A PROSPECTIVE STUDY OF WALKING AS COMPARED WITH VIGOROUS EXERCISE IN THE PREVENTION OF CORONARY HEART DISEASE IN WOMEN

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Abstract

Background The role of walking, as compared with vigorous exercise, in the prevention of coronary heart disease remains controversial, and data for women on this topic are sparse.

Methods We prospectively examined the associations between the score for total physical activity, walking, and vigorous exercise and the incidence of coronary events among 72,488 female nurses who were 40 to 65 years old in 1986. Participants were free of diagnosed cardiovascular disease or cancer at the time of entry and completed serial detailed questionnaires about physical activity. During eight years of follow-up, we documented 645 incident coronary events (nonfatal myocardial infarction or death from coronary disease).

Results There was a strong, graded inverse association between physical activity and the risk of coronary events. As compared with women in the lowest quintile group for energy expenditure (expressed as the metabolic-equivalent [MET] score), women in increasing quintile groups had age-adjusted relative risks of 0.77, 0.65, 0.54, and 0.46 for coronary events (P for trend <0.001). In multivariate analyses, the inverse gradient remained strong (relative risks, 0.88, 0.81, 0.74, and 0.66 for women in increasing quintile groups as compared with those in the lowest quintile group; P for trend=0.002). Walking was inversely associated with the risk of coronary events; women in the highest quintile group for walking, who walked the equivalent of three or more hours per week at a brisk pace, had a multivariate relative risk of 0.65 (95 percent confidence interval, 0.47 to 0.91) as compared with women who walked infrequently. Regular vigorous exercise ($\geq$6 MET) was associated with similar risk reductions (30 to 40 percent). Sedentary women who became active in middle adulthood or later had a lower risk of coronary events than their counterparts who remained sedentary.

Conclusions These prospective data indicate that brisk walking and vigorous exercise are associated with substantial and similar reductions in the incidence of coronary events among women. (N Engl J Med 1999;341:650-8.)

In epidemiologic studies, physical activity has been associated with a decrease in the risk of coronary heart disease,[1,2] but data on women have been sparse. Moreover, the specific role of walking, the most common form of exercise among women,[3] has not been fully elucidated. The most recent federal guidelines from the Centers for Disease Control and Prevention and the American College of Sports Medicine,[4] as well as the Surgeon General's report on physical activity and health,[3] endorse at least 30 minutes of moderate-intensity physical activity on most, and preferably all, days of the week, whereas earlier guidelines recommended vigorous endurance exercise for at least 20 minutes three or more times per week.[5] Although the current guidelines encourage a level of activity that is safe, achievable, and feasible for most Americans (60 percent of whom do not engage in regular physical activity),[6,7] the potential benefits of moderate-intensity activity in preventing coronary heart disease remain unclear.

We therefore assessed the comparative roles of walking and vigorous exercise in the prevention of coronary events in a large cohort of women enrolled in the prospective Nurses' Health Study. Detailed and repeated assessments of physical activity were performed to examine the degree to which total physical activity, walking time and pace, vigorous exercise, and change in activity level were associated with the incidence of coronary events in this cohort.

METHODS

Study Population

The Nurses' Health Study was initiated in 1976, when 121,700 female registered nurses 30 to 55 years old who were residing in 11 large U.S. states completed a mailed questionnaire on their medical history and lifestyle. Every two years, follow-up questionnaires have been sent to obtain updated information on potential risk factors and to identify newly diagnosed cases of coronary heart disease or other illnesses. For the primary analyses in the

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present study, the base-line data were those gathered in 1986, when detailed information on physical activity was first collected, and the duration of follow-up was eight years. After women who reported a diagnosis of cardiovascular disease or cancer at base line were excluded, the population for analysis was made up of 72,488 women 40 to 65 years old in 1986.

Assessment of Physical Activity

Detailed information on physical activity was first collected in 1986 and was updated in 1988 and 1992. Participants were asked to report the average amount of time spent per week during the previous year in walking or hiking outdoors (including walking to work or while playing golf), jogging (at a speed slower than 10 minutes per mile [6 minutes per kilometer]), running (at 10 minutes per mile or faster), bicycling (including the use of a stationary bicycle), swimming laps, playing tennis or squash, or participating in calisthenics, aerobics, or aerobic dance; in addition, the women were asked to report the average number of flights of stairs they climbed each week. Women also reported their usual walking pace: easy or casual (<2.0 miles per hour [mph] [3.2 km per hour]), average (2.0 to 2.9 mph [3.2 to 4.6 km per hour]), brisk (3.0 to 3.9 mph [4.8 to 6.2 km per hour]), or very brisk (≥4.0 mph [6.4 km per hour]). Using a standardized classification of the energy costs of physical activities,[8] we calculated a weekly metabolic-equivalent (MET) score for total physical activity, vigorous activity (≥6 MET per hour), nonvigorous activity (<6 MET per hour), and walking (2.5 to 4.5 MET per hour, depending on the pace). One MET is the caloric need per kilogram of body weight per hour of activity, divided by the caloric need per kilogram per hour at rest. Physical-activity scores were expressed as MET-hours per week. Validation of the questionnaire for assessing physical activity has been described previously in a similar cohort[9]; the overall correlation between physical activities reported on the questionnaire and those recorded in four one-week diaries was 0.62, and the correlation was 0.79 for activities reported on the questionnaire and those recalled after one week.[9]

