Usefulness of Self-Reported Leisure-Time Physical Activity to Predict Long-Term Survival in Patients With Coronary Heart Disease

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Self-reported leisure-time physical activity level correlates well with both cardiovascular (CV) and non-CV mortality in subjects without coronary heart disease (CHD). The impact of leisure-time physical activity on long-term outcomes has not been well studied in patients with preexisting CHD, who are often physically limited because of symptoms, medications, and co-morbid conditions. The aim was to determine the long-term prognostic value of self-reported leisure-time physical activity in a large CHD cohort. Leisure-time physical activity was evaluated using a self-administered questionnaire and categorized using a 4-level scale (sedentary, mild, moderate, and strenuous) in 14,021 of 24,958 subjects from the Coronary Artery Surgery Study Registry with suspected or proven CHD who underwent cardiac catheterization from 1974 to 1979. Median long-term follow-up was 14.7 years (interquartile range 9.8 to 16.2). Clinical outcomes were evaluated according to physical activity level and adjusted for potential confounders. Long-term all-cause and CV mortality progressively increased from most to least active subjects, with sedentary patients showing a 1.6-fold increase in mortality for both these outcomes (hazard ratio [HR] 1.63, 95% confidence interval [CI] 1.34 to 1.97, p <0.0001 for all-cause mortality). Similar trends were noted for men and women and in adjusted models, although HRs were attenuated after adjusting for age, gender, smoking, hypertension, diabetes mellitus, total cholesterol, body mass index, and ejection fraction (adjusted HR 1.23, 95% CI 1.01 to 1.49, p = 0.03 for all-cause mortality; adjusted HR 1.25, 95% CI 0.99 to 1.57, p = 0.05 for CV mortality). In conclusion, leisure-time physical activity independently predicted long-term survival in men and women with chronic stable CHD. **(Am J Cardiol 2008;xx:xxx)**

Self-reported physical activity is part of a screening cardiovascular (CV) assessment in the general population. Its ability to predict CV risk in subjects with coronary heart disease (CHD) has not been studied in detail. We therefore sought to document the long-term prognostic value of self-reported leisure-time physical activity in a large sample of subjects with suspected or proven CHD.

Methods

The Coronary Artery Surgery Study (CASS) Registry includes 24,958 patients with suspected or proven CHD who were enrolled at 15 North American centers from 1974 to 1979.[1] Patients had scheduled follow-up on an annual basis until 1982. Vital status was subsequently obtained through a mail-in survey completed from 1989 to 1991. Vital status for nonresponders was obtained from the National Death Index for patients in the United States and by next of kin, medical records, and death certificates in Canada. Follow-up was complete for 96% of patients in the registry by the closing date of December 31, 1992. Patients without medical records confirming death were considered alive. CV mortality was defined according to the *International Classification of Diseases, Eighth Revision* using codes 390 to 458. Intermediate-term end points were defined as those occurring by the end of scheduled follow-up in 1982, whereas long-term end points were defined as those occurring by December 31, 1992. Data for nonfatal events were available until 1982 from annual scheduled follow-up visits and are included in the intermediate-term end points. Nonfatal events studied included hospitalization for incident myocardial infarction, stroke, or congestive heart failure.

The clinical variables used were derived from the CASS Registry and obtained at the time of enrollment. Clinical variables studied included age; gender; family history of premature CHD; medical history of diabetes, hypertension, hypercholesterolemia, and smoking; and medication use. Additional variables studied were systolic and diastolic blood pressure, serum cholesterol, triglycerides, fasting plasma glucose, exercise tolerance from baseline exercise testing, left

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Table 1
Baseline characteristics according to physical activity level

