PHYSICAL FITNESS AS A PREDICTOR OF MORTALITY AMONG HEALTHY, MIDDLE-AGED NORWEGIAN MEN

LEIV SANDVIK, M.SC., JAN ERIKSSEN, M.D., D.SC., ERIK THAULOW, M.D., D.SC., GUNNAR ERIKSSEN, M.D., REIDAR MUNDAL, M.D., AND KAARE RODAHL, M.D., D.SC.

Abstract *Background.* Despite many studies suggesting that poor physical fitness is an independent risk factor for death from cardiovascular causes, the matter has remained controversial. We studied this question in a 16-year follow-up investigation of Norwegian men that began in 1972.

Methods. Our study included 1960 healthy men 40 to 59 years of age (84 percent of those invited to participate). Conventional coronary risk factors and physical fitness were assessed at base line, with physical fitness measured as the total work performed on a bicycle ergometer during a symptom-limited exercise-tolerance test.

Results. After an average follow-up time of 16 years, 271 men had died, 53 percent of them from cardiovascular disease. The relative risk of death from any cause in fitness quartile 4 (highest) as compared with quartile 1 (lowest) was 0.54 (95 percent confidence interval, 0.32 to 0.89; P = 0.015) after adjustment for age, smoking status, serum lipids, blood pressure, resting heart rate, vital capacity, body-mass index, level of physical activity, and glucose tolerance. Total mortality was similar among the subjects in fitness quartiles 1, 2, and 3 when the data were adjusted for these same variables.

The adjusted relative risk of death from cardiovascular causes in fitness quartile 4 as compared with quartile 1 was 0.41 (95 percent confidence interval, 0.20 to 0.84; P = 0.013). The corresponding relative risks for quartiles 3 and 2 (as compared with quartile 1) were 0.45 (95 percent confidence interval, 0.22 to 0.92; P = 0.026) and 0.59 (95 percent confidence interval, 0.28 to 1.22; P = 0.15), respectively.

Conclusions. Physical fitness appears to be a graded, independent, long-term predictor of mortality from cardiovascular causes in healthy, middle-aged men. A high level of fitness was also associated with lower mortality from any cause. (N Engl J Med 1993;328:533-7.)

PHYSICAL activity beyond a certain level and duration is necessary to improve physical fitness[1] and may be an important factor in the prevention of death from ischemic heart disease.[2] Since physical activity is more difficult to quantify than the level of physical fitness, however, the latter has gained popularity in the assessment of both cardiovascular function and long-term cardiovascular health. Recent reports[3-11] conclude that a low level of physical fitness is associated with increased mortality from cardiovascular causes during the subsequent five to eight years, a finding that corroborates our observations over a seven-year period in 2014 apparently healthy men 40 to 59 years of age.[12]

The aims of the present study were to search for a possible graded association between physical fitness and overall mortality or mortality from cardiovascular causes and to determine whether our results after 7 years[12] would persist after the substantially longer observation period of 16 years.

METHODS

Subjects

The subjects participating in this study were recruited from five companies in Oslo, Norway, from 1972 through 1975. The male employees of these companies included both white-collar and blue-collar workers considered to be typical of the healthy working male population of Norway. All 2341 healthy men 40 to 59 years of age working for the companies were invited to participate in the study, and 2014 of them (86 percent) accepted. None were using cardioactive drugs or drugs that might affect exercise performance or heart-rate response.

A subject was considered healthy if none of the following disorders were present, as determined by a thorough screening of the health file or by medical examination: coronary heart disease, other heart diseases, hypertension treated with drugs, diabetes mellitus, cancer, advanced pulmonary disease, advanced renal disease, liver disease, and miscellaneous diseases, including disorders of the musculoskeletal system preventing the subject from taking a symptom-limited bicycle exercise test. The details of the selection procedures have been presented elsewhere.[13]

From the Medical Department, Central Hospital of Akershus, Nordbyhagen, Norway (L.S., J.E., G.E.), and the National University Hospital (E.T.), the Ullevaal Hospital (R.M.), and the Department of Work Physiology, University of Oslo (K.R.) — all in Oslo, Norway. Address reprint requests to Dr. Jan Erikssen at the Medical Department, Central Hospital of Akershus, N-1474 Nordbyhagen, Norway.