For secondary analyses, we used data from a shorter questionnaire about physical activity that was administered in 1980 and 1982. On the 1980 questionnaire, women were asked to report the average number of hours they spent each week during the previous year engaged in moderate or vigorous recreational activities, including vigorous sports, jogging, bicycling, brisk walking, heavy gardening, or heavy housework. On the 1982 questionnaire, women were asked the question: "For how many hours per week, on average, do you engage in activity strenuous enough to build up a sweat?" To analyze this information, we calculated the cumulative average number of hours per week spent in moderate or vigorous recreational activities (all the activities listed above except for walking at a casual or average pace), as assessed in 1980, and (with updated information) in 1982, 1986, 1988, and 1992.

Ascertainment of End Points

The primary end points for this study were coronary events (defined as nonfatal myocardial infarction or death due to coronary disease) that occurred after the return of the 1986 questionnaire and before June 1994. We requested permission to review the medical records of women who reported a nonfatal myocardial infarction on a follow-up questionnaire. Study physicians who had no knowledge of the women's self-reported risk factors reviewed the records. Nonfatal myocardial infarction was confirmed if data in the medical records met World Health Organization criteria for this condition — namely, symptoms and either diagnostic electrocardiographic changes or elevated cardiac-enzyme levels.[10] Myocardial infarctions that required hospital admission and for which confirmatory information was obtained by interview or letter but for which no medical records were available were designated as probable infarctions (and constituted 17 percent of all reported nonfatal infarctions). We included all confirmed and probable cases of infarction in the analyses because the results were the same whether probable cases were included or excluded. Follow-up information for nonfatal infarction was obtained for more than 95 percent of the potential person-time of follow-up.

Deaths were reported by family members or the Postal Service or were ascertained through state registries or the National Death Index. We estimate that follow-up for deaths was more than 98 percent complete.[11] Fatal coronary disease (codes 410 through 414 of the *International Classification of Diseases, 8th Revision*[12]) was confirmed by review of the hospital or medical autopsy records or by review of the death certificate if coronary disease was the stated cause of death and evidence of previous coronary disease was available. We designated deaths for which coronary disease was listed as the underlying cause on the death certificate, but for which no records were available, as due to presumed fatal coronary disease. These cases constituted 14.7 percent of all fatal coronary events. We also included sudden deaths (12.3 percent of all fatal coronary events). Analyses limited to confirmed cases yielded results similar to those in which confirmed and presumed cases of fatal coronary disease were combined.

Statistical Analysis

For primary analyses, we used the detailed assessment of physical activity performed in 1986 as the base line. Person-time for each participant was calculated from the date of her return of the 1986 questionnaire to the date of an incident coronary event, death from any cause, or June 1, 1994, whichever came first. Data on women who had a coronary event or who died from any cause were censored with respect to subsequent analysis during follow-up. The relative risk of a coronary event was computed as the incidence of the event in each quintile group for MET score, divided by the incidence in the lowest quintile group, with adjustment for five-year age categories. Tests of linear trend for increasing quintiles of MET scores were performed by treating the score as a continuous variable and designating the median score for the category as its value. To represent long-term levels of physical activity for individual women as accurately as possible and to reduce measurement error, we calculated cumulative averages of the MET scores from all the questionnaires available up to the start of each two-year follow-up interval. A similar method for analyzing repeated dietary measurements has been described in detail elsewhere.[13]

For secondary analyses, we used data gathered in 1980 as the base line. We used the continuous values of hours of activity per week to compute the cumulative averages at the start of each interval and grouped the average hours per week of moderate or vigorous exercise into five categories (<1, 1 to 1.9, 2 to 3.9, 4 to 6.9, and ≥7 hours per week). To examine the association between a change in physical activity and the risk of coronary events, we related the change between 1980 and 1986 in hours spent engaged in moderate or vigorous activity to coronary events occurring between 1986 and 1994.

