

Can Adoption of Regular Exercise Later in Life Prevent Metabolic Risk for Cardiovascular Disease?

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OBJECTIVE — To determine the impact of chronic exercise training initiated later in life upon development of metabolic markers of cardiovascular disease risk.

RESEARCH DESIGN AND METHODS — Two inception cohorts of previously sedentary healthy adults aged 55–75 years at baseline (1989), one initiating regular supervised physical exercise training and the other a geographical similar sedentary control, were assessed for anthropometric, biochemical, and clinical markers of the metabolic syndrome and comorbidity over 10 years.

RESULTS — At baseline, active individuals aged 68 years compared with sedentary individuals aged 67 years had similar fitness levels (5.7 vs. 5.8 metabolic equivalents). At follow-up, complete data were obtained for 161 active and 136 sedentary subjects. Drop out occurred primarily because of failure to adhere to the exercise regimen and poor physical health for active and sedentary individuals, respectively. More metabolic abnormalities were seen in the sedentary group than in the active group for one or two (64 vs. 36%, $P < 0.001$) and three or more (35 vs. 22%, $P < 0.003$) abnormalities, respectively. In those assessed at follow-up, the sedentary group compared with the active group had lower fitness levels (5.0 [13.8% decrease] vs. 5.9 [3.5% increase] metabolic equivalents), had a greater likelihood of a positive exercise electrocardiogram or symptom (32 vs. 10%, $P < 0.001$), and had more comorbid conditions (Charlson Comorbidity Index score 0.9 vs. 0.4, $P < 0.01$).

CONCLUSIONS — Higher fitness achieved over 10 years of regular exercise training in older adults was associated with reduced development of metabolic risk factors for cardiovascular disease, fewer exercise-induced cardiac abnormalities, and reduced comorbidity.

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Despite an overall reduction in cardiovascular mortality over the past decade, an aging population has seen a shift in risk for cardiovascular disease to the older adult (1). However, few longitudinal studies of predictors and modifiers of this risk in the older population are available. This gap in evidence is

critical as an aging population becomes increasingly sedentary, whereas the importance of physical activity as a modifier of cardiovascular risk remains unequivocal (2–6).

Coincident with an older more sedentary population at risk for type 2 diabetes, hypertension, and cardiovascular disease

(7–9) is an increased prevalence of the clustering of metabolic risk factors (10–13). The importance of metabolic risk factors from both a clinical and public health perspective is that their prevention, detection, and reversal can occur before the development of overt cardiovascular disease (14). Coupled with particularly poor treatment and control rates for type 2 diabetes, hypertension, and cardiovascular disease (15), prevention and screening strategies early in the cardiovascular disease continuum are essential.

Recent evidence from both the Finnish Diabetes Prevention Study (16) and the U.S. Diabetes Prevention Program (17) showed that even modest lifestyle intervention could have a major impact on reduction in risk for type 2 diabetes in middle-aged (mean 50 years) glucose-intolerant individuals. However, to date, no studies have identified whether regular exercise training, adopted late in life, can prevent the metabolic risk factors in older adults at a time when risk increases most.

Although higher levels of physical activity and fitness are associated with reduction in cardiovascular risk (4,18–21), it appears that higher intensity or dose is optimal in producing increased fitness and measurable metabolic risk factor protection (22–25). We have previously shown that regular high-intensity exercise prescription can improve fitness in institutionalized and community-dwelling older adults (26–28) up to 12 months and that these changes in fitness can be maintained with regular updating of the exercise prescription at high intensity over 7 years (29).

The primary purposes of the present study were 1) to assess the prevalence of clustering of markers of metabolic syndrome, cardiovascular symptoms, and comorbidity in a community-based cohort of older adults at baseline and over 10 years and 2) to determine association among cardiovascular fitness, metabolic markers of the metabolic syndrome, cardiac symptoms and signs, and comorbidity by comparing two groups: one that

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Abbreviations: HOMA-IR, homeostasis model assessment of insulin resistance; MET, metabolic equivalent; RPP, rate-pressure product; sBP, systolic blood pressure.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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adopted and engaged in a regular exercise training program during that time and another that did not.

