Physical Activity and Mortality among Male Survivors of Myocardial Infarction

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ABSTRACT

AL-SHAAR, L., Y. LI, E. B. RIMM, J. E. MANSON, B. ROSNER, F. B. HU, M. J. STAMPFER, and W. C. WILLETT. Physical Activity and Mortality among Male Survivors of Myocardial Infarction. *Med. Sci. Sports Exerc.*, Vol. 52, No. 8, pp. 1729–1736, 2020. **Purpose:** An inverse association between physical activity (PA) and risk of CHD has been seen in many studies, but evidence for benefits of PA after myocardial infarction (MI) in reducing mortality is limited. **Methods:** Using data from the Health Professionals Follow-up Study cohort, we followed male survivors of MI. Short- and long-term changes in PA from before to after MI were calculated, and participants without ambulation impairment were classified into maintained low, decreased, increased, or maintained high PA categories. Cox models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for mortality across PA and PA change categories. **Results:** During a mean of 14 yr of follow-up of 1651 incident nonfatal MI cases, we documented 678 deaths, 307 were due to cardiovascular disease. The adjusted HR for all-cause mortality comparing ≥21 with ≤1.5 MET·wk^{-1} of PA before MI was 0.73 (95% CI = 0.59–0.89, P_{trend} = 0.03). Compared with men who maintained low PA before and after MI, men who maintained high PA had a 39% (95% CI = 25–50) lower risk of all-cause mortality, and those who had a long-term increase in PA from before to after MI had a 27% (95% CI = 6–43) lower risk. Walking for ≥30 min·d^{-1} after MI was associated with a 29% lower mortality (HR = 0.71, 95% CI = 0.58–0.84), independent of walking pace, and walking pace after MI was inversely associated with mortality (HR = 0.67, 95% CI = 0.49–0.92). **Conclusions:** Maintaining a high PA or having a long-term increase in PA from before to after MI was associated with lower mortality among male MI survivors. Walking time and walking pace after MI were each inversely associated with mortality. **Key Words:** EXERCISE, MYOCARDIAL INFARCTION, SURVIVAL, WALKING, RISK FACTORS

Physical activity (PA) has been associated with lower risk of CHD in many epidemiologic studies (1–3). Several mechanisms are likely to explain this association, including improved blood lipid profile and blood pressure, decreased blood coagulability, increased insulin sensitivity, and better weight control (4–6). Since the 1950s, exercise has been an essential component of cardiac rehabilitation (CR) for patients with CHD (7–9). Exercise and other components of the CR programs, namely, healthy diet, weight loss, smoking cessation, and blood pressure/glucose/lipid control, were found to reduce the rate of hospital readmission and cardiovascular disease (CVD) mortality (7,8). Despite the substantial evidence for the benefits of CR, only a small percentage of patients with myocardial infarction (MI) are referred to, participate, or complete CR programs (10). Moreover, in recent analyses, the financial sustainability of CR has been questioned (10,11). Although efforts are being made to enhance the outreach of CR, some have alternatively advocated for transforming CR to a broader healthy lifestyle prevention program (11,12) to reach a larger patient population and extend beyond the traditional CR's 12-wk window (12). Given this interest in longer-term interventions, there is a growing need for additional information on habitual PA and long-term outcomes among patients with MI.

We therefore evaluated discretionary PA, its intensity and changes, among male survivors of MI in the Health Professionals Follow-up Study (HPFS) cohort, using repeated measurements of PA, diet, and smoking during three decades of follow-up.

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METHODS

Study population. The HPFS was initiated in 1986 after enrolling 51,529 male health professionals, 40 to 75 yr of age. Mailed questionnaires were administered biennially to obtain updated medical, lifestyle, and other health-related information.

From the 45,396 men who were free of CVD or cancer at the time of enrollment, we included participants who survived a documented incident MI during follow-up between 1988 and January 31, 2010, until the end of the 2-yr follow-up period during which the MI occurred (n = 2476). We excluded those who reported cancer (n = 156) or stroke (n = 40) at or before the time of MI diagnosis or difficulty in walking eight blocks or climbing a flight of stairs before MI diagnosis (n = 226). Participants were also excluded if they reported impaired PA on the first questionnaire cycle post-MI diagnosis (n = 301), had body mass index (BMI) < 18.5 $kg \cdot m^{-2}$ (n = 21), or had missing data on PA in the last questionnaire before MI (n = 3) or first questionnaire after reporting MI (n = 428). After exclusion for one or more reasons, a total of 1651 eligible participants were followed up until 2016.

The study protocol was approved by the institutional review boards of Brigham and Women's Hospital and the Harvard T. H. Chan School of Public Health.