We used pooled logistic regression[14] to adjust simultaneously for potential confounding variables, including age (in five-year categories), period during the study (four two-year periods), smoking status (never smoked, previously smoked, or currently smokes 1 to 14, 15 to 24, or ≥25 cigarettes per day), body-mass index (the weight in kilograms divided by the square of the height in meters, in five categories), alcohol consumption (0, 1 to 4, 5 to 14, or ≥15 g per day), menopausal status (premenopausal, postmenopausal without hormone-replacement therapy, postmenopausal with previous hormone-replacement therapy, or postmenopausal with current hormone-replacement therapy), history of diabetes, history of hypercholesterolemia, history of hypertension, parental history of myocardial infarction before the age of 60 years, use of multivitamin supplements, use of vitamin E supplements, and use of aspirin (none, one to six doses per week, or seven or more doses per week). Covariates were updated according to questionnaire information every two years. The population attributable risk was calculated from multivariate models with use of the following formula: ([1 − relative risk] ÷ relative risk) × (proportion of inactive cases) (×100).[15]

TABLE 1. DISTRIBUTION OF INDICATORS OF CORONARY RISK ACCORDING TO QUINTILE GROUP FOR TOTAL PHYSICAL-ACTIVITY SCORE AT BASE LINE (1986).*

VARIABLE	QUINTILE GROUP FOR TOTAL PHYSICAL ACTIVITY†				
	1	2	3	4	5
No. of women	13,859	15,065	14,598	14,326	14,640
Total physical-activity score (MET-hr/wk)					
Median	0.8	3.2	7.7	15.4	35.4
Range	0–2.0	2.1–4.6	4.7–10.4	10.5–21.7	>21.7
			percentage of group		
Risk indicator					
Currently smoking	28.2	23.7	19.6	17.4	17.5
History of hypertension	26.1	25.1	24.0	22.4	21.0
History of diabetes	4.2	3.3	3.7	2.8	2.6
History of hypercholesterolemia	12.0	11.4	11.7	11.6	10.6
Parent with myocardial infarction before age of 60 yr	14.0	14.4	13.9	14.2	14.0
Current postmenopausal hormone-replacement therapy‡	19.5	21.5	23.1	23.8	24.1
Use of multivitamin supplement	36.9	39.9	43.0	45.0	47.2
Use of vitamin E supplement	12.8	13.9	15.8	17.5	19.4
			mean		
Age (yr)	52.1	52.3	52.2	52.2	52.3
Alcohol consumption (g/day)	5.9	5.8	6.0	6.4	7.0
Body-mass index	25.1	24.6	24.2	23.9	23.5
Waist-to-hip ratio	0.79	0.79	0.78	0.78	0.77
Saturated fat (% of caloric intake)	12.3	11.9	11.7	11.5	11.2
Polyunsaturated fat (% of caloric intake)	6.2	6.1	6.2	6.1	6.1
Trans fat (% of caloric intake)	1.8	1.7	1.7	1.6	1.5
Dietary cholesterol (mg/1000 cal)	154	152	151	149	148

*Percentages and means for variables other than age have been standardized according to the age distribution of the overall study group.

†The total physical-activity score was expressed as MET-hours per week, calculated as the average time per week spent in each of eight activities, multiplied by the MET value of each activity. The MET value is the caloric need per kilogram of body weight per hour of activity divided by the caloric need per kilogram per hour at rest.

‡Values are percentages of postmenopausal women who used hormone-replacement therapy among all the postmenopausal women in each quintile group.

RESULTS

The distribution at base line of several indicators of coronary risk varied according to quintile group for total physical-activity score (expressed as MET-hours per week) in this cohort (Table 1). Women who were more physically active were less likely to be current smokers and, as expected, were leaner and had a lower prevalence of reported hypertension, diabetes, and hypercholesterolemia than less active women. More physically active women were also more likely to use postmenopausal hormone-replacement therapy, multivitamin and vitamin E supplements, and alcohol. In contrast, the activity level was not appreciably related to age, parental history of myocardial infarction, or dietary intake of fats or cholesterol.

The eight years of follow-up, from 1986 to 1994, included 559,435 person-years. During this follow-up period we documented 645 coronary events (475 nonfatal myocardial infarctions and 170 deaths from coronary disease) among the 72,488 women who in 1986 were 40 to 65 years old, had neither cardiovascular disease nor cancer, and completed a detailed physical-activity questionnaire. The total physical-activity score (expressed as MET-hours per week) in 1986 was strongly inversely related to the risk of coronary events during the eight-year follow-up (Table 2). In age-adjusted analyses from 1986 to 1994 (in which MET scores, first computed in 1986, were calculated as cumulative updated averages in 1988 and 1992), the risk of coronary events decreased monotonically with increasing quintiles for MET score (relative risks, 0.77, 0.65, 0.54, and 0.46 as compared with the risk in the lowest quintile group; P for trend <0.001). In multivariate analyses, after simultaneous control for age, smoking status, body-mass index, and other covariates (Table 2), the total physical-activity score remained a powerful predictor of the subsequent risk of coronary events; relative risks for increasing quintile groups for physical activity, as compared with the lowest quintile group, were 0.88, 0.81, 0.74, and 0.66 (P for trend $=0.002$). There was a significant risk reduction for the two highest quin-

