Fitness versus Physical Activity Patterns in Predicting Mortality in Men

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PURPOSE: To compare the contributions of fitness level and physical activity patterns to all-cause mortality.

METHODS: Of 6213 men referred for exercise testing between 1987 and 2000, 842 underwent an assessment of adulthood activity patterns. The predictive power of exercise capacity and activity patterns, along with clinical and exercise test data, were assessed for all-cause mortality during a mean (±SD) follow-up of 5.5 ± 2 years.

RESULTS: Expressing the data by age-adjusted quartiles, exercise capacity was a stronger predictor of mortality than was activity pattern (hazard ratio [HR] = 0.56; 95% confidence interval [CI]: 0.38 to 0.83; $P < 0.001$). In a multivariate analysis that considered clinical characteristics, risk factors, exercise test data, and activity patterns, exercise capacity (HR per quartile = 0.62; CI: 0.47 to 0.82; $P < 0.001$) and energy expenditure from adulthood recreational activity (HR per quartile = 0.72; 95% CI: 0.58 to 0.89; $P = 0.002$) were the only significant predictors of mortality; these two variables were stronger predictors than established risk factors such as smoking, hypertension, obesity, and diabetes. Age-adjusted mortality decreased per quartile increase in exercise capacity (HR for very low capacity = 1.0; HR for low = 0.59; HR for moderate = 0.46; HR for high = 0.28; $P < 0.001$) and physical activity (HR for very low activity = 1.0; HR for low = 0.63; HR for moderate = 0.42; HR for high = 0.38; $P < 0.001$). A 1000-kcal/wk increase in activity was approximately similar to a 1 metabolic equivalent increase in fitness; both conferred a mortality benefit of 20%.

CONCLUSION: Exercise capacity determined from exercise testing and energy expenditure from weekly activity outperform other clinical and exercise test variables in predicting all-cause mortality. **Am J Med. 2004;117:912–918.** ©2004 by Elsevier Inc.

Increasing evidence of the association between physical inactivity and cardiovascular or all-cause mortality (1) has led health authorities around the world to make physical activity promotion part of broad health care policy goals (1–3). More recent studies (3–6) have observed strong associations between physical fitness, measured by a maximal exercise test, and survival from cardiovascular and noncardiovascular causes. Physical fitness is related to physical activity patterns, and thus current physical activity guidelines generally consider fitness a surrogate measure of physical activity. However, other attributes, such as genetics, subclinical disease, and behavioral and environmental factors, determine individual fitness levels (7). There has been some recent debate as to whether daily physical activity patterns largely determine one's fitness level and therefore its inverse association with mortality, or whether fitness level predicts mortality independently from activity pattern (8,9). In addition, while these issues have been studied largely in asymptomatic populations (10–13), less is known about these associations in patients with existing cardiovascular disease.

In the present study, we assessed all-cause mortality using fitness measured in subjects referred for exercise testing for clinical reasons, and quantified adulthood physical activity patterns by questionnaire. Our objectives were to compare the independent contributions of fitness and physical activity patterns to overall mortality, to determine the predictive power of fitness and activity patterns as compared with other clinical and exercise test variables, and to assess the interaction between fitness and activity in predicting mortality.

METHODS

Sample

The sample was drawn from 6213 consecutive men (mean [±SD] age, 59 ± 11 years) who were referred for exercise testing for clinical reasons between April 1987 and July 2000. Of these, a subgroup of 842 subjects underwent a detailed evaluation of current and past activity patterns. The subgroup represented a convenience sample tested on a particular day of the week in which research assistants were assigned to oversee the data collection.