Characteristic	Strenuous Activity (n = 365)	Moderate Activity (n = 2,572)	Mild Activity (n = 6,369)	Sedentary (n = 4,715)	p Value
Age (yrs)	48 ± 10	52 ± 9	53 ± 9	53 ± 9	<0.0001
Body weight (kg)	79 ± 12	77 ± 12	76 ± 13	74 ± 13	<0.0001
Body mass index (kg/m^2)	26 ± 3	26 ± 3	26 ± 4	26 ± 4	0.96
Left ventricular ejection fraction (%)	60 ± 14	60 ± 15	59 ± 15	58 ± 15	<0.0001
Exercise tolerance (METs)	8 ± 3	7 ± 3	7 ± 4	6 ± 3	<0.0001
Systolic blood pressure (mm Hg)	130 ± 19	130 ± 19	131 ± 20	131 ± 21	0.27
Diastolic blood pressure (mm Hg)	81 ± 11	81 ± 12	81 ± 12	81 ± 12	0.20
Serum total cholesterol (mg/dl)	230 ± 46	230 ± 47	230 ± 49	233 ± 52	0.042
Serum triglycerides (mg/dl)	184 ± 98	203 ± 147	206 ± 193	207 ± 146	0.0030
Fasting plasma glucose (mg/dl)	100 ± 26	103 ± 27	103 ± 30	100 ± 26	<0.0001
Men	330 (90%)	2,171 (84%)	4,858 (76%)	3,301 (70%)	<0.0001
Active smokers	99 (27%)	809 (31%)	2,161 (34%)	1,927 (41%)	<0.0001
Family history of premature CHD	151 (41%)	1,080 (41%)	2,739 (43%)	2,162 (46%)	0.0012
Hypertension history	104 (28%)	800 (31%)	2,136 (33%)	1,641 (35%)	<0.0001
Diabetes mellitus	19 (5%)	203 (8%)	710 (11%)	544 (11%)	<0.0001
Previous myocardial infarction	127 (35%)	1,100 (43%)	3,029 (47%)	2,341 (50%)	<0.0001
Abnormal coronary angiogram	277 (76%)	2,107 (82%)	5,214 (82%)	3,944 (84%)	0.0006
No. of coronary arteries narrowed >50%					
0	129 (35%)	698 (27%)	1,733 (27%)	1,276 (27%)	0.035
1	58 (16%)	539 (21%)	1,315 (21%)	954 (20%)	
2	82 (22%)	600 (23%)	1,407 (22%)	1,108 (24%)	
3	96 (26%)	723 (28%)	1,880 (30%)	1,351 (29%)	
Antihypertensive therapy	25 (7%)	216 (8%)	530 (8%)	398 (8%)	0.77
β-Blocker use	125 (34%)	925 (36%)	2,774 (43%)	2,371 (50%)	<0.0001
Aspirin use	12 (3%)	89 (3%)	305 (5%)	162 (3%)	0.0010
Lipid-lowering therapy	17 (5%)	122 (5%)	266 (4%)	175 (4%)	0.19
Oral hypoglycemic agents	5 (1%)	77 (3%)	287 (4%)	214 (4%)	0.0002
Insulin therapy	5 (1%)	30 (1%)	120 (2%)	85 (2%)	0.10

Values expressed as mean ± SD or number (percent).

ventricular ejection fraction, and extent of coronary disease. All blood marker measurements were obtained at the time of blood collection from fresh samples. The number of diseased coronary arteries was based on whether the left anterior descending, left circumflex, or right coronary artery had ≥70% diameter stenosis or whether the left main artery had ≥50% diameter stenosis. Left main artery disease was considered 2-vessel disease in the presence of a right-dominant coronary circulation and 3-vessel disease in the presence of a left-dominant coronary circulation. Coronary angiograms were interpreted using visual estimation in the CASS Registry.

All subjects were questioned about typical daily recreation or physical activity level during the last 6 months. This meant activities in addition to regular employment or homemaking. Self-reported physical activity was evaluated using a 4-level activity scale, namely strenuous, moderate, mild, and sedentary.[2] Categories of activity were defined as strenuous, physically demanding recreational activity usually involving competition or endurance, including team efforts; moderate recreation, carried out for pleasure and relaxation, but without competition or endurance; mild recreation, carried out for pleasure and relaxation and involving only slight physical activity; and sedentary, including activities performed while sitting.

Results were expressed as mean ± SD or median, minimum, and maximum for continuous variables and frequency and percent for categorical variables. Univariate analyses (1-way analysis of variance or Kruskal-Wallis test for continuous variables and Pearson's chi-square test for categorical variables) were used to compare the different physical activity level groups. Univariate Cox proportional hazard regression models were used to evaluate the influence of physical activity level on outcomes. Multivariate Cox regression models were also created adjusting for potential confounders (baseline characteristics and clinical variables). Survival analyses using the Kaplan-Meier method and log-rank test were used to study freedom from outcomes according to physical activity level. A p value <0.05 was considered statistically significant. Statistical analyses were performed using SAS, version 8.02 (SAS Institute, Cary, North Carolina).

Results

Decreasing physical activity level was associated with a higher proportion of women and older age and a higher prevalence of smoking, diabetes, hypertension, and family history of premature CHD (Table 1). Body mass index was similar between groups, although body weight was lower in less active individuals. As expected, higher physical activity level corresponded to better physical fitness. Fasting plasma glucose and triglycerides were also higher in less active subjects.