TABLE 2. RELATIVE RISK OF CORONARY EVENTS ACCORDING TO QUINTILE GROUP FOR TOTAL PHYSICAL-ACTIVITY SCORE.*

VARIABLE	QUINTILE GROUP FOR TOTAL PHYSICAL ACTIVITY					P FOR TREND
	1	2	3	4	5	
MET-hr/wk						
Median	0.8	3.2	7.7	15.4	35.4	
Range	0–2.0	2.1–4.6	4.7–10.4	10.5–21.7	>21.7	
No. of coronary events	178	153	124	101	89	
Person-yr of follow-up	106,252	116,175	112,703	110,886	113,419	
	relative risk (95% CI)					
Type of analysis						
Age-adjusted	1.0	0.77 (0.62–0.96)	0.65 (0.52–0.82)	0.54 (0.42–0.69)	0.46 (0.36–0.60)	<0.001
Multivariate†	1.0	0.88 (0.71–1.10)	0.81 (0.64–1.02)	0.74 (0.58–0.95)	0.66 (0.51–0.86)	0.002
Multivariate, excluding first 2 yr†‡	1.0	0.91 (0.71–1.16)	0.79 (0.61–1.03)	0.69 (0.52–0.92)	0.66 (0.49–0.88)	0.004
Multivariate, excluding biologic intermediates†§	1.0	0.85 (0.69–1.06)	0.78 (0.62–0.99)	0.69 (0.54–0.88)	0.60 (0.46–0.77)	<0.001

*The total physical-activity score was computed as the cumulative updated average number of MET-hours per week for 1986, 1988, and 1992. The primary end point, events due to coronary heart disease, included nonfatal myocardial infarction and death due to coronary causes. In each type of analysis, the women in the lowest quintile group served as the reference group. CI denotes confidence interval.

†The model included variables for age (in five-year categories), period during the study (four two-year periods), smoking status (never smoked, previously smoked, or currently smokes 1 to 14, 15 to 24, or ≥25 cigarettes per day), body-mass index (in five categories), menopausal status (premenopausal, postmenopausal without hormone-replacement therapy, postmenopausal with previous hormone-replacement therapy, or postmenopausal with current hormone-replacement therapy), parental history with respect to myocardial infarction before the age of 60 years, multivitamin-supplement use, vitamin E supplement use, alcohol consumption (0, 1 to 4, 5 to 14, or ≥15 g per day), history of hypertension, history of diabetes, history of hypercholesterolemia, and aspirin use (none, one to six doses per week, or seven or more doses per week).

‡In this analysis, data from the first two years of follow-up after the completion of the physical-activity questionnaire were excluded in order to minimize potential bias due to subclinical disease.

§In this analysis, biologic intermediary covariates that may have had a role in mediating the effect of exercise (body-mass index, hypertension, high cholesterol level, and diabetes) were excluded from the model.

tile groups, with a total of 10.5 MET-hours per week or more (the equivalent of ≥3 hours per week of brisk walking or 1.5 hours per week of vigorous exercise). In a separate analysis in which data from the first two years of follow-up after completion of the activity questionnaires were excluded (to minimize potential bias due to the influence of subclinical disease on activity level), the results were not materially altered (Table 2). Exclusion of biologic variables that may have a role in mediating the effect of activity (e.g., body-mass index) strengthened the inverse association between physical-activity level and risk of a coronary event (relative risk, 0.60 [95 percent confidence interval, 0.46 to 0.77] for the highest vs. the lowest quintile group for total physical-activity score) (Table 2).

To assess the potential modifying effects of cigarette-smoking status, body-mass index, and parental history with respect to premature myocardial infarction on the relation between physical activity and coronary events, analyses were repeated within subgroups defined by these variables (Fig. 1). Physical activity was inversely related to the risk of coronary events in all strata for smoking (never, previously, and currently), for both nonobese and obese women, and for women with and those without a parental history of premature myocardial infarction.

We next used the 1980 questionnaire to assess the long-term association between moderate and vigorous recreational activity (from data updated in 1982, 1986, 1988, and 1992) and the incidence of coronary events from 1980 to 1994. The activities included were vigorous sports, jogging, bicycling, brisk walking, heavy gardening, heavy housework, and activities "strenuous enough to build up a sweat." The number of hours per week of moderate or vigorous activity were strongly inversely related to the risk of coronary events. In multivariate analyses, averages of 4.0 to 6.9 and 7 or more hours per week spent in these activities were associated with risk reductions of 31 percent and 37 percent, respectively, as compared with an average of less than 1 hour per week (P for trend <0.001).