Exercise Testing

The exercise laboratory was directed in a consistent fashion by two of the authors (VF and JM). A thorough clinical history, listing of medications, and risk factors (beginning in 1987) were recorded prospectively at the

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time of the exercise tests using computerized forms (14,15) that included standard definitions of clinical conditions and exercise responses. Patients underwent symptom-limited treadmill testing using standardized graded (16) or individualized ramp treadmill (17) protocols. Before ramp testing, patients answered a questionnaire to estimate exercise capacity; the questionnaire allowed most patients to reach maximal exercise within the recommended range of 8 to 12 minutes (18). We previously observed that this protocol provides the closest relation between measured and estimated metabolic equivalents (METs) (17). Patients were discouraged from using the handrails for support. Heart rate targets were not used as predetermined endpoints. Medications were not changed or stopped prior to testing. ST-segment depression was measured visually at the J junction, and slope was determined over the following 60 ms and classified as upsloping, horizontal, or downsloping. Ventricular tachycardia was defined as three or more consecutive premature ventricular contractions, and frequent premature ventricular contractions were defined as ≥10% of the total ventricular contractions (19). Blood pressure was measured manually, and exercise capacity (in METs) was estimated from peak treadmill speed and grade (20). No test was classified as indeterminate (21). The exercise tests were performed, analyzed, and reported according to a standardized protocol and utilizing a computerized database (22).

Physical Activity Questionnaire

On the day of exercise testing, physical activity patterns were quantified in the convenience sample of 842 subjects. The quantification of physical activity was performed by questionnaire and modeled after the Harvard Alumni studies of Paffenbarger and colleagues (23). Although the questionnaire was self-administered, subjects were encouraged to ask questions if clarification was required. Responses were recorded using Microsoft Access (Redmond, Washington). Metabolic costs of occupational and recreational activities were computed, and energy expenditure was expressed in kilocalories per week (24). Energy costs of activities were estimated from the compendium of physical activities developed by Ainsworth et al (25). Energy cost of stairs climbed per week was calculated using the estimation of Basset et al (26). One flight of stairs was considered 10 steps, and 12 blocks were considered 1 mile. Energy expenditure was expressed in terms of lifetime adulthood recreational and occupational activity. Recreational activity was also expressed separately as energy expended during the year before undergoing exercise testing (recent activity). For both fitness (in peak METs achieved) and activity patterns, data were categorized by quartiles.

Follow-up

The Social Security Death Index was used to match all patients using name and social security number. Vital status was determined as of July 2000.

Statistical Analysis

Total (all-cause) mortality was used as the endpoint for survival analysis. Survival analysis was performed using Kaplan-Meier curves to compare variables and cutpoints, and a Cox proportional hazards model was used to determine which variables were associated significantly with time to death, and to develop relative risks for quartiles of exercise capacity and physical activity. Hazard ratios were calculated along with their 95% confidence intervals. Age adjustment was performed with age stratified by decade. Number Crunching Statistical Software (Salt Lake City, Utah) was used for all analyses.

RESULTS

In the convenience subgroup, the mean (±SD) follow-up period was 5.5 ± 2.0 years, and the average annual mortality was 2%. A total of 1256 deaths occurred during follow-up in the total group of subjects (n = 6213) undergoing exercise testing; 89 occurred among those in the subgroup who had physical activity patterns assessed. No major complications occurred during testing, although sustained ventricular tachycardia occurred during 1.3% of the exercise tests. In the subgroup, 230 patients had ischemic responses to exercise: 42 had ≥1.0-mm horizontal or downsloping ST depression, 130 had angina during exercise, and angina was the main reason for stopping in 58. The prevalence of these responses was similar between the total group of subjects and the subgroup. The current sample in which exercise testing and physical activity patterns were assessed was compared with the remainder of the group of subjects referred for exercise testing (n = 5371). Demographic, historical, and clinical characteristics were generally similar, including for age and medication use, although small differences were observed in the prevalence of stroke, heart failure, and myocardial infarction (Table 1).