Base-Line Measurements

The study was carried out at the National University Hospital of Oslo (the Rikshospitalet). The examination included a comprehensive medical history, physical examination, a panel of blood tests (including a lipid profile and an intravenous glucose-tolerance test), phonocardiography, chest radiography, a spirographic study, resting electrocardiography, and a symptom-limited bicycle exercise-tolerance test.[12] Physically active men were defined as those who exercised at least twice a week to the level of sweating and becoming short of breath, participated in sports competitions, or both.[14] With respect to smoking habits, the participants were described as having never smoked, as having formerly smoked, or as currently smoking either 1 to 9 or 10 or more cigarettes daily. Resting blood pressure and heart rate were measured after the patient had been in the supine position for five minutes. Cholesterol and triglyceride concentrations were determined by standardized methods, as reported elsewhere,[15] as were details of the intravenous glucose-tolerance test.[16] To measure glucose tolerance, the rate of disappearance of glucose, expressed as the percentage disappearing per minute (the K value), was used.[16] In the spirographic study, vital capacity and forced vital capacity in one second were measured with a Bernstein spirometer, and peak expiratory flow with a Wright peak flowmeter, as described elsewhere.[17] All the participants were examined between 7:30 a.m. and 10:30 a.m. after abstaining from eating and smoking for at least 12 hours.

The exercise tests were conducted on an electrically braked Elema bicycle that was repeatedly calibrated during the study. When set at a particular workload, the cycle ergometer demands a constant output of energy from the test subject, regardless of the rate at which the subject pedals. The initial workload was set at 1.405 kcal per minute in all but 2 percent of the subjects, who started at 0.703 kcal per minute because their state of physical fitness appeared to be very poor. Increments of 0.703 kcal per minute were added every six minutes. The subjects were encouraged to continue exercising until they were exhausted. If a subject stated that he felt unable to continue the test, without giving specific reasons, the test was always terminated, regardless of other findings. The exercise protocol specified the following reasons for terminating a test: major cardiac arrhythmias, a drop in the systolic blood pressure of at least 10 percent on two successive measurements one minute apart toward the end of the test, heart block, ST-segment depression greater than 3 mm, severe dyspnea, or increasing chest pain.

Work capacity was calculated as the sum of the work performed (in kilocalories) at each workload until the termination of the test. Physical fitness was measured as the difference between the observed and expected work capacities according to the subject's body weight (as defined below under Statistical Analysis).

Exercise testing was repeated within two weeks in 130 participants. The two measurements of work capacity were within 5 percent of each other for 90 percent of the men and within 10 percent of each other for the entire group.

Identification of Deaths

Information about the times and causes of death was 100 percent complete by December 31, 1989. These data were obtained from the Norwegian Central Bureau of Statistics, as described elsewhere.[12] The specific causes of death are given according to the *International Classification of Diseases, 9th Revision*. On the basis of this information, each death was classified as having either a cardiovascular or a noncardiovascular cause.

Statistical Analysis

A graph of work capacity and body weight suggested linear associations in the group with a body weight of ≤75 kg and in the group with a body weight of >75 kg, with a shallower slope in the latter group. Linear regression analysis was performed separately in the two groups, with work capacity used as the dependent variable and body weight as the independent variable. The resulting regression function was calculated for each subject, and this value was labeled "expected working capacity according to body weight."

The association between the subject's fitness level and mortality (from cardiovascular, noncardiovascular, and all causes) was first assessed by presenting annual mortality according to the fitness quartiles. The relation between the fitness level and the variables studied was assessed by determining the mean values for the variables in each fitness quartile.

The association between the time to death (from cardiovascular causes or all causes) and the measurement of fitness, as well as selected variables, was investigated by means of the proportional-hazards model.[18] Three models were investigated. The first referred to mortality from cardiovascular causes and included physical fitness, age, and smoking status. The second model included, in addition, resting systolic blood pressure, resting heart rate, cholesterol and triglyceride levels, body-mass index (the weight in kilograms divided by the square of the height in meters), vital capacity, physical-activity level, and glucose tolerance as assessed by the intravenous glucose-tolerance test (the K value).[16] The third model referred to overall mortality and included the same variables as the second model.