Ascertainment of MI. MI was initially self-reported and confirmed by medical records documenting symptoms and either diagnostic electrocardiographic changes or elevated cardiac specific enzyme levels (13). Medical records were reviewed by physicians blinded to the participants' exposure status. For those whose medical records were unavailable, the diagnosis was considered probable if supported by telephone interview or additional corroborating information.

Ascertainment of mortality. Deaths were identified from searches of vital records, the National Death Index, and reports by the participant's next of kin or the postal system (14). Cardiovascular mortality included fatal MI, fatal stroke, and CHD, confirmed by a review of death certificates, medical records, and/or autopsy reports after obtaining the permission of the next of kin.

Assessment of PA. We assessed total and moderate to vigorous PA (MVPA), as the latter has been strongly associated with incidence of CVD (1,15). Participants reported the average time spent per week in the previous year on specific activities by choosing one of the 10 different duration options, ranging from 0 to ≥11 $h \cdot wk^{-1}$. MVPA included brisk walking, moderate and heavy outdoor work, weight training, jogging (<10 min per mile), running (≥10 min per mile), bicycling, lap swimming, tennis/squash/racquetball, and rowing. Data on walking pace, categorized as easy (<2 mph), normal (2–2.9 mph), brisk (3–3.9 mph), or striding (≥4 mph), were also collected (16). A weekly energy expenditure score ($MET \cdot h \cdot wk^{-1}$) was computed for each participant after summing up the MET score associated with each activity (17). The validity and the reproducibility of these measurements have been previously reported (18,19). Briefly, correlations between PA reported in diaries and that in the questionnaire were 0.62 in women and 0.58 in men. A new validation study conducted on a subgroup of our HPFS cohort and other non–health professional participants in 2011–2013 showed moderate correlation between our PA questionnaire and the doubly labeled water–determined PA energy expenditure (r = 0.40 for total PA and 0.43 for MVPA), as well as with two accelerometer measures (r = 0.44 for total PA and 0.39 for MVPA) (unpublished data). In addition, independent associations were observed between PA and several biomarkers of obesity and CVD risk such as HDL cholesterol, leptin, and C-peptide (20).

PA before MI was derived from the last questionnaire before MI diagnosis. PA after MI was analyzed from the first questionnaire after reporting MI diagnosis. The difference between these PA measurements represented short-term PA change in this study. To represent long-term PA change, we calculated the difference between the cumulative average of repeated measurements of PA in the periods before and after MI.

Assessment of covariates. Covariates, including age, race, marital status, family history of diabetes, MI and cancer, in addition to a dietary quality index (in quintiles), alcohol consumption (0, 0.1–4.9, 5.0–14.9, 15–29.9, or ≥30.0 $g \cdot d^{-1}$), cigarette smoking (never smoked, previously smoked, currently smokes 1–14, 15–24, or ≥25 cigarettes per day, or not reported), year of MI diagnosis, and aspirin use, were used in the multivariate adjustment. Dietary information was collected from validated food frequency questionnaires every 4 yr (21,22). Diet quality was assessed using the 2010 Alternate Healthy Eating Index (23); scores range between 0 and 110 with higher scores indicating a healthier diet. Heart failure during hospitalization, incidence of cancer, and stroke were further included in the models assessing the association of PA after MI with mortality to minimize confounding. BMI, diabetes, hypertension, hypercholesterolemia, and their respective medications were included in a sensitivity analysis because these are likely to be in the causal pathway relating PA to mortality and, therefore, could potentially attenuate the true association of PA with mortality. To account for potential bias attributed to MI severity, we further adjusted in a sensitivity analysis for other available clinical data collected during hospital admission: peak levels of cardiac enzymes (> median levels of peak hospital troponin or CKMB) and left ventricular ejection fraction dysfunction (ejection fraction <50%), or the occurrence of ST elevation MI. To account for changes in medical treatment of MI participants across the study period, we included indicator variables to reflect year of MI diagnosis.

Statistical analysis. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards models, with number of months since the return of the first questionnaire after MI diagnosis as the time scale. Person-time was calculated from the time of the return of the first post-MI questionnaire until death or end of follow-up, whichever came first. Pre-MI data were obtained on average 13 months before MI diagnosis and post-MI data on average 34 months after MI diagnosis.

MVPA values before and after MI were categorized as ≤1.5, 1.6–7.4, 7.5–20.9, and ≥21 $MET \cdot h \cdot wk^{-1}$; 21 $MET \cdot h \cdot wk^{-1}$ is

equivalent to 7 h·wk^{-1} of moderate-intensity exercise. Changes in PA were classified based on cutoffs of 7.5 MET·h·wk^{-1}, which is equivalent to 2.5 h·wk^{-1} of moderate-intensity exercise: maintained low, decreased, increased, and maintained high.

Effect modifications were assessed by including interaction terms between continuous PA and each of BMI, age at MI diagnosis, alcohol drinking, and smoking.

