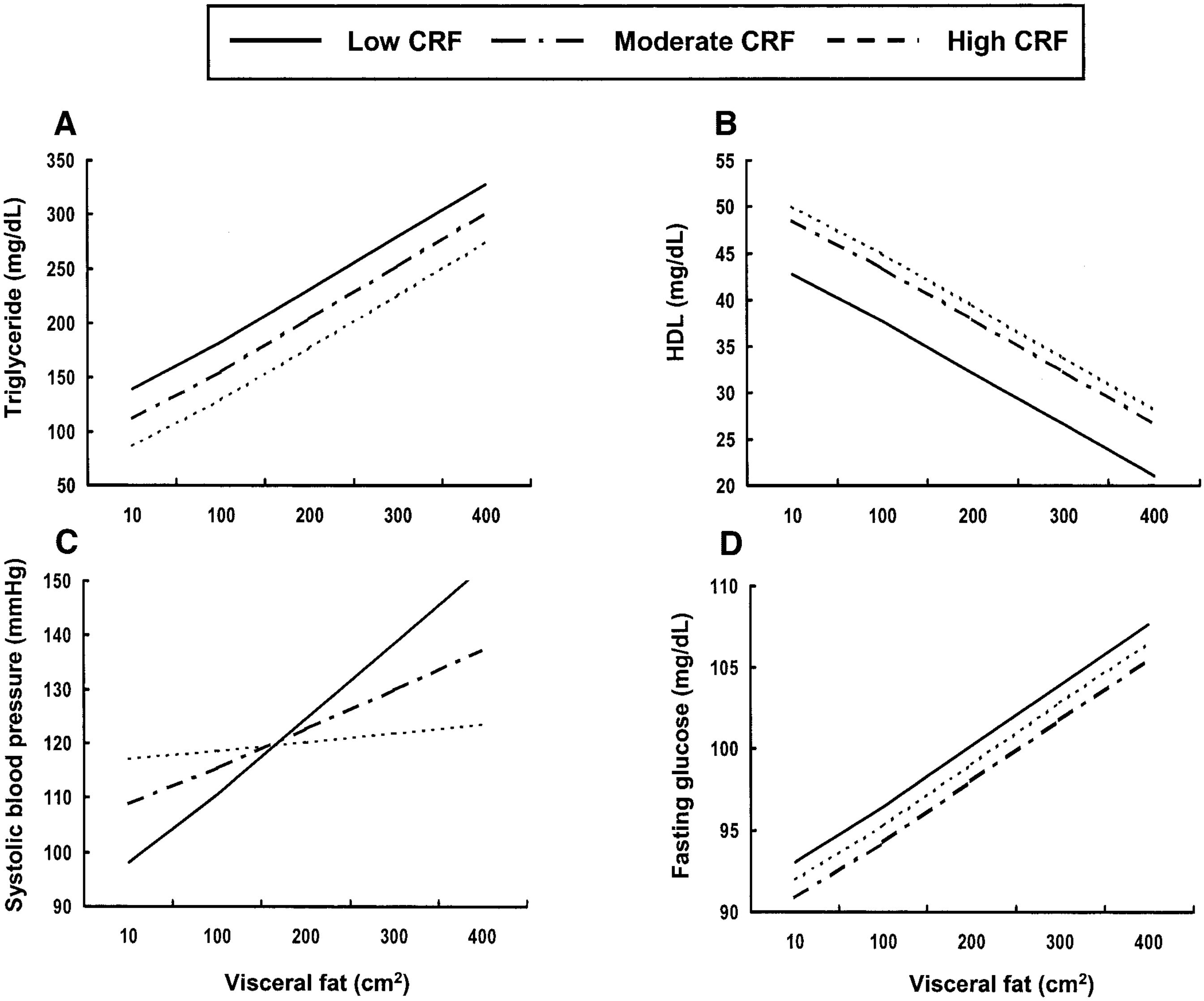

Figure 2—*Relationship between visceral fat (VAT) and metabolic risk, standardized to 40 years of age.* A: *Low CRF,* y = *183.13 − 1.21 (age) + 0.48 (VAT); moderate CRF,* y = *156.46 − 1.21 (age) + 0.48 (VAT); high CRF,* y = *129.48 − 1.21 (age) + 0.48 (VAT).* B: *Low CRF,* y = *30.13 + 0.33 (age) − 0.06 (VAT); moderate CRF,* y = *35.89 + 0.33 (age) − 0.06 (VAT); high CRF,* y = *37.36 + 0.33 (age) − 0.06 (VAT).* C: *Low CRF,* y = *85.72 + 0.28 (age) + 0.14 (VAT); moderate CRF,* y = *97.26 + 0.28 (age) + 0.07 (VAT); high CRF,* y = *105.99 + 0.28 (age) + 0.02 (VAT).* D: *No group or group × VAT effect.*

vides an objective evaluation of an individual's recent activity patterns and accounts for 70–80% of the variance in detailed activity records (22). CRF is stronger than self-reported physical activity as a predictor of many health outcomes, most likely because fitness measurements are less prone to misclassification and because factors other than activity may influence both fitness and health through related biological factors (26,27). The mechanisms through which CRF would be independently associated with the components of the metabolic syndrome are not firmly established. Assuming that CRF reflects the recent physical activity patterns of our participants, it is reasonable to suggest that the lower levels of insulin resistance (28), blood pressure (29), and blood lipids (30) that are normally associated with routine physical activity are at least partially responsible for our findings.