RESEARCH DESIGN AND METHODS

From two large samples of older adults from the same geographic location, one group (active) contacted the Canadian Center for Activity and Aging for participation in supervised exercise programming ($n = 266$), whereas the other (sedentary) was assembled as part of a randomly selected cohort of sedentary older adults ($n = 420$) to study the long-term effects of aging on aerobic fitness (26). After baseline screening, active subjects included 193 healthy men and women (73 excluded in this study, including 26 for presence of metabolic risk factors). Subjects were aged 55–75 years and completed a physical examination including a maximal exercise treadmill test on entry and annually during their participation in a structured exercise program at the Canadian Center for Activity and Aging. These subjects attended regular (30–45 min) exercise sessions three times per week of aerobic activity (walking, jogging) with a training intensity heart rate corresponding to 75–85% VO_{2max} according to published recommendations (30).

Subjects monitored heart rate during each session and were supervised by a certified instructor. No active retention program was used during participation in the program. Compliance with this program has been previously reported (31). Only those who attended at least 80% of available exercise sessions (46 weeks yearly) per year and recorded target heart rate in a class log (more than two sessions per week) received a training heart rate update. In the sedentary group, 110 lived outside the defined geographic area, whereas 187 participants were identified for observation (123 were excluded, including 36 with presence of metabolic risk factors). All sedentary individuals were aged 55–75 years and were included in a larger longitudinal study on aging (26). No further regular exercise training was provided, while any involvement in formal/informal exercise programs during the observation period was gathered at the final visit and confirmed by post-study activity questioning. The study was reviewed and approved by the University of Western Ontario Review Board, and all subjects provided informed consent.

Baseline assessment of both groups was similar and included current medical diagnoses, presence of cardiovascular risk factors, markers of the metabolic syndrome, anthropometric measures, resting and exercise electrocardiograms, clinic and exercise blood pressure, and a maximal treadmill exercise tolerance test. Individual morbid conditions were combined into the Charlson Comorbidity Index score (32), a prospectively validated weighted index that includes the number and severity of comorbidities. Those in the sedentary group also had simultaneous collection of respired gases during exercise treadmill testing to determine VO_{2max} (33).

Cardiovascular fitness

All exercise tests were performed using a modified Balke protocol, where speed and grade were increased every minute to elicit oxygen demand of $1\text{--}3 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ so that the test achieved maximal effort in 8–12 min. Workload was expressed in metabolic equivalents (METs) for the active group and METs and VO_{2max} in the sedentary group. The value for METs was estimated from standard tables on the basis of protocol duration of exercise (34). Predicted maximal functional aerobic capacity (VO_{2max}) was calculated from published equations that included adjustment for age and sex (34). In the sedentary group, oxygen consumption was measured during treadmill exercise using a bidirectional turbine and volume transducer (SensorMedics VMM-2A). VO_{2max} was determined as previously described (33). Predicted VO_{2max} was compared with measured VO_{2max} in the sedentary group at baseline and follow-up. A correlation of 0.87 and 0.91 was observed, respectively. This is similar to previous reports in our laboratory (27,33). Subjects in both groups were stratified further into three groups defined on the basis of age, sex, and achieved METs as previously described (12). Briefly, those with METs in the lowest 20% of each age-sex distribution were classified as low fitness; those within the 21st to 59th percentile for age-sex were categorized as low to moderate fitness, and those at or higher than the 60th percentile were categorized as moderate to high fitness. The average values based on the treadmill test METs for low, moderate, and high fitness in men and women in both groups are given in Table 1.

Assessment of components of the metabolic syndrome, metabolic risk factors, and anthropometrics

The metabolic syndrome risk factors (9) and their definitions used in this study have been previously described. Diabetes was defined as blood glucose $>7 \text{ mmol/l}$ or a clinical diagnosis of diabetes with diet, oral, or insulin therapy. Impaired fasting glucose was defined as fasting blood glucose of 6.1–6.9 mmol/l.

Blood pressure was measured with a mercury sphygmomanometer and the mean of three seated resting values recorded. BMI was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was calculated as the average of two measurements taken after expiration at the midpoint between the lowest rib and the iliac crest. Participants fasted 12 h and were free of caffeine, smoking, and alcohol more than 4 h before blood sampling. Blood glucose was measured using glucose dehydrogenase methodology. LDL and HDL fractions were separated from fresh serum by ultracentrifugation. Lipoprotein fraction cholesterol and triglycerides were measured by standard enzymatic spectrophotometric techniques. Insulin was measured with a radioimmunoassay kit (Novo Nordisk). In each subject, the degree of insulin resistance was estimated by homeostasis model assessment of insulin resistance (HOMA-IR) according to the method of Mathews et al. (35). In particular, an insulin resistance score (HOMA-IR) was computed with the following formula: fasting plasma glucose (mmol/l) \times fasting serum insulin (mIU/ml) \div 22.5.