For analyses of linear trends, medians of PA categories were modeled as a continuous variable. Nonlinear trends were tested with likelihood ratio tests of restricted cubic splines.

To reduce potential bias from excluding participants who did not survive until the time of the first questionnaire cycle after MI diagnosis or had missing post-MI PA data, a sensitivity analysis was conducted using pre-MI PA. We included those who died at the time of or after MI (thus including fatal CHD and sudden cardiac deaths) but did not answer a subsequent questionnaire, those who had missing post-MI PA data, and those who reported PA impairment in the first questionnaire cycle post-MI. Because changes in PA might be confounded by the underlying health status, we generated a new variable and combined data on long-term changes in PA, weight, and diet quality from before to after MI in a sensitivity analysis. For example, poor health status would be likely if a participant reduced his PA from high to low, while losing weight and not improving diet quality.

Data were analyzed in SAS software (version 9.4; SAS Institute, Cary, NC) at a two-tailed alpha level of 0.05.

RESULTS

Study participants. A total of 1651 participants with incident nonfatal MI were included in the analysis with a mean age of 65 yr (range 40–89) at MI diagnosis.

Characteristics of participants categorized by MVPA levels after and before MI are presented in Table 1 and Supplemental Table 1 (see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940). Physically more active men tended to have a higher Alternate Healthy Eating Index score, consumed more alcohol, and were less likely to be current smokers or diabetic as compared with those with lower PA levels after MI.

All-cause and CVD mortality. We documented 678 deaths from all-causes and 307 deaths from CVD among survivors of MI during a mean of 14 yr of follow-up after the first post-MI questionnaire. MVPA values before and after MI diagnosis were both inversely associated with all-cause mortality (HR comparing ≥21 to ≤1.5 MET·h·wk^{-1} = 0.73, 95% CI = 0.59–0.89, P_{trend} = 0.03) before MI and 0.74 (95% CI = 0.60–0.92, P_{trend} = 0.02) after MI diagnosis. A significant nonlinear inverse association was noted between PA before MI and CVD mortality (P for nonlinearity = 0.03, Table 2). Further adjustment for BMI, hypertension, diabetes, and hypercholesterolemia and their respective medications modestly attenuated these associations (Table 2) and were therefore not included in further models.

In a model with simultaneous adjustment for PA before and after MI diagnosis, MVPA before MI remained an important predictor for all-cause and CVD mortality. The association of post-MI PA with mortality became nonsignificant (HR comparing ≥21 to ≤1.5 MET·h·wk^{-1} = 0.82, 95% CI = 0.65–1.04, P_{trend} = 0.20) (Supplemental Table 2, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

Change in PA from before to after MI diagnosis. After MI diagnosis, participants tended to increase their PA, and the majority of those in the highest pre-MI PA categories (≥7.5 MET·h·wk^{-1}) remained active (Supplemental Table 3, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940). Compared with men who remained in the low PA category, those who maintained high PA both before and after MI had 24% lower all-cause mortality (HR = 0.76, 95% CI = 0.62–0.92) and 30% lower CVD mortality risk (HR = 0.70, 95% CI = 0.52–0.95) (Table 3). Short-term increase in PA was not associated with lower risk of mortality. In analyses of long-term PA change, compared with men who maintained low long-term PA, those who increased from low to high PA or maintained their high PA from before to after MI were at a lower risk of mortality (HR = 0.73, 95% CI = 0.57–0.94, for those who increased PA, and HR = 0.61, 95% CI = 0.50–0.75, for those who maintained high PA) (Table 3). To address the possibility that men may have reduced their PA due to disease symptoms during the follow-up period, i.e., reverse causation, we stopped updating the data on PA once a participant reported ambulation impairment anytime during the follow-up. Similar associations were observed, and also a lower mortality risk was observed among those who changed from high to low cumulative average PA as compared with those who remained physically inactive (Table 3).

Because long-term changes in PA could be confounded by the underlying health status of a participant, a more detailed analysis was carried out among participants with available data on their cumulative average weight and diet in the periods before and after MI (N = 1541). Compared with those who maintained low PA and did not experience weight loss from before to after MI, participants who maintained low PA while experiencing weight loss without diet improvement were at a 54% higher risk of all-cause mortality (HR = 1.54, 95% CI = 1.04–2.27). By contrast, those who maintained their high PA levels, reduced their weight, and improved their diet were at a lower risk of mortality (HR = 0.61, 95% CI = 0.40–0.94) (Supplemental Table 4, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

After further adjustment for MI severity, the associations between PA post-MI and change in PA in relation with all-cause and CVD mortality were similar (Supplemental Table 5, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

The inverse associations between PA (pre- and post-MI) and mortality were similar across categories of BMI, age, and alcohol drinking groups (P > 0.05, for interaction) but were stronger among never smokers as compared with ever smokers (P = 0.03 for interaction) (Supplemental Table 6, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

TABLE 1. Age-adjusted characteristics of participants in the health professionals follow-up study by categories of MVPA (MET·h·wk^{-1}) after MI (N = 1651).