The results obtained with the models are presented as relative risks. For a continuous variable, the relative risk of death from cardiovascular causes associated with a given change in the variable is presented after adjustment for all other variables in the model. The change studied was 2 SD (in the direction of increased risk) above the mean values for systolic blood pressure, cholesterol level, triglyceride level, vital capacity, and body-mass index; for age, the change studied was an increase of 10 years. For the graded variables (e.g., fitness level and smoking status) and the binary variables (e.g., K value and physical-activity level), the relative risks of death from cardiovascular causes between groups are presented. All the P values presented are two-tailed.

The assumptions of the proportional-hazards model were checked for all three models and found to be adequately met. The models were computed with the use of the proportional-hazards general procedure for a linear model in the SAS computer package.[19]

Results

All 2014 men included in the study completed the exercise test according to the protocol, and 97.4 percent started the second stage of the test. Twenty-two exercise tests were terminated because the subjects had increasing chest pain during the test. None had reported chest pain during their usual activities. Three exercise tests were interrupted because the subject's blood pressure reached 300 mm Hg; 1 had a decrease in blood pressure of at least 10 percent; 21 had arrhythmias; none had heart block; and 9 had ST-segment depressions of more than 3 mm. Of the 54 men who had at least one of these complications 32, 11, 5, and 6 belonged to fitness quartiles 1, 2, 3, and 4, respectively, when all 2014 men were categorized in fitness quartiles. Because of the possibility that these 54 men had cardiovascular disease at base line, they were excluded from further analysis. The remaining 1960 men, who stopped exercising because of obvious exhaustion, because they said they were unable to exercise further, or both, make up the present series. Their mean age was 49.9 years (range, 40.0 to 59.9). The average follow-up period was 15.9 years (range, 14 to 17), during which 271 of the men died, 143 (52.8 percent) of them from cardiovascular diseases (89 percent of these men died from myocardial infarction or had sudden and unexpected deaths). Of the 143 men who died of cardiovascular causes, 61 were in fitness quartile 1, 45 in quartile 2, 26 in quartile 3, and 11 in quartile 4. There were 45, 32, 38, and 13 deaths from other causes in the respective quartiles, for an overall mortality of 106, 77, 64, and 24, respectively.

Table 1 shows the values in each fitness quartile for a number of selected base-line variables. The higher the level of fitness, the higher the vital capacity and the lower the resting heart rate, blood pressure, cholesterol level, and prevalence of smoking. A high level of fitness was also strongly associated with a high level of physical activity in leisure time. All these associations were statistically significant ($P<0.001$). Virtually identical results were found when the data were corrected for differences in mean age among the quartiles (data not shown).

The relation between the fitness measure and annual mortality (from cardiovascular, noncardiovascular, and all causes) is shown in Table 2. Age-adjusted mortality from cardiovascular causes decreased with increasing fitness among both smokers and nonsmokers, and in all but the highest fitness quartile, smokers had a higher mortality due to cardiovascular causes than nonsmokers. In the highest fitness quartile, smokers and nonsmokers had similar mortality from cardiovascular causes.

The relation between fitness level and age-adjusted cumulative mortality from cardiovascular causes over the 16-year period is shown in Figure 1. Mortality from cardiovascular causes was very low in all the fitness subgroups during the first four years of observation, whereas the difference in mortality between quartile 1, the lowest fitness quartile, and the other three began to appear only after five years. The difference between quartile 4, the highest fitness quartile, and quartiles 2 and 3 was first observed after seven years and increased consistently thereafter. Mortality from cardiovascular causes was similar in quartiles 2 and 3 during the first 13 years, whereas a tendency toward a difference in favor of quartile 3 was seen at 16 years.