Anthropometric measurements included four skinfold thicknesses (triceps, biceps, subscapular, and suprailiac) taken with Harpenden calipers on the subjects' right side. The sum of skinfolds, percentage body fat, and fat-free mass (in kilograms) were calculated for each subject as previously described (26). Measures were done by a certified fitness appraiser skilled in the technique.

Ascertainment of end points

Electrocardiographic evidence for ischemia was defined using the conventional criteria of $>1 \text{ mm}$ of horizontal or down-sloping ST-segment depression or elevation for at least 60–80 ms after the end of the QRS complex (36). An independent

Table 1—Baseline characteristics of both groups according to cardiorespiratory fitness level

	Overall	All	Low	Average	High	Dropouts
Age (years)	68 ± 6					
Active		68 ± 5	67 ± 6	65 ± 8	73 ± 7	67 ± 6
Sedentary		67 ± 4	71 ± 6	73 ± 4	74 ± 5	66 ± 4
Male (%)						
Active		38	44	28	28	35
Sedentary		36	38	31	31	40
Height (cm)	170 ± 2					
Active		171 ± 1	171 ± 2	171 ± 2	172 ± 1	170 ± 1
Sedentary		169 ± 2	170 ± 2	168 ± 3	171 ± 2	173 ± 2
Weight (kg)	80.0 ± 1.5					
Active		79.8 ± 0.9	78.5 ± 1.6	81.0 ± 1.8	80.3 ± 1.6	80.8 ± 1.1
Sedentary		80.5 ± 1.2	81.5 ± 1.2	79.7 ± 2.0	81.1 ± 1.5	81.3 ± 1.8
BMI (kg/m ²)	27.5 ± 0.3					
Active		27.3 ± 0.2	26.0 ± 4.3	28.6 ± 6.1	26.9 ± 4.1	27.0 ± 3.1
Sedentary		27.6 ± 0.4	27.4 ± 4.1	28.1 ± 7.1	27.4 ± 3.4	27.4 ± 3.7
Fat-free mass (kg)	55.5 ± 1.6					
Active		56.6 ± 1.0	58.2 ± 5.1	57.3 ± 5.3	54.4 ± 5.5	59.4 ± 6.1
Sedentary		54.4 ± 1.5	51.4 ± 4.3	55.6 ± 4.8	56.1 ± 4.6	57.1 ± 5.1
Waist circumference (cm)	91.3 ± 6.1					
Active		92.5 ± 4.5	94.3 ± 4.1	93.7 ± 3.9	89.4 ± 4.8	91.0 ± 3.8
Sedentary		90.5 ± 6.3	91.1 ± 5.0	93.1 ± 4.3	87.3 ± 4.5	91.3 ± 4.1
sBP (mmHg)	129 ± 6					
Active		129 ± 7	133 ± 19	128 ± 20	129 ± 15	130 ± 10
Sedentary		131 ± 8	135 ± 12	130 ± 17	127 ± 10	128 ± 8