Limitations of this study warrant mention. The cross-sectional design does not allow us to infer a causal relationship. Therefore, our findings require confirmation from prospective and intervention trials with serial measurements of CRF, abdominal obesity, and metabolic risk factors, which would reinforce the independent relationships between these factors. It is suggested that ~40% of the variation in CRF is attributable to genetic factors (31). This does not discount our observed relationship between CRF and health risk; however, it merely suggests that CRF may be a surrogate measure for both physical activity and genotype. The absence of dietary intake data is a limitation because dietary factors are known to influence some components of the metabolic syndrome. Finally, whether our findings remain true for women or other ethnic groups is unknown.

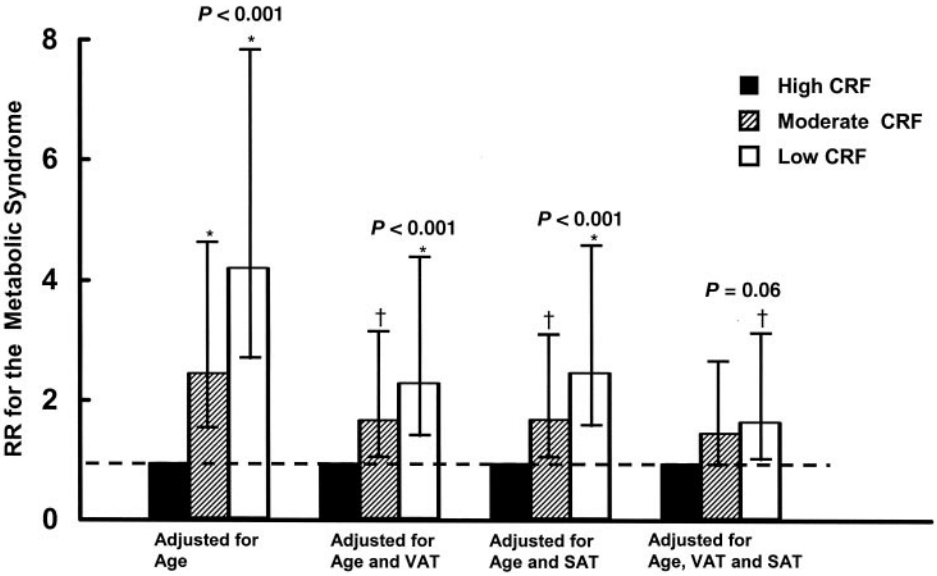

Figure 3—*RRs and 95% CIs for the metabolic syndrome after adjusting for age and visceral fat (VAT) or subcutaneous fat (SAT) in men with low, moderate, and high CRF. *Significantly greater than high-CRF group,* $P < 0.01$*; †significantly greater than high-CRF group,* $P < 0.05$*.* P *values are for tests of linear trend across the CRF groups.*

In conclusion, our findings suggest that high CRF is associated with a substantially lower metabolic health risk for a given level of visceral fat, subcutaneous fat, or waist circumference. Furthermore, there was an inverse dose-response relationship between CRF and metabolic syndrome independent of abdominal fat. These findings suggest that moderate CRF levels protect against obesity-related health risk and, therefore, reinforce the recommendation that adults adopt a physically active lifestyle.

Acknowledgments— This research was supported, in part, by research grants from the Canadian Institutes of Health Research (MT13448; to R.R.) and the National Institutes of Health (AG06945; to S.N.B. and T.S.C.).