Relative Risks among Fitness Quartiles

Mortality from Cardiovascular Causes

The relative risk of death from cardiovascular causes in quartile 4 as compared with quartile 1 was 0.30 (95 percent confidence interval, 0.15 to 0.61; P<0.001) after adjustment for age and smoking status. This relative risk was 0.41 (95 percent confidence interval, 0.20 to 0.84; P = 0.013) after further adjustment for systolic blood pressure, cholesterol level, triglyceride level, vital capacity, K value, resting heart rate, body-mass index, and physical-activity level (Table 3). The relative risk of death from cardiovascular causes in quartile 4 as compared with quartile 3 was 0.50 (95 percent confidence interval, 0.23 to 1.05; P = 0.068) after adjustment for age and smoking status.

A high level of physical activity as defined in the present study had no independent prognostic value, nor did body-mass index, resting heart rate, or fasting triglyceride level. All the other variables were significantly and independently associated with mortality from cardiovascular causes (Table 3).

Overall Mortality

After adjustment for the same variables that were used in the model for mortality from cardiovascular causes, the relative risk of mortality from any cause was as follows when the three other quartiles were compared with quartile 1: for quartile 4, 0.54 (95 percent confidence interval, 0.32 to 0.89; P = 0.015); for quartile 3, 1.00 (95 percent confidence interval, 0.71 to 1.41; P = 0.92); and for quartile 2, 0.92 (95 percent confidence interval, 0.66 to 1.28; P = 0.58). It is noteworthy that a comparison between quartiles 4 and 3 revealed a relative risk in quartile 4 of 0.53 (95 percent confidence interval, 0.32 to 0.87; P = 0.010), whereas the comparison of quartile 4 with quartile 2 revealed a relative risk of 0.59 (95 percent confidence interval, 0.36 to 0.96; P = 0.031). Thus, overall mortality was significantly lower in quartile 4 than in all three other quartiles.

Discussion

Our study has demonstrated a graded, inverse association between physical fitness and mortality from cardiovascular causes over a period of 16 years that is independent of age and conventional coronary risk factors. These findings corroborate and amplify our previous reports after a follow-up of seven years[3,12] and are in close accord with the findings of other recent studies.[4-11]

After adjustment for age and smoking status, overall mortality and mortality from cardiovascular causes were both observed to be lower among men in the quartile with the highest level of fitness than among the men in the remaining quartiles. Thus, although physical fitness appears to be more closely associated with mortality from cardiovascular causes than with overall mortality, the men in the quartile with the highest level of fitness appeared to be protected from death from all causes. In a previous study, Blair et al. reported an inverse relation between fitness and

Table 1. Base-Line Clinical and Laboratory Values in 1960 Healthy Men 40 to 59.9 Years of Age, According to Fitness Level.*

Variable	Fitness Quartile			
	1 (lowest) (n = 490)	2 (n = 491)	3 (n = 492)	4 (highest) (n = 487)
	mean±SD			
Total work performed (kcal)	16.3±4.3	22.2±4.3	27.5±4.1	40.2±10.0
Duration of exercise test (min)	9.6±2.1	12.2±1.8	14.3±1.5	18.5±3.0
Age (yr)	52.6±5.2	51.0±5.2	48.8±5.1	46.6±4.6
Resting heart rate (beats/min)	64±10	62±10	61±9	59±9
Blood pressure (mm Hg)				
Systolic	137±20	131±18	127±16	125±15
Diastolic	91±11	88±10	86±10	85±10
Cholesterol (mg/dl)	263±46	263±46	255±46	247±46
Triglycerides (mg/dl)	126±68	121±68	113±58	101±48
Body-mass index	25.5±2.8	24.6±2.9	24.0±2.5	24.0±2.5
Vital capacity (ml)	4029±860	4304±800	4539±857	4827±867
	percent			
K value ≤0.9	9.2	7.1	6.5	4.3
Current smokers	53	49	43	28
Physically active†	5	6	12	29

*To convert values for cholesterol to millimoles per liter, multiply by 0.02586, and to convert values for triglycerides to millimoles per liter, multiply by 0.01129.

†As defined in the Methods section.

Table 2. Annual Age-Adjusted Mortality from Cardiovascular, Noncardiovascular, and All Causes in 1960 Men during 16 Years of Follow-up, According to Fitness Level and Smoking Status.