dBP (mmHg)	77 ± 4					
Active		76 ± 6	75 ± 7	75 ± 5	76 ± 6	77 ± 7
Sedentary		79 ± 7	80 ± 5	77 ± 3	79 ± 5	78 ± 4
RPP (×10 ³)	26,988 ± 5,975					
Active		26,759 ± 6,104	22,625 ± 6,278	25,334 ± 5,981	29,645 ± 6,332	2,734 ± 5,831
Sedentary		27,345 ± 5,879	28,767 ± 7,534	26,794 ± 6,768	27,117 ± 6,995	2,844 ± 6,531
Current smokers (%)	6 ± 2					
Active		5 ± 3	6 ± 2	7 ± 3	2 ± 4	3 ± 2
Sedentary		7 ± 3	7 ± 5	9 ± 3	6 ± 4	4 ± 3
METs	5.7 ± 1.1					
Active		5.7 ± 0.8	4.9 ± 0.4	5.1 ± 1.1	6.5 ± 1.9	5.8 ± 0.9
Sedentary		5.8 ± 1.0	4.4 ± 0.9	6.0 ± 0.8	7.2 ± 1.3	5.8 ± 1.1
Glucose (mmol/l)	5.6 ± 0.08					
Active		5.6 ± 1.4	5.9 ± 2.6	5.3 ± 2.5	5.5 ± 1.6	5.7 ± 1.1
Sedentary		5.6 ± 1.7	5.7 ± 2.1	5.5 ± 2.5	5.6 ± 1.9	5.6 ± 1.8
Total cholesterol (mmol/l)	5.35 ± 1.6					
Active		5.4 ± 1.6	5.5 ± 1.2	5.2 ± 1.0	5.6 ± 1.3	5.4 ± 2.0
Sedentary		5.3 ± 1.3	5.3 ± 1.6	5.1 ± 0.8	5.5 ± 0.9	5.5 ± 1.9
LDL cholesterol (mmol/l)	2.9 ± 0.4					
Active		2.6 ± 0.7	2.1 ± 0.9	2.1 ± 0.7	2.2 ± 0.7	2.5 ± 0.9
Sedentary		2.9 ± 0.9	2.4 ± 1.0	2.4 ± 0.6	2.2 ± 0.6	2.7 ± 1.1
HDL cholesterol (mmol/l)	1.1 ± 0.2					
Active		1.1 ± 0.3	1.1 ± 0.3	1.0 ± 0.1	1.3 ± 0.2	1.0 ± 0.4
Sedentary		1.1 ± 0.3	1.2 ± 0.4	1.1 ± 0.3	1.1 ± 0.2	1.2 ± 0.5
Triglycerides (μmol/l)	2.17 ± 0.9					
Active		2.14 ± 1.1	2.32 ± 1.0	2.00 ± 0.5	2.10 ± 0.9	2.2 ± 1.3
Sedentary		2.20 ± 1.2	2.55 ± 1.2	2.44 ± 1.0	2.38 ± 0.8	2.3 ± 1.6
Insulin-free (pmol/l)	280 ± 189					
Active		276 ± 200	245 ± 210	320 ± 315	264 ± 283	280 ± 251
Sedentary		311 ± 234	238 ± 203	329 ± 264	270 ± 276	297 ± 266
HOMA-IR	7.08 ± 0.66					
Active		6.86 ± 0.31	7.11 ± 0.24	6.99 ± 0.43	6.81 ± 0.37	7.08 ± 0.60
Sedentary		7.07 ± 0.40	7.16 ± 0.38	7.11 ± 0.45	6.98 ± 0.59	7.12 ± 0.38
Charlson Comorbidity Index score	0.4 ± 0.4					
Active		0.4 ± 0.2	0.3 ± 0.9	0.4 ± 1.0	0.5 ± 0.8	0.5 ± 0.3
Sedentary		0.4 ± 0.4	0.3 ± 0.4	0.4 ± 1.0	0.5 ± 0.8	0.4 ± 0.6