After a median long-term follow-up of 14.7 years (interquartile range 16.2 to 9.8), 109 (29.9%), 905 (35.2%), 2,537

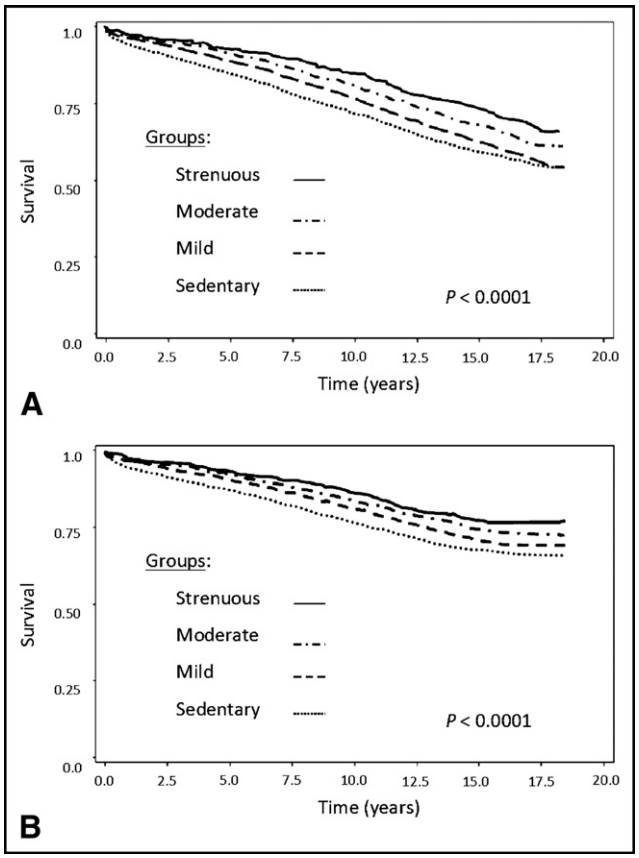

Figure 1. Cumulative survival according to self-reported physical activity level and *(A)* freedom from long-term all-cause death in the entire cohort and *(B)* and freedom from long-term CV death in the entire cohort.

(39.8%), and 1,980 patients (42.0%) had died in the strenuous, moderate, mild, and sedentary groups, respectively ($p < 0.0001$; Figure 1). CV disease accounted for 22.0%, 25.1%, 28.1%, and 30.5% of all deaths in the same groups, respectively ($p < 0.0001$; Figure 1). Unadjusted risk of all-cause mortality was significantly higher in patients in the moderate, mild, and sedentary groups relative to subjects performing strenuous physical activity. After adjusting for age, gender, history of smoking, hypertension, diabetes, total cholesterol, body mass index, and ejection fraction, hazard ratios (HRs) for all-cause mortality were attenuated, with only sedentary subjects showing a significantly higher risk of death. Similar results were obtained for long-term CV mortality. HRs for combined intermediate-term end points (5-year follow-up) were higher than those for long-term mortality, but showed the same trend of increasing risk with decreasing physical activity level. Both men and women showed similar relations between physical activity level and mortality. Unadjusted and adjusted outcomes are listed in Table 2.

Discussion

Our findings showed for the first time in a very large prospectively collected CHD cohort that self-reported leisure-time physical activity predicted both intermediate- and long-term clinical outcomes. In unadjusted models, a clear risk gradient was evident from the most to the least active groups, with a 1.6- to 2-fold increase in risk of major CV events in sedentary subjects. The impact of physical activity level on outcomes was similar for men and women. Adjusted models showed similar risk gradients, although differences between physical activity groups were attenuated. In adjusted models, only sedentary subjects showed a higher risk of all-cause death.

The prognostic value of self-reported physical activity has been confirmed in several large epidemiologic studies of healthy subjects without known CV disease.[3–9] For example, in the Oxford and Collaborators Health Check Trial (OXCHECK) study, self-reported frequency of vigorous-intensity leisure-time physical activity was associated with a significantly lower risk of all-cause mortality.[10] In a large Finnish cohort study involving >30,000 women and men followed up for >20 years, moderate to high occupational and leisure-time physical activity decreased CV and all-cause mortality by approximately 25%.[11] Similarly, data from the British Regional Heart Study, a prospective British cohort study involving >7,000 men aged 40 to 59 years, showed that regular physical activity in subjects without known CV disease may reduce all-cause and CV mortality by 30% to 40% during 15 years.[12,13] Data from the Nurses Health Study confirmed the protective effects of regular leisure-time physical activity in healthy women.[14,15] Finally, in a Finnish monozygotic twin study, in twin pairs discordant for CHD, regular physical activity was associated with a 50% lower risk of CHD at long-term follow-up, indicating the influence of physical activity over genetic considerations and other risk factors.[16]