Smoking Status and Cause of Death*	Fitness Quartile†			
	1 (lowest)	2	3	4 (highest)
	annual mortality per 100			
Never smoked				
CVD	0.62	0.29	0.24	0.23
Other	0.25	0.34	0.24	0.17
All	0.87	0.63	0.48	0.40
Former smokers				
CVD	0.53	0.35	0.22	0.14
Other	0.28	0.31	0.40	0.23
All	0.81	0.66	0.62	0.37
1–9 cigarettes daily				
CVD	0.55	0.88	0.41	0.26
Other	0.55	0.26	0.69	0.26
All	1.10	1.14	1.10	0.52
≥10 cigarettes daily				
CVD	0.70	0.66	0.68	0.26
Other	0.67	0.53	0.93	0.39
All	1.37	1.19	1.61	0.65

*CVD denotes cardiovascular disease.

†Among the men included in this analysis who never smoked, 113 were in quartile 1, 113 in quartile 2, 110 in quartile 3, and 159 in quartile 4. Among former smokers, there were 119, 135, 172, and 190 in the respective quartiles; among men smoking 1 to 9 cigarettes daily, 77, 91, 86, and 65; and among men smoking 10 or more cigarettes daily, 181, 152, 124, and 73.

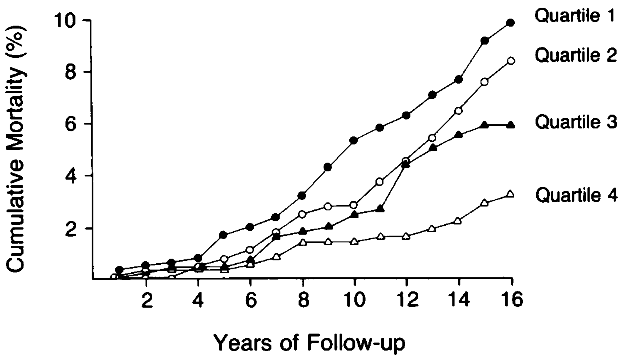

Figure 1. Cumulative Age-Adjusted Mortality from Cardiovascular Causes over 16 Years of Follow-up, According to Fitness Quartile.

death from cancer.[6] However, their data were not adjusted for smoking status.

Maximal work capacity, as defined in the present study, has been shown to be highly correlated with maximal oxygen uptake,[20] indicating that our measure of fitness is closely related to this most accepted measure of physical fitness.[1] To our knowledge, no study has suggested reduced survival in the presence of a high level of physical fitness. Instead, all major published studies, both North American[4,6-8,10] and European,[3,5,9] suggest a favorable long-term outcome in subjects with high as compared with low levels of physical fitness, regardless of how fitness is measured and defined.[4-10] The unadjusted risk ratio of 4.8 for mortality from cardiovascular causes over seven years in our study when subjects from the lowest fitness quartile were compared with those from the highest[3] is close to the risk ratios reported by others during follow-up periods of seven to nine years.[4,6,10,11]

We also observed a marked difference in mortality from cardiovascular causes between the subjects with intermediate levels of physical fitness (quartiles 2 and 3) and those with high levels (quartile 4). This finding would have remained undetected if our cohort had been followed for only 10 years (Fig. 1), as was the case in previous studies.[4-7]

These associations between fitness and mortality from cardiovascular causes can be used to assess the risk of cardiovascular disease among healthy subjects only if the subjects tested in the cited studies were truly healthy.[3-10] This prerequisite seems to have been met despite variation in the methods of selecting subjects.[3-10] Our selection procedure ought to have been reasonably successful in excluding subjects with preexisting cardiovascular disease, as the very low initial mortality suggests (Fig. 1).