Data are means ± SD. Low, average, and high represent low, average, and high fitness tertiles for the study groups. dBP, diastolic blood pressure.

Table 2—Percent change in metabolic indices between 1987 and 1997 for the active and sedentary men and women

	Active				Sedentary				P
	Baseline	Follow-up	$\Delta B - F$	% Δ	Baseline	Follow-up	$\Delta B - F$	% Δ	
BMI (kg/m ²)	27.3 ± 0.2	27.2 ± 0.4	-0.1	-0.37	27.6 ± 0.4	28.9 ± 0.3	+1.3	1.09	NS
sBP (mmHg)	129 ± 7	135 ± 5	+6	+4.65	131 ± 8	141 ± 5	+10	7.63	<0.03
Glucose (mmol/l)	5.6 ± 1.4	5.8 ± 1.2	+0.2	+3.57	5.6 ± 1.7	5.8 ± 1.3	+0.2	3.57	NS
Total cholesterol (mmol/l)	5.4 ± 1.6	5.4 ± 1.4	+0.1	-0.06	5.3 ± 1.3	5.5 ± 1.3	+0.2	3.77	<0.05
LDL cholesterol (mmol/l)	2.6 ± 0.7	2.7 ± 1.0	+0.1	3.85	2.9 ± 0.9	3.1 ± 1.2	+0.2	6.89	<0.02
HDL cholesterol (mmol/l)	1.1 ± 0.3	1.2 ± 0.8	+0.1	+9.09	1.1 ± 0.3	0.9 ± 0.8	-0.2	-18.18	<0.001
Triglycerides (μmol/l)	2.14 ± 1.1	1.96 ± 1.6	-0.18	-8.41	2.2 ± 1.2	2.9 ± 1.4	+0.7	31.82	<0.001
Insulin (pmol/l)	276 ± 200	273 ± 212	-3	-1.09	311 ± 234	299 ± 230	-12	-3.86	<0.05
HOMA-IR	6.86 ±	7.04 ± 0.8	+0.18	+6.04	7.71 ± 0.40	7.74 ± 0.33	+0.03	+4.6	NS
Waist circumference (cm)	92.5 ± 4.5	94.5 ± 5.5	+2	2.12	90.5 ± 6.3	101.3 ± 9.5	+10.8	10.66	<0.001
METs	5.7 ± 0.8	5.9 ± 0.9	+0.2	3.51	5.8 ± 1.0	5.0 ± 1.0	-0.8	-13.79	<0.001

Data are means ± SD. $\Delta B - F$, absolute baseline minus follow-up; % Δ , percent change from baseline to follow-up.

blinded physician corroborated exercise-induced electrocardiogram signs.

Cardiac end points including cardiac death, nonfatal myocardial infarction, or congestive heart failure were ascertained from medical records by linkage to the hospital computer system using health card and date of birth and corroborated by an independent blinded nurse with 100% follow-up of all subjects. Deaths were classified with ICD-9, with 390–459 classified as cardiovascular deaths. Nonfatal myocardial infarction was a clinical definition that included electrocardiographic and/or elevated cardiac enzyme levels confirmed on review of hospital records. Congestive heart failure was based on clinical definition or self-report plus clinical confirmation by the attending primary physician, including medications for that condition.

Smoking history was considered in the data analyses by use of dichotomous classification: current nonsmokers (never smoked and exsmokers with no smoking at least 1 year) versus current smokers.

Data analysis

Descriptive statistics were computed within and between groups and then across cardiorespiratory fitness categories for each of the independent variables in the analysis. Bivariate associations between the groups were tested using χ^2 tests for categorical data and *t* tests for continuous variables.

Zero-order and partial correlations were computed using the variables as continuous scale measures to assess the relationships among the various metabolic abnormalities, comorbidity, and

cardiorespiratory fitness. Each of the pairwise partial correlations were adjusted for all the other variables in the analysis. Serum triglycerides were converted to a log-linear scale for correlational analyses. Each group was then categorized for analyses according to the number of metabolic abnormalities (0–4) and their level of cardiorespiratory fitness (low, moderate, high) based on entire cohort tertiles. The association between fitness and the accumulated number of metabolic abnormalities was assessed using sex-specific age-adjusted proportional odds logit models.

Cox proportional hazard models were constructed to determine the association of predictor variables, including fitness levels, age, sex, cardiac risk factors (hypertension, diabetes, smoking, hyperlipidemia), and Charlson Comorbidity Index score, with metabolic markers. Proportionality of the odds logit models was tested and met. We performed an intent-to-treat analysis using imputation and analysis of those in our active group who achieved at least 80% compliance with training on at least 8 of 10 years follow-up. Significance was considered to be *P* < 0.05. All statistical analyses were performed using SPSS version 11.0 (SPSS, Chicago, IL).

RESULTS

Baseline characteristics

Both groups were similar at baseline in terms of age, sex, fitness level, and anthropometric measures (Table 1). A total of 193 active (68 years of age; 46% male) and 187 sedentary (67 years of age; 48%

male) individuals were followed over the study period. Active individuals did have a higher Charlson Comorbidity Index score, but this was not statistically significant. No difference in use of aspirin, hormone replacement therapy, or vitamin preparations including folate was observed. The fitness levels (low, moderate, and high in active/sedentary) are described in Table 1. The average METs were 4.9/4.4, 5.1/6.0, and 6.5/7.2, respectively. None of these were statistically significant between groups.