Physical Activity versus Physical Fitness in Predicting Mortality

Physical fitness was poorly related to energy expenditure from adulthood physical activity ($r = 0.09$). Age-adjusted univariate predictors of mortality, in rank order, were peak exercise capacity, recreational energy expenditure during adulthood, recreational energy expenditure over the last year, and energy expended from blocks walked and flights of stairs climbed per week (Table 2). Although energy expended from occupational activity ($P = 0.13$) and the combination of occupational and recreational activity ($P = 0.16$) were associated with approximately 15% reductions in mor-

Table 1. Comparison of Demographic and Clinical Characteristics of the Study Sample and the Larger Patient Group Referred for Exercise Testing during the Study Period

Characteristic	Study Sample (n = 842)	Other Referrals (n = 5371)	*P* Value
	Mean ± SD or Number (%)		
Age (years)	58.9 ± 11.7	58.9 ± 11.2	0.96
Duration of follow-up (years)	4.6 ± 1.8	6.9 ± 4.0	<0.001
Height (inches)	69.0 ± 3.4	69.2 ± 3.2	0.30
Weight (lbs)	193.4 ± 37.6	189.8 ± 37.6	0.01
Medications			
Digoxin	23 (3)	321 (6)	<0.001
Calcium antagonist	221 (26)	1519 (28)	0.48
Beta-blocker	147 (18)	1048 (20)	0.32
Nitrate	142 (17)	1344 (25)	<0.001
Antihypertensive	185 (22)	1343 (25)	0.15
History			
Atrial fibrillation	31 (4)	813 (15)	0.29
Pulmonary disease	75 (9)	367 (7)	0.02
Stroke	43 (5)	185 (3)	0.01
Claudication	37 (4)	304 (6)	0.19
Typical angina	141 (17)	1213 (23)	0.04
Myocardial infarction	204 (24)	1658 (31)	<0.001
Heart failure	46 (6)	481 (9.0)	0.001
Coronary bypass surgery	74 (8.8)	507 (9.4)	0.75
Percutaneous coronary intervention	68 (8)	324 (6)	0.01

tality per quartile increase, they did not appear to be strong predictors of survival. Age-adjusted multivariate predictors of survival, in rank order, were exercise capacity, followed by energy expenditure from recreational activity during adulthood. Past occupational energy expenditure was not associated with survival by multivariate analysis. A 1000-kcal/wk increase in adulthood activity was approximately equal to an increase of 1 MET in fitness; both conferred a survival benefit of 20%.

In age-adjusted analyses, exercise capacity and weekly energy expenditure were stronger predictors of mortality than historical data, other exercise test responses, and risk factors such as hypertension, hyperlipidemia, diabetes, and obesity (Table 3). Each quartile increase in exercise capacity was associated with an overall 38% reduction in mortality, whereas each quartile increase in energy expenditure from weekly activity was associated with an overall 28% reduction in mortality. However, the reduction in mortality risk between quartiles was not linear; the largest reduction occurred between the least fit or least active group and the next least fit or active group, with smaller differences observed between the other groups.

Kaplan-Meier survival curves applying commonly recognized indexes for exercise capacity (≤5 METs vs. >5

Table 2. Age-Adjusted Predictors of Mortality among Measures of Activity and Fitness*

Variable	Univariate Analysis: Hazard Ratio (95% Confidence Interval)	Univariate Analysis: *P* Value	Multivariate Analysis†: Hazard Ratio (95% Confidence Interval)	Multivariate Analysis†: *P* Value
Exercise capacity	0.53 (0.41–0.69)	<0.001	0.56 (0.38–0.83)	<0.001
Recreational activity/week, lifetime	0.70 (0.56–0.87)	<0.001	0.68 (0.49–0.95)	0.02
Recreational activity/week, last year	0.77 (0.61–0.98)	0.03	—	
Blocks walked/flights of stairs climbed per week	0.74 (0.55–0.98)	0.04	0.78 (0.56–1.09)	0.13
Occupational activity/week, lifetime	0.85 (0.69–1.06)	0.13	—	
Combined occupational and recreational activities/week	0.86 (0.71–1.05)	0.16	—	

* Data are from Cox proportional hazards analysis, categorized by quartiles. Activity data calculated from questionnaire, expressed in kcal/wk; exercise capacity is expressed in quartiles of metabolic equivalents calculated from peak treadmill speed and grade.
† Adjusted for age.