References

1. Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE, Fujimoto WY: Visceral adiposity is an independent predictor of incident hypertension in Japanese Americans. *Ann Intern Med* 140:992–1000, 2004
2. Kannel WB, Cupples LA, Ramaswami R, Stokes J 3rd, Kreger BE, Higgins M: Regional obesity and risk of cardiovascular disease: the Framingham Study. *J Clin Epidemiol* 44:183–190, 1991
3. Lakka TA, Laaksonen DE, Lakka HM, Mannikko N, Niskanen LK, Rauramaa R, Salonen JT: Sedentary lifestyle, poor cardiorespiratory fitness, and the metabolic syndrome. *Med Sci Sports Exerc* 35:1279–1286, 2003
4. Lee CD, Blair SN, Jackson AS: Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr* 69:373–380, 1999
5. Wei M, Kampert JB, Barlow CE, Nichaman MZ, Gibbons LW, Paffenbarger RS Jr, Blair SN: Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *JAMA* 282:1547–1553, 1999
6. Blair SN, Kohl HW 3rd, Barlow CE, Paffenbarger RS Jr, Gibbons LW, Macera CA: Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. *JAMA* 273:1093–1098, 1995
7. Ross R, Katzmarzyk PT: Cardiorespiratory fitness is associated with diminished total and abdominal obesity independent of body mass index. *Int J Obes Relat Metab Disord* 27:204–210, 2003
8. Wong SL, Katzmarzyk P, Nichaman MZ, Church TS, Blair SN, Ross R: Cardiorespiratory fitness is associated with lower abdominal fat independent of body mass index. *Med Sci Sports Exerc* 36:286–291, 2004
9. Janssen I, Katzmarzyk PT, Ross R, Leon AS, Skinner JS, Rao DC, Wilmore JH, Rankinen T, Bouchard C: Fitness alters the associations of BMI and waist circumference with total and abdominal fat. *Obes Res* 12:525–537, 2004
10. Ross R, Dagnone D, Jones PJ, Smith H, Paddags A, Hudson R, Janssen I: Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomized, controlled trial. *Ann Intern Med* 133:92–103, 2000
11. Ross R, Janssen I, Dawson J, Kungl AM, Kuk JL, Wong SL, Nguyen-Duy TB, Lee S, Kilpatrick K, Hudson R: Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res* 12:789–798, 2004
12. Physical Activity and Health: *A Report of the Surgeon General*. Atlanta, GA, Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996
13. Nagano M, Kai Y, Zou B, Hatayama T, Suwa M, Sasaki H, Kumagai S: The contribution of cardiorespiratory fitness and visceral fat to risk factors in Japanese patients with impaired glucose tolerance and type 2 diabetes mellitus. *Metabolism* 53:644–649, 2004
14. Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE: Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. *Diabetes* 46:1579–1585, 1997
15. Janssen I, Katzmarzyk PT, Ross R: Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 79:379–384, 2004
16. Expert Panel on Detection, Evaluation, and Treatment of High Blood Pressure in Adults: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 285:2486–2497, 2001

17. Ross R, Leger L, Morris D, de Guise J, Guardo R: Quantification of adipose tissue by MRI: relationship with anthropometric variables. *J Appl Physiol* 72:787–795, 1992
18. Lee SJ, Janssen I, Ross R: Inter-individual variation in abdominal subcutaneous and visceral adipose tissue: influence of measurement site. *J Appl Physiol* 97:948–954, 2004
19. Balke B, Ware RW: An experimental study of physical fitness of Air Force personnel. *U S Armed Forces Med J* 10:875–888, 1959
20. Pollock ML, Bohannon RL, Cooper KH, Ayres JJ, Ward A, White SR, Linnerud AC: A comparative analysis of four protocols for maximal treadmill stress testing. *Am Heart J* 92:39–46, 1976
21. Katzmarzyk PT, Church TS, Blair SN: Cardiorespiratory fitness attenuates the effects of the metabolic syndrome on all-cause and cardiovascular disease mortality in men. *Arch Intern Med* 164:1092–1097, 2004
22. Paffenbarger RS Jr, Blair SN, Lee IM, Hyde RT: Measurement of physical activity to assess health effects in free-living populations. *Med Sci Sports Exerc* 25:60–70, 1993
23. Hunter GR, Kekes-Szabo T, Treuth MS, Williams MJ, Goran M, Pichon C: Intra-abdominal adipose tissue, physical activity and cardiovascular risk in pre- and post-menopausal women. *Int J Obes Relat Metab Disord* 20:860–865, 1996
24. Hunter GR, Kekes-Szabo T, Snyder SW, Nicholson C, Nyikos I, Berland L: Fat distribution, physical activity, and cardiovascular risk factors. *Med Sci Sports Exerc* 29:362–369, 1997
25. Walsh MC, Hunter GR, Sirikul B, Gower BA: Comparison of self-reported with objectively assessed energy expenditure in black and white women before and after weight loss. *Am J Clin Nutr* 79:1013–1019, 2004
26. Blair SN, Cheng Y, Holder JS: Is physical activity or physical fitness more important in defining health benefits? *Med Sci Sports Exerc* 33:S379–S399, S419–S320, 2001
27. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, Buchner D, Ettinger W, Heath GW, King AC, Kriska A, Leon AS, Marcus BH, Morris J, Paffenbarger RS, Patrick K, Pollock ML, Rippe JM, Sallis J, Wilmore JH: Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 273:402–407, 1995
28. Perseghin G, Price TB, Petersen KF, Roden M, Cline GW, Gerow K, Rothman DL, Shulman GI: Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. *N Engl J Med* 335:1357–1362, 1996
29. Fagard RH: Physical activity in the prevention and treatment of hypertension in the obese. *Med Sci Sports Exerc* 31 (11 Suppl.):S624–S630, 1999
30. Stefanick ML: Physical activity for preventing and treating obesity-related dyslipoproteinemias. *Med Sci Sports Exerc* 31 (11 Suppl.):S609–S618, 1999
31. Bouchard C: Genetics of aerobic power and capacity. In *Sports and Human Genetics.* Champaign, IL, Human Kinetics, 1986