Follow-up

At follow-up, 161 active and 136 sedentary individuals were studied (Table 2). There was no difference in withdrawals between groups. For dropouts, we conducted two methods of imputation. First, we imputed the last number carried forward for fitness, metabolic risk factors, and anthropometrics. Next, we carried the worst-case value forward (i.e., presence of three metabolic risk factors or lowest fitness level). There was no significant difference between these two approaches for fitness, metabolic risk factors, or anthropometrics. For those completing follow-up, the proportion achieving >80% compliance with exercise training for at least 8 of 10 years follow-up in the active group was very high, with only 12 not fulfilling our criteria. Some sedentary individuals (8%) did report engaging in community-based exercise programs over the follow-up period; however, none participated more than 18 consecutive months (mean 21 ± 16 weeks), and none reported that a specific training prescription or guidelines were

used. Only 23 of the entire sample (7 active/16 sedentary) entered a nursing home facility. Six deaths in the sedentary group and four in the active group were of cardiac origin.

Clinical outcomes

Men had higher BMI and fat-free mass ($P < 0.001$) across all fitness categories, lower HDL ($P = 0.08$), and lower total cholesterol ($P = 0.07$) than women. In the highest fitness category in both groups, glucose was higher among men than women. Otherwise, there were no sex differences. The sedentary group had higher Charlson Comorbidity Index scores (0.9) versus the active group (0.8) ($P < 0.002$), and nonfatal MI was 7 vs. 2 ($P < 0.05$), stable angina was 8 vs. 2 ($P < 0.05$), and positive electrocardiogram findings on exercise treadmill testing was 21 vs. 6, respectively ($P < 0.01$). The presence of angina or positive electrocardiographic exercise changes was uncommon and was associated with neither fitness nor metabolic factors. Both groups increased aspirin and hormone replacement therapy medication use at follow-up, but this was not significant nor was there a difference between groups. The sedentary group used more medications for cardiovascular indications than the active group at follow-up ($P < 0.05$).

Cardiorespiratory fitness

Overall, peak MET was inversely associated with age. The active group showed a 3.5% increase in METs (5.7 to 5.9) versus the 13.8% decrease in the sedentary group (5.8 to 5.0) ($P < 0.001$) (Table 2) and achieved higher peak METs ($P < 0.001$) at follow-up. Overall, men had higher peak METs than women ($P < 0.05$); however, in the sedentary group, women had higher peak METs than men ($P < 0.05$) at all levels of fitness. Systolic blood pressure (sBP) during exercise was higher ($P = 0.09$) and rate-pressure product (RPP) (heart rate \times sBP) greater in active versus sedentary individuals ($P < 0.05$). More subjects in the sedentary group moved to the lowest tertile for peak METs (21 vs. 4) ($P < 0.01$), whereas more active individuals moved to a higher tertile (most in low to moderate fitness level) ($P < 0.05$). A high correlation between VO_{2max} predicted from peak METs and measured VO_{2max} ($r = 0.95$) was observed in the sedentary group, which

is similar to that observed at baseline ($r = 0.92$).

Metabolic markers

Overall, the prevalence of each of the markers of the metabolic syndrome was inversely related to fitness level at follow-up in both groups. At follow-up, the percent increase in sBP was significantly less in the active group versus the sedentary group ($P < 0.03$), whereas total cholesterol, triglycerides, insulin, waist circumference, percent body fat, and METs showed similar direction of significant changes (Table 2). The largest % Δ between groups was observed for HDL cholesterol, where the active group showed a 9% increase and the sedentary group showed an 18% decrease (Table 2).

The most prevalent marker for both groups was elevated sBP, with 22% of men and 26% women having values >140 mmHg. We included those on hypertension medications in this group. The next most prevalent marker was elevated serum triglycerides followed by waist girth, with 21% of men having values >150 mg/dl and 21% having waist girth >100 cm, whereas 14 and 9% of women had these abnormalities, respectively. The combination of elevated sBP, elevated serum triglycerides, and waist girth was found in 23% of men and 21% of women.

Overall, the prevalence of the triumvirate combination of sBP, elevated triglycerides, and waist circumference was inversely graded across fitness categories, with 28% of the low fit, 23% of the moderately fit, and 8% of the high fit having more than two of these metabolic markers.