Although the genetic component of physical fitness, as defined by a subject's maximal oxygen uptake, has been suggested to be approximately 40 percent,[21] this leaves about 60 percent of the variation between people attributable to other causes. Among these, physical activity, the key determinant,[1,2] is known to influence favorably a number of risk factors for coronary heart disease, such as the levels of cholesterol and triglycerides, and blood pressure.[3,22-25] Moreover, physical activity improves glucose tolerance and insulin sensitivity,[26] increases fibrinolysis,[27,28] increases levels of high-density lipoprotein cholesterol,[25] improves oxygen uptake in the heart as well as in peripheral tissues,[1] and increases the dimensions of coronary arteries and the formation of collateral vessels in animals.[29-31] Physical training also reduced the tendency to coronary vasospasm in one animal model[29] and increased the threshold for ventricular fibrillation in exercising rats.[32,33] Regular exercise also lowers the resting heart rate by increasing vagal tone.[34] A low heart rate is associated with a low mortality rate in humans[35,36] and appears to protect against the development of coronary atherosclerosis in monkeys.[37] Platelet aggregation has also been shown to decrease in exercising subjects.[38,39] Furthermore, a high level of physical activity appears to protect against death from cardiovascular disease.[2]

Although physical activity is not an independent predictor of mortality from cardiovascular causes, a close, direct correlation between reported physical activity and level of physical fitness was found in our study, as in previous studies.[4,40] Our estimates of physical activity during leisure hours are too crude, however, to allow speculation about its role in the prevention of death from cardiovascular disease.[14]

The associations in the present report, as in most others, have been corrected for differences in well-recognized coronary risk factors.[3-12] Thus, although our findings may conceivably be explained by important, currently unrecognized risk factors, a low level of physical fitness appears to be an important coronary risk factor.

Table 3. Relative Risk of Death from Cardiovascular Causes in 1960 Healthy Men during 16 Years of Follow-up, Associated with Specific Changes or Comparisons of Base-Line Variables.

Variable*	Relative Risk	95 Percent Confidence Interval	P Value
Age (increase of 10 yr)	2.9	2.0–4.3	<0.001
Smoking status (vs. those who never smoked)			
≥10 cigarettes/day	1.8	1.1–2.8	0.032
1–9 cigarettes/day	2.0	1.2–3.2	0.003
Former smokers	1.0	0.6–1.6	0.95
Fitness level (vs. quartile 1)			
Quartile 4	0.41	0.20–0.84	0.013
Quartile 3	0.45	0.22–0.92	0.026
Quartile 2	0.59	0.28–1.22	0.15
K value (≤0.9 vs. >0.9)	2.0	1.3–3.4	0.005
Systolic blood pressure (increase of 36 mm Hg)	1.5	1.1–2.1	0.010
Cholesterol (increase of 93 mg/dl [2.4 mmol/liter])	1.5	1.1–2.1	0.004
Vital capacity (decrease of 1702 ml)	1.4	1.05–2.1	0.029
Triglycerides (increase of 120 mg/dl [1.36 mmol/liter])	1.1	0.7–1.7	0.62
Body-mass index (increase of 5.4)	1.1	0.7–1.7	0.56
Physical activity (active vs. not active)	1.1	0.7–1.7	0.53
Resting heart rate (increase of 18 beats/min)	1.2	0.8–1.8	0.20

*For categorical variables, the risks for categories are compared, whereas for continuous variables, risks are given for an increase in the variable of 2 SD in the direction of increased risk, as described in the Methods section.

Although studies showing a favorable association between fitness and mortality might be more likely to be published than negative studies, the uniformity of the published literature and the observed graded relation argue against a publication bias of any consequence. Many previous studies may be criticized for possible selection biases or inadequate descriptions of selection procedures,[3-12] but these shortcomings notwithstanding, the results from all these studies are remarkably similar.[3-12] Accordingly, the aggregate data in the literature represent a body of evidence that, according to epidemiologic principles,[41] suggests a causal relation between physical fitness and mortality from cardiovascular causes. The associations observed worldwide are consistent, strong, graded, plausible, coherent, appropriately sequenced, and reasonably unbiased.[41] Only experimental evidence, difficult to obtain in humans, is still lacking in the final chain of proof.[41]

Whether genetic superiority among fit subjects explains these findings is unknown, but the close association between fitness level and mortality from cardiovascular causes tends to argue against it as the only explanation. Instead, one may speculate whether low fitness in the absence of disease often signifies a lifestyle with inherent unfavorable consequences for cardiovascular health.