To assess the role of changes in activity level during the follow-up period, we categorized information from women according to their activity in 1980 relative to that in 1986. In an analysis restricted to women who were sedentary (exercised less than once per week) in 1980 (54 percent of the cohort at that time), women who remained sedentary in 1986 had substantially higher rates of coronary events than women who became active. As compared with the risk among women who remained sedentary, the multivariate risks of coronary events from 1986 to 1994 for women in increasing quintile groups for total phys-

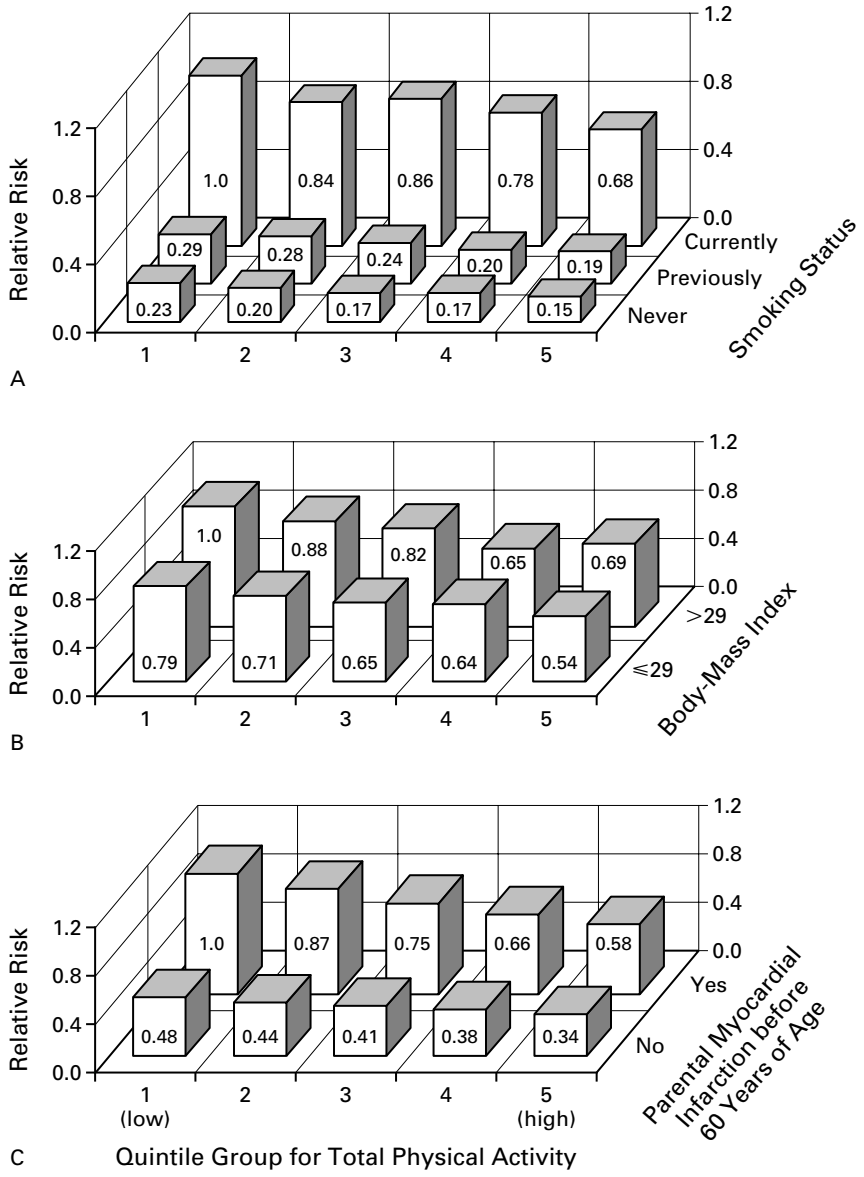

Figure 1. Multivariate Relative Risk of Coronary Events (Nonfatal Myocardial Infarction or Death from Coronary Causes) According to Quintile Group for Total Physical Activity within Subgroups Defined According to Smoking Status (Panel A), Body-Mass Index (Panel B), and Presence or Absence of a Parental History of Premature Myocardial Infarction (Panel C).

For each risk factor, the reference group is the category at highest risk. Relative risks have been adjusted for the variables in the full multivariate model (listed in Table 2).

ical activity (MET score) in 1986 were 0.85, 0.79, 0.67, and 0.71 (P for trend=0.03).