	≤1.5 (n = 280)	1.6–7.4 (n = 243)	7.5–20.9 (n = 415)	≥21 (n = 713)	
Continuous Variables	**Mean (SD) or Median (Interquartile Range)**				***P****
MVPA (MET·h·wk^{-1})	0 (0–0)	4.3 (2.5–5.8)	12.7 (10–16)	40.0 (28.0–59.0)	<0.001
MVPA (h·wk^{-1})	0 (0–0)	1.0 (0.5–1.2)	2.5 (2.1–3.5)	8.2 (6.0–11.5)	<0.001
Total PA (h·wk^{-1})	1.0 (0–2.7)	2.0 (1.0–3.5)	4.0 (2.7–5.7)	9.2 (6.5–13.5)	<0.001
Total PA (MET·h·wk^{-1})	3.0 (0–8.0)	7.2 (4.5–12.5)	16.9 (13.0–22.5)	43.4 (31.0–63.5)	<0.001
Age at diagnosis[a]	66.9 (9.9)	66.1 (9.2)	64.8 (8.5)	64.5 (8.4)	<0.001
BMI (kg·m^{-2})	26.4 (3.8)	26.4 (3.9)	26.3 (3.5)	25.7 (3.5)	0.01
Alternate Healthy Eating Index score	56 (11)	57 (13)	59 (12)	62 (12)	<0.001
Alcohol intake (g·d^{-1})	8.1 (13.2)	10.6 (15.3)	10.8 (14.0)	10.5 (14.0)	0.03
Categorical Variables	**Pct.**	**Pct.**	**Pct.**	**Pct.**	
White race	90	93	93	92	0.84
Married	72	76	80	82	<0.001
Family history of MI	40	44	44	42	0.99
Family history of diabetes	26	22	24	24	0.68
Family history of cancer	34	33	32	36	0.59
Types of PA					
Walking ≥1 h·wk^{-1}	54	67	75	78	<0.001
Running ≥1 h·wk^{-1}	0	0	0.2	5	0.002
Jogging and rowing ≥1 h·wk^{-1}	0	4	21	36	<0.001
Biking and swimming ≥1 h·wk^{-1}	0	14	34	35	<0.001
Racquet sports ≥1 h·wk^{-1}	0	1	4	11	<0.001
Moderate to heavy outdoor work ≥1 h·wk^{-1}	0	15	40	61	<0.001
Weight training ≥1 h·wk^{-1}	0.4	2	12	27	<0.001
Smoking					
Never smoker	36	40	37	40	0.41
Former smoker	58	53	60	58	0.62
Current smoker	7	6	4	3	0.001
Comorbidities					
Diabetes	22	13	14	11	<0.001
Hypertension	59	53	55	54	0.43
Hypercholesterolemia	63	65	67	70	0.02
Medication use					
Aspirin	75	80	82	86	<0.001
Antihypertensives	80	80	83	78	0.67
Antihypercholesterolemia	50	54	63	68	<0.001
Heart failure during hospital admission	11	9	7	6	0.01
ST elevation MI	65	60	58	62	0.74[b]
Abnormal ejection fraction	45	36	33	33	0.01[b]
Peak cardiac enzymes >median	79	82	82	81	0.53[b]
Cancer after MI	7	11	8	9	0.35
Stroke after MI	3	4	2	2	0.11

* P value for linear trends.
[a]Not age adjusted; racquet sports included tennis, squash, and racquetball. Peak cardiac enzymes include peak troponin or CKMB levels. Variables were assessed on average 34 months post-MI diagnosis.
[b]Based on valid data for 1191 (ST elevation MI), 996 (abnormal ejection fraction), and 634 (peak cardiac enzymes) participants.

Type of PA. Walking for 2.5 h or more per week after MI was associated with lower all-cause mortality (HR = 0.71, 95% CI = 0.58–0.87, for 2.5–5.0 h·wk^{-1}, and HR = 0.65, 95% CI = 0.51–0.85, for >5 h·wk^{-1}, P < 0.001 for nonlinearity). Brisk walking (pace ≥3 mph) was independently associated with lower mortality as compared with walking at an easy pace (HR = 0.71, 95% CI = 0.51–0.97) (Supplemental Tables 7 and 8, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940). The joint associations between walking and pace of walking in relation to risks of all-cause and CVD mortality are shown in Figure 1. In comparison with men who walked 1 h or less per week at a low pace after MI, men who walked 2.5 h or more had a 27% lower risk of all-cause mortality if their pace was <3 mph and 38% lower risk if their pace was ≥3 mph (Fig. 1, Supplemental Table 9, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940). Similar associations were observed with simultaneous adjustment for walking duration and pace before their MI. When including all other types of activities in the same model, walking remained inversely associated with all-cause mortality.