Table 3. Age-Adjusted Multivariate Predictors of Mortality among Clinical Variables, Fitness Level, and Physical Activity Patterns*

Variable	Hazard Ratio (95% Confidence Interval)	*P* Value
Fitness level		
Very low (reference)†	1.0	–
Low	0.59 (0.52–0.68)	<0.001
Moderate	0.46 (0.39–0.55)	<0.001
High	0.28 (0.23–0.34)	<0.001
Activity level		
Sedentary (reference)	1.0	–
Low	0.63 (0.36–1.10)	0.10
Moderate	0.42 (0.23–0.78)	<0.01
High	0.38 (0.19–0.73)	<0.01
Cardiovascular disease	1.62 (0.96–2.73)	0.06
History of smoking	1.58 (0.86–2.87)	0.15
History of hypertension	1.32 (0.82–2.13)	0.31
Family history of coronary artery disease	1.22 (0.74–2.02)	0.50
Diabetes	1.26 (0.70–2.27)	0.52
Obesity	0.81 (0.47–1.38)	0.47
Cholesterol level >220 mg/dL	1.08 (0.61–1.90)	0.79

* Activity data expressed as quartiles in kcal/wk of adulthood recreational activity; exercise capacity expressed in quartiles of METs; all other variables are dichotomous.
† <5.0 METs.
MET = metabolic equivalent.

METs for the entire referred group of 6213 subjects) and energy expenditure from physical activity (>2000 kcal/wk vs. subjects reporting no activity for the subgroup) showed that both higher exercise capacity and activity were associated with improved survival (Figure 1). Subjects with a higher exercise capacity or greater levels of activity had progressively lower mortality ($P < 0.001$; Figure 2). Age-adjusted interactions between fitness and activity, and the respective hazard ratios associated with being fit or active, demonstrated that being comparatively fit or active was associated with >50% reductions in mortality risk, regardless of categorization at the time of assessment (Figure 3). For example, among the least fit subjects (those achieving <5 METs), being relatively active (>1500 kcal/wk) was associated with a 68% reduction in mortality. Alternatively, among the least active subjects (those reporting no activity), being relatively fit was associated with a 55% reduction in mortality.

DISCUSSION

Our results demonstrate that both exercise capacity and energy expenditure from adulthood recreational physical activity are inversely associated with all-cause mortality in patients referred for exercise testing. These two variables were stronger predictors of mortality than other clinical and exercise data; in multivariate analyses, they outperformed established risk factors such as smoking, hypertension, hyperlipidemia, and diabetes. However, exercise capacity was a stronger predictor of mortality than were measures of recent or adulthood habitual physical activity, supporting the concept that physical fitness is a stronger predictor than activity level (8). Previous studies demonstrating an association between physical activity pattern or exercise tolerance and health outcomes generally involved apparently healthy cohorts (10–13), and few such analyses have been performed in more clinically relevant populations, such as patients referred for exercise testing for clinical reasons, which was the sample we studied.

The extent to which the benefits of physical activity on health and longevity are mediated through one's fitness