Group differences

The active group showed a significantly lower prevalence (11%) of the metabolic syndrome than the sedentary group (28%) at 10 years. Those subjects who moved from low to moderate or high fitness in the active group had significantly fewer ($P < 0.001$) metabolic markers compared with those who remained or moved to a lower fitness level. Within the sedentary group, those who moved from moderate or high to low fitness were not significantly different in terms of prevalence of metabolic markers from those who began in a lower tertile and moved to a higher level of fitness from baseline.

The presence of two or more risk factors with lower fitness was associated with

a higher Charlson Comorbidity Index score ($P < 0.001$), lower max METs ($P < 0.003$), and a positive exercise treadmill test ($P < 0.002$) among men in the sedentary group but not the active group. No similar association was observed in women in either group.

Among active individuals, a 1-MET increase in fitness was associated with an 11% reduction in presence of any metabolic risk factor, a 14% reduction in Charlson Comorbidity Index score, and a 50% reduction in the presence of a positive exercise stress test.

Among sedentary individuals, a 1-MET decrease in fitness was associated with a 52% increase in the prevalence of any metabolic risk factor and a 59% increase in the prevalence of the Charlson Comorbidity Index score in contrast to a 1-MET decrease in fitness in the active group, where this was associated with a 32% increase in prevalence of at least one metabolic risk factor and a 43% increase in the Charlson Comorbidity Index score.

Remaining active resulted in less morbidity and metabolic risk factor prevalence over 10 years among older adults. Changes in fitness were associated with altered RPP, suggesting cardiovascular function may mitigate the protective effect of regular exercise independent of the role of improved fitness.

Significant associations were observed for both men and women. For the men, age-adjusted cumulative odds ratios for abnormal markers of the syndrome were 3.0 (95% CI 2.7–3.4; $P < 0.001$) for low-fit when compared with moderate-fit ones and 10.1 (9.1–11.2; $P < 0.001$) when compared with high-fit men. Among women, age-adjusted cumulative odds ratios were 2.7 (2.1–3.5; $P < 0.001$) for least-fit compared with moderately fit ones and 4.9 (3.8–6.3; $P < 0.001$) when compared with most-fit women.

CONCLUSIONS — In this geographically defined older community-dwelling population, regular participation in an exercise training program resulted in a small increase in fitness compared with a 13% decline among sedentary control subjects over 10 years. Further, adoption of regular exercise training later in life was associated with a lower prevalence of metabolic risk factors for cardiovascular disease, fewer comorbid conditions, and fewer signs and symptoms of cardiovascular disease during exercise. Interesting-

ly, although moving from lower to higher relative fitness in those who exercised regularly resulted in fewer metabolic risk factors and comorbidity, this was not observed in the sedentary group. Individuals in the sedentary group who increased fitness in the absence of regular exercise training did not significantly change their prevalence of metabolic risk or comorbidity. Hence, regular physical activity alone may be metabolically advantageous.

Lakka et al. (9) recently reported increased cardiovascular disease prevalence and all-cause mortality in men with the metabolic syndrome >11 years. They reported a 9–14% incidence of metabolic syndrome at baseline, which was substantially lower than the 30% prevalence reported among men aged 40–89 years in the Third National Health and Nutrition Examination Survey (10) but similar to the 7.9% observed in the present study at baseline. Differing prevalence may be related to differing demographics or definitions used for the metabolic syndrome (9). Regardless, high prevalence suggests that prevention strategies that target metabolic risk are required to combat the potential epidemics of type 2 diabetes and hypertension among adults (8).

Recent evidence from the Finnish Diabetes Prevention Study (16) and the U.S. Diabetes Prevention Program (17) suggest even modest lifestyle intervention can have a major impact on decreasing the risk of type 2 diabetes in middle-aged glucose-intolerant individuals. Men who engaged in regular moderate and especially more vigorous leisure-time physical activity were less likely to develop the metabolic syndrome during the Kuopio Ischemic Heart Disease Risk Factor Study (37). Church et al. (38) also reported similar association between fitness and the metabolic syndrome in middle-aged adults. However, until the present study, few trials have shown that regular physical exercise training can modify the presence of metabolic risk factors among older adults.

Although our subjects were sedentary at entry, none of the subjects in either group were referred for diagnostic testing and none had detectable cardiovascular symptoms or signs at entry screening. Hence, subjects were healthy, and pre-existing “silent” cardiac disease was not likely a factor in the adoption of exercise training nor was a preexisting active lifestyle likely to have affected the develop-

ment of risk factors. The active group was self-referred to our regular exercise program, whereas the age-matched sedentary group was randomly selected from the same community. Hence, it is unlikely that other environmental factors could have influenced the results.