To minimize any confounding of the association between walking and MI by high-intensity PA, we restricted the analysis to men who reported less than 1 h of weekly vigorous exercise (<6 MET·h·wk^{-1}, n = 961). Compared with men who walked 1 h or less at a low pace after MI, those who walked 2.5 h or more were at a lower risk of all-cause mortality (HR = 0.66, 95% CI = 0.50–0.86, for walking pace <3 mph, and HR = 0.63, 95% CI = 0.46–0.87, for walking pace ≥3 mph) (Supplemental Figure 1, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

In an exploratory analysis of other types of PA, practicing racquet sports after MI for more than 1 h·wk^{-1} was associated with 36% (95% CI = 4–57) lower risk of all-cause mortality as compared with participants who did not practice this activity, after accounting for all other types of PA. Spending >1 h·wk^{-1} on biking or rowing after MI was independently associated

TABLE 2. Age- and multivariate-adjusted HR (95% CI) of all-cause and CVD mortality according to categories of MVPA in MET-hours per week, shortly before and after MI diagnosis (N = 1651).

MVPA (MET·h·wk^{-1})	N_{events} (N_{total})	Age Adjusted	Multivariate Adjusted[a]	+Comorbidities[b]	+BMI	+Comorbidities + BMI
Before MI diagnosis						
All-cause mortality						
≤1.5	168 (338)	Reference	Reference	Reference	Reference	Reference
1.6–7.4	131 (287)	**0.79 (0.62–0.99)**	0.81 (0.64–1.02)	0.87 (0.69–1.10)	0.84 (0.66–1.06)	0.89 (0.70–1.13)
7.5–20.9	158 (404)	**0.68 (0.55–0.85)**	**0.71 (0.57–0.89)**	**0.76 (0.61–0.96)**	**0.74 (0.59–0.93)**	**0.79 (0.63–0.99)**
≥21	221 (622)	**0.68 (0.56–0.83)**	**0.73 (0.59–0.89)**	**0.76 (0.62–0.94)**	**0.76 (0.61–0.93)**	**0.79 (0.64–0.98)**
$P_{nonlinearity}$		0.13	0.13	0.24	0.19	0.24
$P_{linearity}$		**0.005**	**0.03**	**0.04**	0.06	0.07
CVD mortality						
≤1.5	87 (338)	Reference	Reference	Reference	Reference	Reference
1.6–7.4	56 (287)	**0.65 (0.46–0.91)**	**0.69 (0.47–0.94)**	**0.70 (0.50–0.99)**	**0.69 (0.49–0.98)**	0.72 (0.51–1.03)
7.5–20.9	69 (404)	**0.57 (0.42–0.79)**	**0.60 (0.43–0.83)**	**0.63 (0.45–0.87)**	**0.62 (0.45–0.86)**	**0.65 (0.46–0.90)**
≥21	95 (622)	**0.56 (0.42–0.76)**	**0.62 (0.46–0.84)**	**0.65 (0.48–0.88)**	**0.64 (0.47–0.87)**	**0.66(0.49–0.91)**
$P_{nonlinearity}$		**0.007**	**0.03**	**0.04**	**0.04**	**0.047**
$P_{linearity}$		**0.005**	**0.04**	0.05	0.06	0.07
After MI diagnosis						
All-cause mortality						
≤1.5	147 (280)	Reference	Reference	Reference	Reference	Reference
1.6–7.4	113 (243)	**0.77 (0.60–0.98)**	0.79 (0.62–1.01)	0.82 (0.64–1.06)	0.79 (0.61–1.01)	0.82 (0.64–1.06)
7.5–20.9	176 (405)	0.83 (0.67–1.04)	0.91 (0.73–1.14)	0.95 (0.75–1.19)	0.91 (0.73–1.14)	0.95 (0.76–1.19)
≥21	242 (713)	**0.66 (0.54–0.81)**	**0.74 (0.60–0.92)**	**0.78 (0.63–0.97)**	**0.76 (0.61–0.94)**	**0.80 (0.64–0.99)**
$P_{nonlinearity}$		0.57	0.89	0.80	0.96	0.73
$P_{linearity}$		**<0.001**	**0.02**	0.05	**0.04**	0.08
CVD mortality						
≤1.5	72 (280)	Reference	Reference	Reference	Reference	Reference
1.6–7.4	52 (243)	0.73 (0.51–1.05)	0.77 (0.53–1.10)	0.81 (0.56–1.17)	0.76 (0.53–1.09)	0.81 (0.56–1.17)
7.5–20.9	75 (405)	**0.71 (0.52–0.99)**	0.81 (0.58–1.13)	0.85 (0.61–1.20)	0.80 (0.57–1.12)	0.85 (0.61–1.19)
≥21	108 (713)	**0.60 (0.49–0.81)**	**0.71 (0.52–0.97)**	0.77 (0.56–1.06)	**0.72 (0.53–0.99)**	0.79 (0.57–1.08)
$P_{nonlinearity}$		0.14	0.43	0.67	0.42	0.66
$P_{linearity}$		**0.005**	0.09	0.21	0.13	0.29