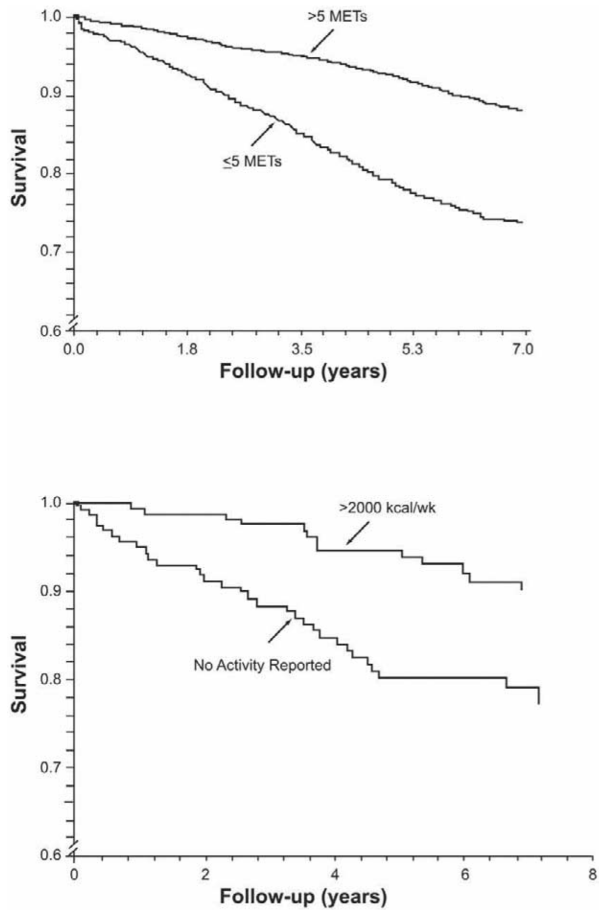

Figure 1. Kaplan-Meier survival curves for subjects achieving an exercise capacity ≤5 METs compared with >5 METs (top; for entire sample of 6213 subjects; $P < 0.001$ between groups) and in the subgroup of subjects expending >2000 kcal/wk in adulthood recreational activity compared with those reporting no physical activity (bottom; $P < 0.01$ between groups). MET = metabolic equivalent.

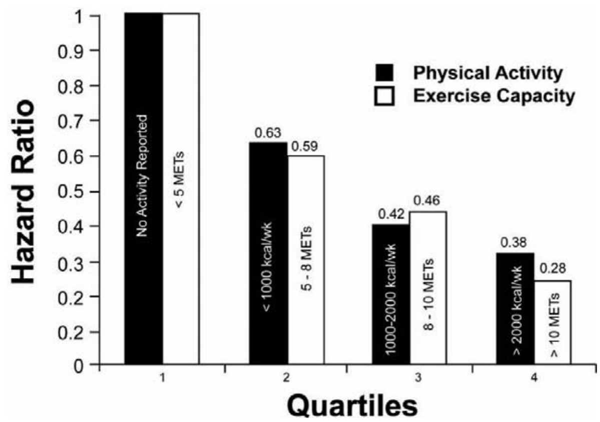

Figure 2. Age-adjusted hazard ratios for exercise capacity and adulthood recreational activity, expressed in quartiles, with the least fit or least active group as the reference group (quartile 1). MET = metabolic equivalent.

level has been debated (8,9). We found a correlation of 0.09, suggesting independence of these two measures. This association is lower than that reported previously (27), in which the correlation ranged between 0.30 and 0.60. We also observed a comparatively large reduction in mortality (72%) between the most and least fit subjects. Although comparisons with previous studies are complicated by different approaches to assessing activity, classification of groups, and other methodological differences, our results contrast with those of the majority of studies demonstrating differences in mortality in the order of 50% between the most and least fit groups (28).

We observed a less dramatic but nevertheless strong gradient for the reduction in mortality as physical activity increased. Indeed, fitness more strongly predicted mortality than did activity pattern as evidenced by both univariate and multivariate analyses. This concurs with a recent summary of eight fitness and 30 activity cohorts (8), in which fitness was a considerably stronger predictor of cardiovascular events. However, the strengths of the mortality gradients for fitness and activity that we observed were more similar to one another than those in most previous studies.

Few studies have addressed both fitness and physical activity in the same sample with other clinical and risk factor data, although available data generally suggest that fitness level more strongly predicts outcomes compared with physical activity patterns (8,28). There may be several reasons why this is the case. First, the quantification of fitness is more objective than activity. Fitness is generally determined directly from symptom or sign-limited exercise testing, whereas activity level is dependent on subject recollection, as well as on the judiciousness with which subjects respond and other limitations associated with questionnaires (29). Second, the strength of exercise capacity in stratifying risk, although only recently appreciated (30,31), is increasingly being recognized among both healthy (2,4,5,8,11) and clinically referred subjects (4,6,32-34). For example, in recent studies performed at the Cleveland Clinic (34), the Mayo Clinic (6,33), and the Veterans Administration (4), exercise capacity more strongly predicted cardiovascular events, all-cause mortality, or both, than did other clinical and exercise test variables.