Factors limiting the ability to exercise, including CV symptoms, negative chronotropic medication, and such co-morbid conditions as peripheral vascular disease, might in theory affect the ability of patients with CHD to exercise and the ability of self-reported physical activity to predict future CV events. A medical history of hypertension, previous myocardial infarction, and use of β blockers was present in ⅓ to ½ of patients, whereas diabetes was present in 5% to 10% of patients, respectively. Less physically active patients were generally older, had a higher prevalence of preexisting CHD, and were more likely to have diabetes and hypertension. Despite these concerns, we noted a clear trend of increasing risk of CHD morbidity and mortality with decreasing physical activity level. Adjusted models for both intermediate and long-term outcomes showed similar trends, although HRs were reduced, with only sedentary patients showing a statistically significantly higher risk of death. Although men reported being more physically active than women, the relation between self-reported physical activity and long-term survival did not differ between genders.

Our data were consistent with 1 smaller study of 772 older men with CHD, defined using a self-reported history of myocardial infarction or angina.[17] During a 5-year follow-up, light physical activity was associated with a 50% reduction in risk of all-cause and CV death. Conversely, moderate and moderate-vigorous physical activity was not

Table 2
Risk of cardiovascular (CV) end points according to physical activity level compared with strenuous group

Variable	Long-Term All-Cause Death		Long-Term CV Death		Intermediate-Term Risk of All-Cause Death, MI, CHF, or Stroke		Intermediate-Term Risk of CV Death, MI, CHF, or Stroke	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Moderate								
Unadjusted models	1.22 (1.00–1.49)	0.048	1.18 (0.93–1.49)	0.16	1.31 (0.09–1.73)	0.053	1.29 (0.97–1.72)	0.074
Adjusted models*	1.01 (0.82–1.23)	0.92	1.01 (0.79–1.27)	0.93	1.12 (0.85–1.48)	0.41	1.11 (0.84–1.48)	0.44
Mild								
Unadjusted models	1.47 (1.21–1.78)	<0.0001	1.39 (1.10–1.74)	0.004	1.60 (1.22–2.09)	0.0005	1.50 (1.14–1.98)	0.003
Adjusted models*	1.12 (1.92–1.36)	0.23	1.09 (0.87–1.38)	0.41	1.26 (0.96–1.65)	0.08	1.20 (0.91–1.58)	0.18
Sedentary								
Unadjusted models	1.63 (1.34–1.97)	<0.0001	1.61 (1.28–2.02)	<0.0001	2.03 (1.55–2.65)	<0.0001	1.92 (1.46–2.53)	<0.0001
Adjusted models*	1.23 (1.01–1.49)	0.03	1.25 (0.99–1.57)	0.050	1.57 (1.20–2.06)	0.0009	1.51 (1.14–1.99)	0.0035

* Adjusted for age, gender, smoking status, hypertension, diabetes, body mass index, ejection fraction, and serum total cholesterol.
CHF = congestive heart failure; CI = confidence interval; MI = myocardial infarction.

associated with a significantly lower risk of death, presumably because of a small sample size. The Harvard Alumni Health Study also showed in a cohort of 782 men with reported CHD that subjects using <2,000 kcal/week on leisure-time physical activity had a higher risk of death relative to more active individuals.[18] Similarly, in 1,045 subjects ≥65 years with reported CHD, energy expenditure <1,500 kcal/week during leisure-time physical activity conferred a higher risk of all-cause death relative to higher energy expenditure.[19] The findings of our study confirmed the results of previous work, this time in a cohort of 14,000 subjects with proven CHD with a significantly longer follow-up, and we extended our results to women.

Limitations of the present study included few patients in the strenuous activity group despite our total sample size of >14,000 subjects. A larger sample in this category might have enabled us to detect statistically significant mortality differences among all groups in our models adjusted for potential confounders. Alternatively, any level of physical activity higher than sedentariness may provide a similar degree of CV protection in patients with CHD. Second, we used physical activity level at baseline and were not able to take into account potential changes in activity level over time. Third, physical activity level was self-reported and based on a simple 4-level classification system. However, this tool was considered robust at the time the study was undertaken[20] and has been used as a prognostic instrument in large epidemiologic studies.[21,22] Fourth, although we have no explanation why leisure-time physical activity data were not available for all patients in the CASS Registry, we do not believe our results were significantly biased given their consistency with existing knowledge regarding the relation between self-reported physical activity and outcomes. Finally, CASS was performed during the 1970s and 1980s, and the outcomes we measured necessarily reflected treatment practices at the time the original study was undertaken. Nevertheless, the results are important, perhaps reflecting the natural history of the disease. They must also be interpreted in the context of the growing tendency toward physical inactivity.

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