[a]Adjusted for age; race; family history of MI, cancer, and diabetes; smoking; marital status; alcohol consumption; alternate healthy eating index score; year of MI diagnosis; and aspirin use. Models using PA after MI diagnosis were further adjusted for heart failure during hospital admission and incidence of stroke and cancer after MI diagnosis.
[b]Included diabetes, in addition to hypertension, hypercholesterolemia, and their respective medications.

with higher risk of mortality (Supplemental Tables 10–13, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

Inclusion of fatal and all nonfatal MI. We also evaluated pre-MI PA in an analysis that included men who died of CHD before returning a post-MI questionnaire, including those who died before hospitalization. This included 3419 participants among whom 2347 died, including 1496 CVD deaths. Higher pre-MI levels of MVPA remained inversely associated with all-cause and CVD mortality (Fig. 2, Supplemental Table 14, see Appendix, Supplemental Digital Content 1, Supplemental data, http://links.lww.com/MSS/B940).

DISCUSSION

In this prospective study of male survivors of MI, higher levels of PA before an acute MI were associated with improved survival after MI, and maintaining high PA or having a long-term increase in PA from before to after MI was associated with a lower post-MI risk of all-cause and CVD mortality. Walking at least 2.5 h·wk^{-1}

TABLE 3. Multivariate-adjusted HR (95% CI) of all-cause and CVD mortality according to MVPA change from before to after MI.

Short-Term Change (MET·h·wk^{-1})	Median (IQR) Pre-MI	Median (IQR) Post-MI	N_{deaths}	All-Cause Mortality HR (95% CI)[b]	$N_{CVDdeaths}$	CVD Mortality HR (95% CI)[b]
Low–low (n = 322)	0.8 (0–3)	0.8 (0–3)	170	1	78	1
Low–high (n = 303)	2.1 (0–5)	18.9 (12–37)	129	0.93 (0.73–1.17)	65	1.04 (0.74–1.46)
High–low (n = 201)	17.5 (12–34)	2.0 (0–5)	90	**0.74 (0.57–0.96)**	46	0.86 (0.59–1.26)
High–high (n = 825)	28.5 (16–49)	30 (18–47)	289	**0.76 (0.62–0.92)**	**118**	**0.70 (0.52–0.95)**
Cumulative Average Change (MET·h·wk^{-1})	**Median (IQR) Pre-MI**	**Median (IQR) Post-MI**		**HR (95% CI)[b]**		**HR (95% CI)[b]**
Low–low (n = 252)	1.7 (0–4)	2.6 (1–5)	144	1	71	1
Low–high (n = 281)	3.7 (1–5)	16.4 (12–26)	123	**0.73 (0.57–0.94)**	63	0.73 (0.51–1.04)
High–low (n = 152)	14.6 (11–23)	3.6 (2–6)	75	0.83 (0.62–1.11)	30	0.69 (0.44–1.07)
High–high (n = 966)	25.1 (15–39)	30.4 (18–45)	336	**0.61 (0.50–0.75)**	143	**0.54 (0.40–0.73)**
Cumulative Average Change (MET·h·wk^{-1})[a]	**Median (IQR) Pre-MI**	**Median (IQR) Post-MI**		**HR (95% CI)[b]**		**HR (95% CI)[b]**
Low–low (n = 234)	1.8 (0–4)	2.2 (0.5–5)	140	1	71	1
Low–high (n = 286)	3.7 (1–5)	16.4 (11–26)	127	**0.69 (0.54–0.89)**	63	**0.67 (0.47–0.96)**
High–low (n = 137)	15 (11–23)	3.8 (1–6)	71	**0.73 (0.54–0.98)**	30	0.66 (0.42–1.02)
High–high (n = 971)	25 (15–39)	31 (18–46)	340	**0.61 (0.50–0.75)**	143	**0.53 (0.39–0.71)**

Median (IQR) before and after MI are presented for each category of PA change.
[a]Using cumulative average before and stopping to update the data after reporting PA impairment during the follow-up after MI.
[b]Adjusted for age; race; family history of MI, cancer, and diabetes; smoking; marital status; alcohol consumption; alternate healthy eating index score; year of MI diagnosis; aspirin use; heart failure during hospital admission; and incidence of cancer and stroke after MI. PA was classified based on cutoffs of 7.5 MET·h·wk^{-1}, which is equivalent to 2.5 h·wk^{-1} of moderate-intensity exercise. Low–low represents those whose MVPA remained <7.5 MET·h·wk^{-1} from before to after MI.
IQR, interquartile range.