Detailed information about walking (duration and pace) was first obtained in 1986 and was updated in 1988 and 1992. Approximately 60 percent of the cohort of 72,488 women reported in 1986 that they walked for at least one hour per week, whereas only 26 percent engaged in vigorous exercise (≥6 MET) for at least one hour per week. To address the association between walking and the risk of coronary events while minimizing the potential confounding effect of vigorous activity, we restricted the study population to the women who reported no vigorous exercise (47 percent of the cohort). Women in the two highest quintile groups for walking score (a composite of walking time and pace) had a significantly reduced risk of coronary events as compared with the risk in the lowest quintile group (Table 3). As compared with sedentary women, women who had a walking score of 3.9 to 9.9 MET-hours per week —

TABLE 3. RELATIVE RISK OF CORONARY EVENTS AMONG WOMEN WHO DID NOT ENGAGE IN VIGOROUS EXERCISE, ACCORDING TO QUINTILE GROUP FOR WALKING.*

VARIABLE	QUINTILE GROUP FOR WALKING					P FOR TREND
	1	2	3	4	5	
MET-hr/wk						
Median	0	1.7	3	7.5	20	
Range	≤0.5	0.6–2.0	2.1–3.8	3.9–9.9	≥10	
No. of coronary events	92	78	73	77	57	
Person-yr of follow-up	46,900	51,934	45,413	62,011	51,162	
	relative risk (95% CI)					
Type of analysis						
Age-adjusted	1.0	0.69 (0.50–0.93)	0.71 (0.53–0.97)	0.52 (0.38–0.70)	0.46 (0.33–0.63)	<0.001
Multivariate†	1.0	0.78 (0.57–1.06)	0.88 (0.65–1.21)	0.70 (0.51–0.95)	0.65 (0.47–0.91)	0.02

*The walking score was computed as the cumulative updated average number of MET-hours per week spent walking for 1986, 1988, and 1992. These analyses excluded women who engaged in vigorous exercise. Coronary events included nonfatal myocardial infarction and death due to coronary causes. In each type of analysis, the women in the lowest quintile group served as the reference group. CI denotes confidence interval.

†The model included variables for age (in five-year categories), period during the study (four two-year periods), smoking status (never smoked, previously smoked, or currently smokes 1 to 14, 15 to 24, or ≥25 cigarettes per day), body-mass index (in five categories), menopausal status (premenopausal, postmenopausal without hormone-replacement therapy, postmenopausal with previous hormone-replacement therapy, or postmenopausal with current hormone-replacement therapy), parental history with respect to myocardial infarction before the age of 60 years, multivitamin-supplement use, vitamin E supplement use, alcohol consumption (0, 1 to 4, 5 to 14, or ≥15 g per day), history of hypertension, history of diabetes, history of hypercholesterolemia, and aspirin use (none, one to six doses per week, or seven or more doses per week).

the equivalent of 1 to 2.9 hours of walking per week at a brisk pace ≥3 mph — had a multivariate relative risk of 0.70 (95 percent confidence interval, 0.51 to 0.95) for subsequent coronary events, and those with scores of 10 or more MET-hours per week — the equivalent of 3 or more hours of walking per week at a brisk pace — had a multivariate relative risk of 0.65 (95 percent confidence interval, 0.47 to 0.91) for subsequent coronary events (P for trend=0.02). For those who walked five or more hours per week, the risk reduction exceeded 40 percent (data not shown). Exclusion of the small number of women who reported that they were "unable to walk" on the 1990 or 1992 questionnaire (2 percent of the cohort) did not alter these results.

Walking pace was also an important determinant of the risk of coronary events (Fig. 2). In multivariate analyses that also included control for time spent walking (in MET-hours per week), walking pace emerged as an independent predictor of the risk of coronary events. As compared with women who walked at an easy or casual pace (<2.0 mph), women who usually walked at an average pace (2.0 to 2.9 mph) had a multivariate relative risk of 0.75 (95 percent confidence interval, 0.59 to 0.96), whereas those who walked briskly or very briskly (≥3.0 mph) had a relative risk of 0.64 (95 percent confidence interval, 0.47 to 0.88).

To assess the comparative roles of walking and

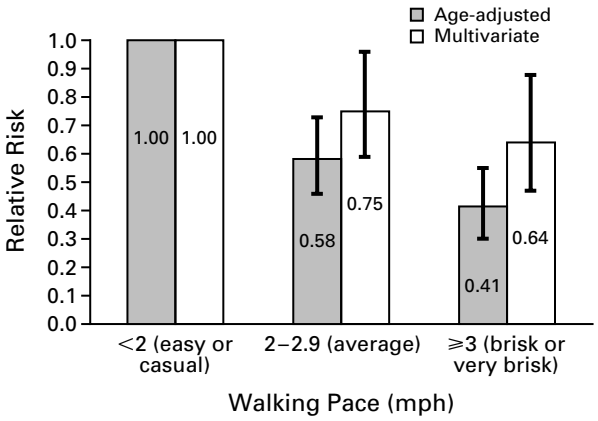

Figure 2. Age-Adjusted and Multivariate Relative Risks of Coronary Events (Nonfatal Myocardial Infarction or Death from Coronary Causes) According to Walking Pace.

