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ORIGINAL RESEARCH

Changes in Physical Activity and Incidence of Nonfatal Cardiovascular Events in 47 153 Survivors of Myocardial Infarction

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BACKGROUND: The majority of patients survive the acute phase of myocardial infarction (MI) but have an increased risk of recurrent cardiovascular disease (CVD) events. To be regularly physically active or change activity level is associated with a lower risk of all-cause mortality. The objective was to explore to what extent physical activity (PA) levels or change in PA levels during the first year post-MI was associated with any recurrent nonfatal CVD events and specific CVD events (eg, MI, ischemic stroke, and vascular dementia).

METHODS AND RESULTS: This cohort study among MI survivors was based on Swedish national registries between 2005 and 2020. PA levels were self-rated at 2 and 12 months post-MI, and patients were classified into remaining physically inactive, increasing, decreasing, or remaining active. A total of 6534 nonfatal CVD events occurred during 6 years of follow-up among the 47 153 included patients. In fully adjusted analyses, the risk of any nonfatal CVD event was lower (P<0.05) among patients remaining active (37%), increasing (22%), or decreasing (18%) PA level compared with remaining inactive. Compared with remaining inactive, the risk of recurring MI and stroke was lower (P>0.05) among remaining active (41% versus 52%, respectively), increasing (20% versus 35%, respectively), or decreasing PA level (24% versus 34%, respectively). For vascular dementia, patients remaining physically active had an 80% lower risk compared with remaining inactive (P<0.05).

CONCLUSIONS: Remaining physically active or change in PA levels during the first year post-MI was associated with a lower risk of recurrent nonfatal CVD events. This emphasizes the importance of supporting patients to continue to be or become physically active.

Key Words: coronary heart disease ■ exercise ■ stroke ■ vascular dementia

Cardiovascular disease (CVD) is the leading cause of disease globally and a major contributor to disability-adjusted life-years. Prevalent cases have increased from 271 million in 1990 to 523 million in 2019, partly due to an aging population.[1] In addition, the acute treatment of myocardial infarction (MI) has improved in recent decades, and a higher proportion of patients survive the acute phase,[2–4] adding to the total CVD population. Thus, the total CVD burden is widespread, contributing to high costs for the health care sector and society. For example, total costs in the United Stated are estimated to reach $1.2 trillion in 2035.[5]

Survivors of MI have higher risks of recurrent cardiovascular events (eg, reinfarction, stroke, and vascular dementia) compared with individuals without a previous MI.[6–8] These entities have joint pathophysiology, with an increased risk of new thrombosis and damaged endothelium[9] as well as similar risk factors.[9–12] However, changing modifiable risk factors, such as smoking

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CLINICAL PERSPECTIVE

What Is New?

- Patients remaining physically active the first year after myocardial infarction had the lowest risk of recurrent nonfatal cardiovascular disease events over a median of 6 years of follow-up.
- However, changes in physical activity level the first year after myocardial infarction is of importance, with a lower risk of total nonfatal cardiovascular disease events in patients increasing or decreasing their physical activity level.
- The large cohort enabled subgroup analyses, showing a lower risk for recurrent myocardial infarction and ischemic stroke among patients remaining active or changing activity level, whereas patients with vascular dementia who remained active had a lower risk than patients remaining inactive.

What Are the Clinical Implications?

- In the health care sector, these findings emphasize the importance of supporting patients to be physically active to reduce the risk of recurrent nonfatal cardiovascular disease events.

Nonstandard Abbreviations and Acronyms

exCR	exercise-based cardiac rehabilitation
PA	physical activity

cessation and statin treatment (decreasing low-density lipoprotein cholesterol), has decreased the risk of recurrent CVD events.[13,14] Habitual physical activity (PA) has been shown to have a meaningful salutogenic effect on several risk factors in secondary prevention[15] and is emphasized in international guidelines on CVD prevention.[11] Therefore, we have shown that patients (n=22 227) who remained physically active or who increased PA levels after MI had lower mortality rates compared with those who remained inactive after MI.[16] Similarly, smaller longitudinal studies and a recent systematic review on patients with coronary heart disease concluded that patients increasing their cardiorespiratory fitness,[17] staying active over time, or increasing their PA levels had lower risks of cardiovascular and all-cause mortality compared with patients who had no to low increase in fitness or remained inactive.[18–20] However, there is limited knowledge about PA levels at repeated assessments after an MI and its association with the risk of recurrent nonfatal CVD events, which could affect the total burden of disease. Data on specific CVD outcomes are also lacking. Therefore, this study aimed to explore to what extent PA level or a change in PA level during the first year after an MI was associated with recurrent nonfatal CVD events. A second aim was to explore the association with specific outcomes, such as recurrent MI, ischemic stroke, and vascular dementia.