This apparently simple pattern, also observed by others,[3-10] is complicated in our study by the finding of strikingly low overall mortality in the men from the highest fitness quartile as compared with those in the other three quartiles. The reason for this finding remains obscure, although several explanations may be conjectured. We have no data to allow further speculations, however, and this finding should be considered an observation that warrants further study.

We are indebted to Mrs. Solveig Eggen for her assistance in the preparation of the manuscript.

References

1. Åstrand P-O, Rodahl K. Textbook of work physiology: physiological bases of exercise. 3rd ed. New York: McGraw-Hill, 1986.
2. Powell KE, Thompson PD, Caspersen CJ, Kendrick JS. Physical activity and the incidence of coronary heart disease. Annu Rev Public Health 1987;8:253-87.
3. Lie H, Mundal R, Erikssen J. Coronary risk factors and incidence of coronary death in relation to physical fitness: seven-year follow-up study of middle-aged and elderly men. Eur Heart J 1985;6:147-57.
4. Ekelund L-G, Haskell WL, Johnson JL, Whaley FS, Criqui MH, Sheps DS. Physical fitness as a predictor of cardiovascular mortality in asymptomatic North American men: the Lipid Research Clinics Mortality Follow-up Study. N Engl J Med 1988;319:1379-84.
5. Sobolski J, Kornitzer M, De Backer G, et al. Protection against ischemic heart disease in the Belgian Physical Fitness Study: physical fitness rather than physical activity? Am J Epidemiol 1987;125:601-10.
6. Blair SN, Kohl HW III, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 1989;262:2395-401.
7. Taylor HL, Klepetar E, Keys A, Parlin N, Blackburn H, Puchner T. Death rates among physically active and sedentary employees of the railroad industry. Am J Public Health 1962;52:1697-707.
8. Peters RK, Cady LD Jr, Bischoff DP, Bernstein L, Pike MC. Physical fitness and subsequent myocardial infarction in healthy workers. JAMA 1983;249:3052-6.
9. Wilhelmsen L, Bjure J, Ekstrøm-Jodal B, et al. Nine years' follow-up of a maximal exercise test in a random population sample of middle-aged men. Cardiology 1981;68:Suppl 2:1-8.
10. Bruce RA, Hossack KF, DeRouen TA, Hofer V. Enhanced risk assessment for primary coronary heart disease events by maximal exercise testing: 10 years' experience of Seattle Heart Watch. J Am Coll Cardiol 1983;2:565-73.
11. Slattery ML, Jacobs DR Jr. Physical fitness and cardiovascular disease mortality: the US Railroad Study. Am J Epidemiol 1988;127:571-80.
12. Erikssen J, Mundal R. The patient with coronary artery disease without infarction: can a high-risk group be identified? Ann N Y Acad Sci 1982;382:438-49.
13. Erikssen J. Aspects of latent coronary heart disease: a prevalence and methodological validation study in apparently healthy, working middle aged men. (Thesis. Oslo, Norway: University Hospital (Rikshospitalet), Med. Dep. B, 1978.)
14. Mundal R, Erikssen J, Rodahl K. Assessment of physical activity by questionnaire and personal interview with particular reference to fitness and coronary mortality. Eur J Appl Physiol 1987;56:245-52.
15. Erikssen J, Skrede S. Serum lipids and latent coronary insufficiency. Scand J Clin Lab Invest 1977;37:243-50.
16. Erikssen J, Enger SC. Intravenous glucose tolerance test in middle-aged men with and without latent coronary heart disease. Acta Med Scand 1977;202:357-62.
17. Rose G, Blackburn H. Cardiovascular survey methods. World Health Organization monograph series no. 56. Geneva: World Health Organization, 1968.
18. Cox DR. Regression models and life-tables. J R Stat Soc [B] 1972;34:187-220.
19. SUGI supplemental library user's guide, version 5 ed. Cary, N.C.: SAS Institute, 1986.
20. Bonjer FH. Measurement of working capacity by assessment of the aerobic capacity in a single session. Fed Proc 1966;5:1363-5.