These analyses excluded women who engaged in vigorous exercise. Multivariate relative risks have been adjusted for the variables in the full multivariate model, as listed in Tables 2 and 3, and for MET score for walking. Women who walked at an easy or casual pace served as the reference group. I bars indicate 95 percent confidence intervals. To convert miles per hour to kilometers per hour, multiply by 1.6.

TABLE 4. MULTIVARIATE RELATIVE RISKS OF CORONARY EVENTS ACCORDING TO CATEGORIES OF VIGOROUS EXERCISE AND WALKING.*

SCORE FOR WALKING (MET-HR/WK)	SCORE FOR VIGOROUS EXERCISE (MET-HR/WK)†		
	0	0.1–6.9	≥7.0
	relative risk (95% CI)		
0–0.6	1.0	0.78 (0.55–1.09)	0.76 (0.49–1.17)
0.7–6.9	0.84 (0.67–1.06)	0.86 (0.65–1.13)	0.59 (0.42–0.82)
≥7.0	0.74 (0.57–0.97)	0.56 (0.36–0.88)	0.70 (0.51–0.95)

*The model included variables for age (in five-year categories), period during the study (four two-year periods), smoking status (never smoked, previously smoked, or currently smokes 1 to 14, 15 to 24, or ≥25 cigarettes per day), body-mass index (in five categories), menopausal status (premenopausal, postmenopausal without hormone-replacement therapy, postmenopausal with previous hormone-replacement therapy, or postmenopausal with current hormone-replacement therapy), parental history with respect to myocardial infarction before the age of 60 years, multivitamin-supplement use, vitamin E supplement use, alcohol consumption (0, 1 to 4, 5 to 14, or ≥15 g per day), history of hypertension, history of diabetes, history of hypercholesterolemia, and aspirin use (none, one to six doses per week, or seven or more doses per week). Coronary events included nonfatal myocardial infarction and death due to coronary causes. The women with the lowest score for each type of activity served as the reference group. CI denotes confidence interval.

†Vigorous exercise was defined as participation in activities that required at least 6 MET per hour and included jogging, running, bicycling, lap swimming, tennis, squash, and calisthenics.

vigorous exercise in relation to coronary risk, we examined the incidence of coronary events according to the joint distribution of MET-hours per week spent in these activities (Table 4). Women who engaged in both walking and vigorous exercise had greater reductions in coronary events than those who participated in either type of activity alone. When examined simultaneously in a multivariate model, walking and vigorous exercise were each associated with a risk reduction. For every 5 MET-hours per week spent walking (the equivalent of 1.5 hours of walking per week at a brisk pace), the multivariate relative risk of coronary events was 0.86 (95 percent confidence interval, 0.74 to 0.99; β coefficient, −0.157), and for every 5 MET-hours per week spent in vigorous exercise (the equivalent of jogging, bicycling, swimming laps, or playing tennis for 45 minutes per week), the multivariate risk was 0.94 (95 percent confidence interval, 0.89 to 0.99; β coefficient, −0.059). Thus, we did not observe a greater magnitude of risk reduction with vigorous exercise than with walking in this cohort when we compared those who walked with those who exercised vigorously a similar number of MET-hours per week. However, our ability to assess the role of vigorous exercise was limited because of the small number of women in this study population (26 percent of the cohort) who engaged regularly in vigorous exercise.

DISCUSSION

These prospective data from a large cohort of women indicate that both walking and vigorous exercise are associated with substantial reductions in the incidence of coronary events. We observed that in this cohort, the magnitudes of risk reduction associated with brisk walking and vigorous exercise were similar when total energy expenditures were similar. These findings lend further support to current federal exercise guidelines, which endorse moderate-intensity exercise for at least 30 minutes on most (preferably all) days of the week.[3,4] Our results suggest that such a regimen (e.g., brisk walking for three or more hours per week) could reduce the risk of coronary events in women by 30 to 40 percent. Increasing walking time or combining walking with vigorous exercise appears to be associated with even greater risk reductions. Given the high prevalence in the United States of a sedentary lifestyle (78 percent of adults engage in less physical activity than currently recommended),[3] we estimate, on the basis of our multivariate relative-risk analyses, that one third of coronary events among middle-aged women in the United States are attributable to physical inactivity.

The strengths of the current study include the prospective design, the large size of the cohort, the long-term follow-up, repeated measures of physical activity, and the uniform and strict criteria for coronary events. Women with diagnosed cardiovascular disease or cancer at base line were excluded from the analyses. These exclusions and the prospective design minimized any influence that underlying disease may have had on physical-activity levels and decreased the potential for biased reporting of activity. Moreover, in our secondary analyses, the first two years of follow-up were excluded in order to minimize bias related to subclinical disease. The repeated measures of physical activity enabled us to calculate more stable, cumulative, and updated classifications of activity status as well as to assess the role of changes in activity level over time. Other advantages include the level of detail of information gathered about walking time and pace on the survey first administered in 1986, the high rate of participation during follow-up, and the collection of information about a large number of potential confounders, including cigarette smoking, body-mass index, family history of myocardial infarction, postmenopausal hormone use, alcohol consumption, diet, and other coronary risk factors. The substantial reduction in the risk of coronary events among women who increased their activity level, as compared with women who remained sedentary, and the strong dose–response gradient observed in each analysis lend credence to the interpretation that there is a causal relation between physical activity and a reduced risk of coronary events and that the risk may be modified through increased activity, even when it is begun in later adulthood.