METHODS

Study Cohort and Setting

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) cohort checklist when writing our report.[21] This study was approved by the regional ethical review board in Stockholm (Dnr 2013/2067–31 and 2021–02433). According to Swedish regulations, no written informed consent is required for registration in national quality registries. However, all patients must have information of their participation in the registry and have the right to withdraw their participation. It was based on a national cohort and consists of all patients (18–79 years of age) with myocardial infarction (*International Classification of Diseases, Tenth Revision* [*ICD-10*] code I21) included in the national quality registry SWEDEHEART-CR (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies-Cardiac Rehabilitation). The SWEDEHEART-CR registry contains data from hospital care for MI and 2 outpatient visits at ≈2 months and 1 year after discharge.[22] Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Uppsala Clinical Research Center at datauttag@ucr.uu.se.

To be included in the analyses of this study, patients had to have their first outpatient visit between January 2005 and December 31, 2019, PA data from the 2 outpatient visits, as well as complete data of all covariates. Patients with an MI before or an additional CVD event during the first year after the index MI were excluded.

Hospital readmissions for nonfatal CVD events (all CVD, MI, ischemic stroke, and vascular dementia) were retrieved from the national patient registry of the National Board of Health and Welfare up to December 31, 2020. Figure 1 illustrates when and from which source exposure, covariates, and outcome were collected.

Self-Reported PA Level

Self-reported PA level was assessed by a validated (r=0.30) single-item question asking the number of sessions during the past 7 days with moderate or vigorous PA lasting ≥30 minutes, ranging from 0 to 7 sessions.[23] Patients reporting 0 to 1 session of PA in the past week were categorized as inactive, and patients reporting 2

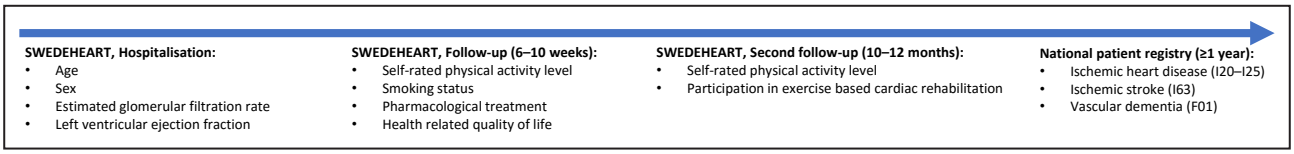

Figure 1. Flowchart describing time point and source of included data.
SWEDEHEART indicates Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies-Cardiac Rehabilitation.

or more sessions were categorized as active. Patients were further categorized into 4 groups according to changes in PA levels between the 2 outpatient visits at cardiac rehabilitation centers as (1) remaining inactive (0–1 session at both assessments), (2) increasing activity (0–1 session to ≥2 sessions), (3) decreasing activity (≥2 sessions to 0–1 session), or (4) remaining active (≥2 sessions at both assessments). These PA categories have previously been used in relation to all-cause mortality in MI survivors.[16]

Covariates

During hospital care, information on age, sex, left ventricular ejection fraction (LVEF), and serum creatinine was collected (Figure 1). LVEF was categorized as ≥50%, 40% to 49%, and ≤39%. Serum creatinine was used to calculate estimated glomerular filtration rate (eGFR) according to the Cockcroft-Gault formula.[24] eGFR was dichotomized at 60 mL/min per 1.73 m^2 to separate normal or mildly decreased eGFR from moderately decreased or more pronounced decreased eGFR.

Pharmacological treatment, health-related quality of life (HQoL), and smoking habits were collected at the first routine follow-up at the cardiac rehabilitation centers. Full pharmacological treatment was identified as being treated with angiotensin-converting enzyme inhibitors, β-blocking agents, statins (or other lipid-lowering agents), and antithrombotic agents and categorized as yes or no. HQoL was estimated by the validated instrument EuroQol-5D, and the values were converted into a single summary index ranging from −0.594 to 1, where 1 represents the best possible health.[25] The HQoL data were then dichotomized into 2 groups based on the median value. Smoking was categorized as persistent smoker, former smoker (>1 month), and no smoker. At the second outpatient visit at the cardiac rehabilitation center, data of participation in exercise-based cardiac rehabilitation (exCR) were collected and categorized as yes (≥3 months) or no (<3 months) (Figure 1).