Previous studies have observed that the dose-response relation between fitness or activity and the risk of heart disease or mortality is generally shaped such that relatively greater health benefits occur at the lower rather than higher end of the spectrum (1,2,8,11). Hence, greater health benefits would occur by increasing physical activity among the most sedentary or least fit persons. Indeed, the various consensus documents on physical activity and health generally acknowledge that "the greatest potential for reduced mortality is in the sedentary who become more active" (35). Our findings concur with these observations. We found that approximately 40% of the reduction in total mortality occurred between the least fit or least active and the next least fit or least active groups, suggesting that levels of fitness or regular activity that are achievable by most adults are sufficient to achieve a significant reduction in mortality.

The interactions that we observed between fitness or activity and mortality are provocative from a public health perspective. Being comparatively unfit was associated with a higher mortality risk even among those who were active, and being relatively inactive was associated with a higher mortality risk regardless of fitness level. No deaths were observed among subjects who were both fit (>10 METs) and active (>1500 kcal/wk). Importantly, regardless of how subjects were classified in terms of fitness or activity status, being more fit or more active was associated with a substantial reduction in mortality.

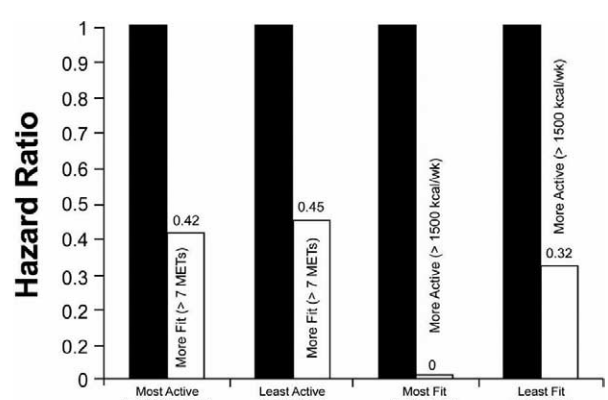

Figure 3. Interaction between fitness and activity, and their association with mortality. The 95% confidence intervals are as follows for the categories of "most active" (0.12 to 1.52), "least active" (0.18 to 1.09), and "least fit" (0.12 to 0.81). MET = metabolic equivalent.

Our study has several limitations. Although dose-response relations between fitness or activity and mortality have been shown to be similar between men and women (2), our sample did not include women. Our sample was comparatively small, but our data confirm results from larger studies that evaluated activity status or fitness separately (10,11,23). As with any questionnaire approach, the responses were dependent on subject recollection and how attentive subjects may have been in their responses. In addition, we had information only on all-cause mortality, and not on specific causes of death. Finally, answering the question of whether fitness or physical activity is more important in terms of health outcomes by multivariate analysis necessitates that they be independent, and this could not be determined from the present study.

In summary, low exercise capacity determined from exercise testing and low energy expenditure from weekly activity were associated with higher mortality risk in men, even more strongly than that of established risk markers such as smoking, hypertension, diabetes, previous myocardial infarction, or a history of heart failure. An approximate 1000-kcal/wk increase in activity, a modest amount achievable by most adults, confers a 20% survival benefit, similar to that which would occur by increasing fitness by 1 MET. Of the two measures, exercise capacity predicted mortality more strongly than did activity pattern. Being unfit carried a marked increase in risk even among persons who were comparatively active; likewise, being inactive was associated with a higher risk even among those who were relatively fit. Given the strong inverse association between fitness and mortality in the present and other recent studies, increasing fitness should be a priority when reviewing test results with patients. In addition, because physical activity in part develops physical fitness, increasing physical activity should remain an important health care policy objective.

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