Because our multivariate analyses controlled for several factors that could be considered intermediate biologic variables (such as body-mass index and a history of hypertension, hypercholesterolemia, or diabetes),[3] the analyses provide a conservative estimate of the relation between physical activity and coronary disease. In analyses that excluded these biologic intermediates, the inverse association between physical activity and coronary events was strengthened (Table 2).

Limitations of the current study must also be considered. Physical activity was assessed by a self-administered questionnaire and, despite the use of repeated measures, there was undoubtedly some misclassification. However, in a validation study, conducted in a separate cohort of nurses, the correlations between physical activity as reported on the questionnaire and as recorded in four one-week diaries or recalled after one week were reasonably high ($r=0.62$ and $r=0.79$, respectively).[9] Random misclassifications would be expected to lead to underestimation of the true association and to bias the estimate of risk toward unity; therefore, misclassification cannot explain the strong inverse associations in our cohort between physical-activity level and the incidence of coronary events. Nevertheless, despite the control for many potential confounding variables in our multivariate analyses, residual confounding by lifestyle factors cannot be excluded. In this regard, it should be noted (Table 1) that the more active women had more favorable risk profiles. Finally, our study population, consisting of registered nurses, is not representative of the general population. The relative homogeneity of the cohort in educational attainment and socioeconomic status may actually serve to enhance the internal validity of this study; confounding by these factors has posed an important problem in many previous studies of physical activity and coronary disease.

More than 40 epidemiologic studies have addressed the relation between exercise and coronary disease,[1,2] but few have included women and presented data on women separately.[16-24] In those that did, results in women were generally similar to those in men, indicating that risk reductions were 30 to 50 percent in both sexes with regular physical activity. Most of these studies were small, however, and did not collect detailed information about walking or report repeated measures of activity. The evidence that moderate-intensity activity is associated with a reduction in the risk of coronary disease, however, has been mounting. In a recent report from the Iowa Women's Health Study, both moderate activity and vigorous activity were inversely related to overall mortality and mortality due to cardiovascular causes,[20] although walking was not assessed separately. In two recent studies among elderly women[24] and men,[25] walking at least four hours per week was associated with substantial reductions in cardiovascular risk.

Even moderate levels of physical fitness (assessed by treadmill testing) have been associated with substantial reductions in mortality due to cardiovascular events and in total mortality.[23] It is unlikely that genetic and constitutional differences in fitness levels and in the ability to exercise explain these findings: in a study of nearly 16,000 men and women in the Finnish Twin Cohort, leisure-time physical activity was associated with reduced mortality, even after the analyses had accounted for genetic, familial, and behavioral factors.[26]

It is also biologically plausible that both moderate exercise and vigorous exercise have an important role in reducing coronary risk. Increasing the intensity or duration of exercise has a graded relation to improvements in lipid concentrations[3,27] and insulin sensitivity.[28] Randomized trials of the effects of different intensities of exercise on blood pressure suggest that moderate- and vigorous-intensity activity may confer similar reductions in diastolic blood pressure and that moderate-intensity activity may confer even greater reductions in systolic blood pressure than vigorous-intensity exercise.[3] In the Insulin Resistance Atherosclerosis Study, both vigorous and nonvigorous levels of physical activity were directly associated with insulin sensitivity.[28] Moreover, equivalent expenditures of energy in moderate or vigorous exercise will lead to similar reductions in adipose mass.[3] A recent study indicated that moderate-intensity exercise reduces the secretion of atherogenic cytokines.[29] Finally, physical activity of all intensities has been linked to improvement in emotional well-being and reduction in anxiety and stress.[3]

In conclusion, these prospective data from a study of a large cohort of women indicate that both walking and vigorous exercise are associated with substantial reductions in the risk of coronary events. We observed a strong, graded inverse relation between energy expenditure in either walking or vigorous activity and the incidence of coronary disease. Among women who either walked briskly at least 3 hours per week or exercised vigorously for 1.5 hours per week, the risk was reduced by 30 to 40 percent. These findings lend support to current federal guidelines that endorse moderate-intensity exercise, which is safe, achievable, and feasible for the majority of the population. Although vigorous exercise should not be discouraged for those who choose a higher intensity of activity, our results indicate that enormous public health benefits would accrue from the adoption of regular moderate-intensity exercise by those who are currently sedentary.

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