21. Bouchard C, Lesage R, Lortie G, et al. Aerobic performance in brothers, dizygotic and monozygotic twins. Med Sci Sports Exerc 1986;18:639-46.
22. Crow RS, Rautaharju PM, Prineas RJ, et al. Risk factors, exercise fitness and electrocardiographic response to exercise in 12,866 men at high risk of symptomatic coronary heart disease. Am J Cardiol 1986;57:1075-82.
23. Schwane JA, Cundiff DE. Relationships among cardiorespiratory fitness, regular physical activity, and plasma lipids in young adults. Metabolism 1979;28:771-8.
24. Gordon DJ, Leon AS, Ekelund LG, et al. Smoking, physical activity, and other predictors of endurance and heart rate response to exercise in asymptomatic hypercholesterolemic men: the Lipid Research Clinics Coronary Primary Prevention Trial. Am J Epidemiol 1987;125:587-600.
25. Enger SC, Herbjørnsen K, Erikssen J, Fretland A. High density lipoproteins (HDL) and physical activity: the influence of physical exercise, age and smoking on HDL-cholesterol and the HDL-/total cholesterol ratio. Scand J Clin Lab Invest 1977;37:251-5.
26. Kemmer FW, Berger M. Exercise and diabetes mellitus: physical activity as part of daily life and its role in the treatment of diabetic patients. Int J Sports Med 1983;4:77-88.
27. Fearnley GR, Lackner R. The fibrinolytic activity of normal blood. Br J Haematol 1955;1:189-98.
28. Rosing DR, Brakman P, Redwood DR, et al. Blood fibrinolytic activity in man: diurnal variation and the response to varying intensities of exercise. Circ Res 1970;27:171-84.
29. Bove AA, Dewey JD. Proximal coronary vasomotor reactivity after exercise training in dogs. Circulation 1985;71:620-5.
30. Kramsch DM, Aspen AJ, Abramowitz BM, Kreimendahl T, Hood WB Jr. Reduction of coronary atherosclerosis by moderate conditioning exercise in monkeys on an atherogenic diet. N Engl J Med 1981;305:1483-9.
31. Wyatt HL, Mitchell J. Influences of physical conditioning and deconditioning on coronary vasculature of dogs. J Appl Physiol 1978;45:619-25.
32. Billman GE, Schwartz PJ, Stone HL. The effects of daily exercise on susceptibility to sudden cardiac death. Circulation 1984;69:1182-9.
33. Noakes TD, Higginson L, Opie LH. Physical training increases ventricular fibrillation thresholds of isolated rat hearts during normoxia, hypoxia and regional ischemia. Circulation 1983;67:24-30.
34. Kenney WL. Parasympathetic control of resting heart rate: relationship to aerobic power. Med Sci Sports Exerc 1985;17:451-5.
35. Berkson DM, Stamler J, Lindberg HA, et al. Heart rate: an important risk factor for coronary mortality — ten-year experience of the Peoples Gas Co.: Epidemiologic study (1958-68). In: Jones RJ, ed. Atherosclerosis: proceedings of the Second International Symposium. New York: Springer-Verlag, 1970:382-9.
36. Dyer AR, Persky V, Stamler J, et al. Heart rate as a prognostic factor for coronary heart disease and mortality: findings in three Chicago epidemiologic studies. Am J Epidemiol 1980;112:736-49.
37. Beere PA, Glagov S, Zarins CK. Retarding effect of lowered heart rate on coronary atherosclerosis. Science 1984;226:180-2.
38. Rauramaa R, Salonen JT, Seppänen K, et al. Inhibition of platelet aggregability by moderate-intensity physical exercise: a randomized clinical trial in overweight men. Circulation 1986;74:939-44.
39. Rauramaa R, Salonen JT, Kukkonen-Harjula K, et al. Effects of mild exercise on serum lipoproteins and metabolites of arachidonic acid: a controlled randomised trial in middle aged men. BMJ 1984;288:603-6.
40. Blair SN. Physical activity leads to fitness and pays off. Physician Sports Med 1985;13(3):153-7.
41. Statistical evidence and inference. In: Bradford Hill A. Principles of medical statistics. 9th ed. New York: Oxford University Press, 1971:309-23.