Reports from the Honolulu Heart Program demonstrated that walking was associated with a decrease in all-cause mortality in older men, which provided an inverse relation between physical activity and incident coronary artery disease (39). Interestingly, the primary mode of exercise used in our active group was walking but likely at a higher intensity than that used by Hakim et al. (39). Certainly, intensity of exercise is an important determinant of risk factor reduction (6,22,24,37). Hence, we attempted to replicate the need for appropriate intensity by using a supervised prescribed long-term exercise training program. Despite the high intensity (~85% VO_{2max}) of the exercise prescribed and updated yearly, we observed a high rate of compliance with the program, and this likely contributed to the observed reductions in risk factor prevalence with each level of fitness, with the greatest reduction in those who moved to the highest fitness level in the active group. Hence, the dose of exercise was not associated with poor adherence; on the contrary, our retention and compliance was high, as was concomitant cardiovascular benefit.

In addition to the interaction between fitness, exercise training, and metabolic risk factor prevalence, we observed similar association with the prevalence of comorbidity using the Charlson Comorbidity Index score and cardiovascular signs and symptoms during exercise testing. Hence, regular exercise training initiated in later life may modify health outcomes, as previously reported in younger populations (3,5,19).

Other healthy lifestyle habits including diet were not captured in our analysis and could have affected the prevalence of metabolic and cardiovascular signs and symptoms. In particular, those in the active group who sought out increasing physical activity may also have sought other healthy lifestyle options. Inclusion of subjects from the same geographic area would have enabled similar environmental exposure (40) among participants in either group to healthy lifestyle choices

and may have reduced the impact of these confounders.

Previous studies of exercise interventions in older populations in particular have had limited external validity. Recruitment of volunteers from the community exposes the cohort to the “healthy volunteer effect” that may differ from the general population. On the other hand, cohorts of patients referred for diagnostic reasons could bias in favor of a sicker population than present in the community. Our sample represented two groups: one who presented to our institution for adoption and participation in a physical activity program for general fitness reasons and one randomly assembled from the same community to serve as a nonactive control. Both were free of predefined clinical outcomes measures. Hence, we believe our samples demonstrated external validity compared with previous studies and enable direct generalizability to similar ambulatory community-dwelling older populations.

The major strength of this study was the longitudinal design, impressive follow-up of most subjects, and inclusion of two groups of older adults from the same community, one of whom adopted and maintained a regular exercise regimen. This allowed both groups to be compared with less fear of spatial exposure differences of time or place. The inclusion of a broad range of ages (55–75 years at baseline), large numbers of both men and women, and absence of symptoms or signs of cardiovascular disease at entry is notable compared with earlier reports (9). Because we stratified for fitness at baseline, we were able to generate odds ratios for risk accumulation with fitness. We measured VO_{2max} in our sedentary cohort and observed a high correlation with fitness determined by exercise treadmill time performance in METs as previously described by our group (41). Hence, our determination of this critical variable was likely sound in both groups.

The major limitation of the study was the self-selection of the active group to adopt exercise training. Hence, this did not allow for full randomization of the exercise training “intervention.” This could have led to volunteer bias and higher rates of compliance with training at higher work rates than might be anticipated in the general population of older adults. However, in the context of the “usual” exposure to lifestyle interventions

in the community, individuals seek out physical activity programs rather than responding to direction from others as reflected in poor adherence rates generally in therapeutic physical activity programs (26). It was not the objective of this study to test the multifaceted issues of exercise adoption and maintenance in the community (42) but rather to determine how older individuals who self-selected participation in an exercise training program differed in terms of metabolic risk from those who did not. We did not discourage sedentary participants from engaging in regular exercise training or fitness programs in the community. Indeed, some did choose to become physically active. However, in our experience and as supported in the literature, retention and compliance with these programs is difficult over the long term (42) and needs ongoing research into reducing barriers to participation and adherence (27).

Finally, as we have demonstrated, the threat of the metabolic syndrome is higher among those older adults who remain sedentary. Hence, as the balance between cardiovascular disease risk and fitness continues to widen with an aging, overweight, and sedentary population, research supporting promotion and adherence to exercise programs among those at risk is critical.

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