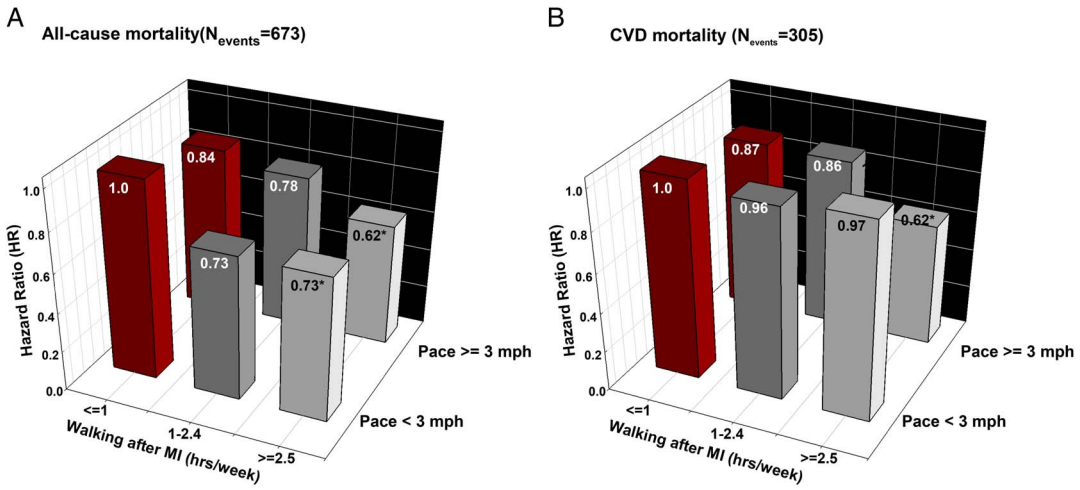

FIGURE 1—Multivariate-adjusted HR of all-cause and CVD mortality for the joint association between walking and pace of walking after MI diagnosis ($N = 1651$). Models were adjusted for age; race; family history of MI, cancer, and diabetes; smoking; marital status; alcohol consumption; alternate healthy eating index score; year of MI diagnosis; aspirin use; heart failure during hospital admission; and incidence of cancer and stroke after MI. Walking ≤1 h·wk^{-1} at a pace <3 mph was considered as the reference group. *P* value for interaction between number of walking hours and pace of walking after MI was 0.06 with all-cause mortality and 0.19 with CVD mortality. *Statistical significance.

after MI diagnosis was associated with substantially lower all-cause mortality, independent of pace or other types of PA.

To our knowledge, this study is the first analysis of PA to include a large number of male survivors of MI whose PA data have been repeatedly measured before and after MI using a validated PA questionnaire, and had a long period of follow-up after their MI diagnosis. Using the prospective design of the cohort and the updated assessment of PA and other important lifestyle factors every 2 yr for over a mean of 15 yr of follow-up after MI, we were able to analyze short- and long-term change in PA from before to after MI in relation to mortality. Several sensitivity analyses were conducted to reduce biases from reverse causation and account for MI severity. Selection bias was also reduced with the inclusion of all fatal CHD and nonfatal MI cases in an analysis examining the association of PA before MI and risk of mortality.

Our results are consistent with previous studies examining change in PA and mortality among survivors of MI. Only two previous studies have examined this association in a cohort design (24,25). The first study (24) included a small number of MI patients (n = 407) followed over 7 yr, using an unvalidated instrument to measure PA. The second study focused on 856 postmenopausal women (25), with a median of 7.2 yr of follow-up after MI. Our results are also consistent with meta-analyses of randomized controlled trials of exercise-based cardiac rehabilitation programs, which reported lower risks of cardiac mortality in the cardiac rehabilitation group as compared with the comparison group (7,8), although these programs often include other lifestyle modifications in addition to PA. The associations observed between PA post-MI and PA changes and mortality were not however as strong as those reported using population-based cohort data of Swedeheart registry (26,27). This could be attributed to the differences in study design in terms of inclusion/exclusion criteria, the use of a validated questionnaire for measuring PA, frequency and time for measuring PA post-MI, definition

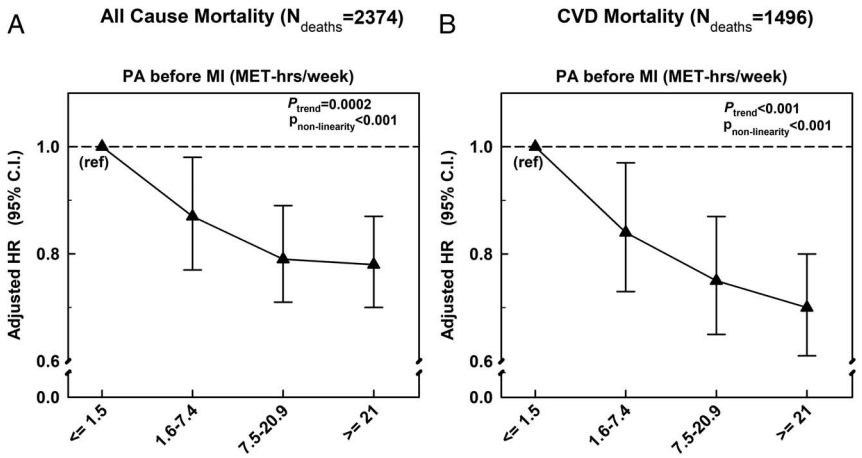

FIGURE 2—MVPA (MET·h·wk^{-1}) before MI in relation to all-cause and CVD mortality among all 3419 men with MI, including those who did not survive up to the post-MI questionnaire cycle or had missing post-MI PA data. Models were adjusted for age; race; family history of MI, cancer, and diabetes; smoking; marital status; alcohol consumption; alternate healthy eating index score; year of MI diagnosis; and aspirin use.

of PA change as the Swedeheart study defined PA change as the difference in PA between two post-MI visits (at 6–10 wk and 10–12 months post-MI), duration of follow-up post-MI, and most importantly the approaches taken to minimize potential reverse causality biases. However, the direction of associations was similar to our findings, and together these findings lend support to the benefits of PA post-MI. In our study, we also extended the research and examined the association between short- and long-term change in PA with mortality taking into account important lifestyle factors, in addition to adjusting for disease severity in a sensitivity analysis. We also examined the different types of PA, including walking in relation to mortality.

Exercise can favorably modulate several physiological and biochemical processes after the cardiac event. In animal models, exercise increases contractility and myofilament Ca^{2+} sensitivity (28,29). It also favorably modulates the renin angiotensin aldosterone system post-MI (30) and myocardial fibrosis and remodeling (31). In addition, increasing PA can improve cardiovascular risk factors, including lipid profile, insulin sensitivity, blood pressure, and weight control (4,5).

On the other hand, further research is needed to confirm the findings observed for the different types of PA, other than walking, in relation to mortality. In our study, these activities were practiced by a very few participants, and therefore analyzing participants who practice these activities more frequently in other cohorts would give a better understanding of the association between these activities post-MI and mortality.

The present study has several limitations. Participants had to survive to the post-MI questionnaire cycle so that short-term PA change could be measured. Therefore, those with severe MI who died at the time of the event or shortly thereafter were not included in the primary analysis.

We conducted a sensitivity analysis using prediagnosis PA after including these patients, who are normally missed in other clinical studies, and the inverse association between pre-MI PA and all-cause and CVD mortality was similar. Also, the use of self-reported PA measurements inevitably includes measurement errors, but in previous validation studies, these assessments were reasonably correlated with detailed assessments of PA (18). The use of repeated assessments of PA in our study will reduce measurement error, but the apparent benefit of PA in our study is almost certainly underestimated. A new validation study conducted on a subgroup of our HPFS cohort and other non–health professional participants in 2011–2013 showed moderate correlation between our PA questionnaire and the doubly labeled water–determined PA energy expenditure (r = 0.40 for total PA and 0.43 for MVPA), as well as with two accelerometer measures (r = 0.44 for total PA and 0.39 for MVPA) (unpublished data). Independent associations between reported PA and biomarkers of obesity and CVD risk were previously reported (20).

Although we adjusted for major confounders, residual and unmeasured confounding is possible. Changes in clinical management of MI over time could have also modified the results. However, we controlled for the year of MI diagnosis, which indirectly accounts for changes in coronary disease management. Lack of a national registry for MI is a limitation, but medical records were reviewed by physicians blinded to the participants' exposure status to ascertain health outcomes. Finally, our patients are mostly non-Hispanic white men, drawn from a cohort of health professionals whose socioeconomic status may not represent the overall population, thus affecting the generalizability of our study findings. However, this homogeneity would have helped to minimize unmeasured confounding related to socioeconomic status.

In summary, our results support the most recent 2018 Physical Activity Guidelines for Americans (32) and the current ACC/AHA guidelines for the management of MI patients, which endorse a posthospitalization plan of care that includes PA and other appropriate lifestyle factor modifications (33). Our findings emphasize the value of maintaining regular PA throughout adult life because greater PA was associated with both lower risk of MI and also better survival among those who experienced an MI. Walking, a common activity among older population, appears to confer a substantial reduction in the risk of mortality. In all cases, cardiac patients are advised to consult their health care providers about the type and amount of PA appropriate for their conditions.

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