Outcome

All nonfatal CVD events in the cohort were extracted from the national patient registry, which has a national coverage, and it is mandatory for Swedish regions to report all inpatient visits.[26] Nonfatal CVD events were defined as readmissions to hospital due to the following main diagnoses: angina pectoris (I20), MI (I21), reinfarction (I22), complications due to MI (I23), other ischemic heart disease (I24 and I25), ischemic stroke (I63), and vascular dementia (F01). The first CVD event registered in the patient registry after the second follow-up at the cardiac rehabilitation center was used. In the analyses, these events were classified as (1) all CVD events (all diagnoses), (2) MI (I21), (3) ischemic stroke (I63), or (4) vascular dementia (F01).

Statistical Analysis

All statistical analyses were performed using the SPSS 27.0 software (IBM, Armonk, NY). Descriptive demographics and clinical characteristics were presented as frequencies and relative frequencies for nominal and ordinal data. For nonparametric continuous data, medians and the interquartile ranges (IQRs) were used. Differences between included and excluded patients were analyzed using the χ^2 test and Mann-Whitney *U* test. Thereafter, baseline differences between the 4 PA categories were explored by χ^2 analyses with Benjamini-Hochberg adjustments and Kruskal-Wallis analyses.

Before hazard ratios (HRs) and their 95% CIs for future CVD events were calculated, the proportionality assumption was checked using the Schoenfeld residuals method. A weak significance for all PA categories (remaining inactive, increase, decrease, and remaining active) was noted for risk time of the different CVD events; thus, an interaction term (risk time × PA) was used in all analyses using Cox regression with a time-dependent covariate module. The HRs for PA categories were analyzed using 2 models. The first model was adjusted for age and sex. The second model was further adjusted using all covariates (sex, age, LVEF, eGFR, HQoL, smoking, participation in exCR, and full pharmacological treatment). HRs were considered statistically significant if the 95% CI did not include 1. Differences in HRs between the categories remaining active and increase were analyzed as interactions based on Altman et al.[27] CIs including 0 were interpreted as having no differences. Therefore, interaction terms were used to explore differences in HR for subgroups (subgroup×exposure) (eg, sex, age groups, LVEF, and eGFR). When differences in subgroups were explored, post hoc analyses were performed based on

Altman et al.[27] Lastly, to assess effect of early morbidity, sensitivity analyses were performed excluding patients with shorter follow-up times than 5 years.

RESULTS

Baseline Characteristics

There were 80 160 patients with an MI included in the SWEDEHEART-CR registry during the study period. Of those, 47 153 patients fulfilled the inclusion criteria and were included in the analyses. The median time of follow-up was 5.94 (IQR, 7.93) years, and 6534 nonfatal CVD events occurred. Figure 2 shows a flowchart of the recruitment of the study population.

Of the included patients, 74% were men and had a median age of 64 (IQR, 13) years. The median HQoL was 0.80 (IQR, 0.26), and ≈70% had a preserved LVEF and full recommended pharmacological treatment. Fifty-five percent did not participate in exCR, and 10% were current smokers. Differences in baseline characteristics among the different PA categories were found, as described in Table 1.

Included and excluded individuals showed similar characteristics, with small, albeit statistically significant, differences ($P<0.001$). Included patients were younger (median, 64 years versus 65 years of age), more often women (26% versus 25%), nonsmokers (90% versus 91%), had better HQoL (median 0.80 versus 0.79), and good eGFR (68% versus 67%). There were greater differences between included and excluded individuals in LVEF ≥50% (69% versus 62%) and participation in exCR (45% versus 42%) (Table S1).

Relation Between Change in PA and Nonfatal Cardiovascular Events

Table 2 describes incidence and HRs for readmission due to CVD for the different PA categories. The incidence for any CVD was 28.3 cases per 1000 person-years. Incidence for recurrent MI was 13.2 cases per 1000 person-years, for ischemic stroke 5.5 cases per 1000 person-years, and for vascular dementia 0.6 cases per 1000 person-years. For all outcomes, the highest incidences were found in groups of patients categorized as remaining physically inactive, during the first year post-MI.

In age- and sex-adjusted models, patients categorized as remaining active had the lowest risk for a recurrent event (40% lower risk of CVD, 49% lower risk of MI, 61% lower risk of ischemic stroke, and 85% lower risk of vascular dementia). Additionally, patients showing a change in PA level between measures had a lower risk compared with those classified as remaining physically inactive at both time points, and no significant difference compared with individuals remaining active for CVD, MI, or ischemic stroke. However, for vascular dementia, patients categorized as remaining active had a significantly lower risk compared with patients who changed their activity level. The association was consistent in a further adjusted model for all CVD outcomes. In sensitivity analyses, there were

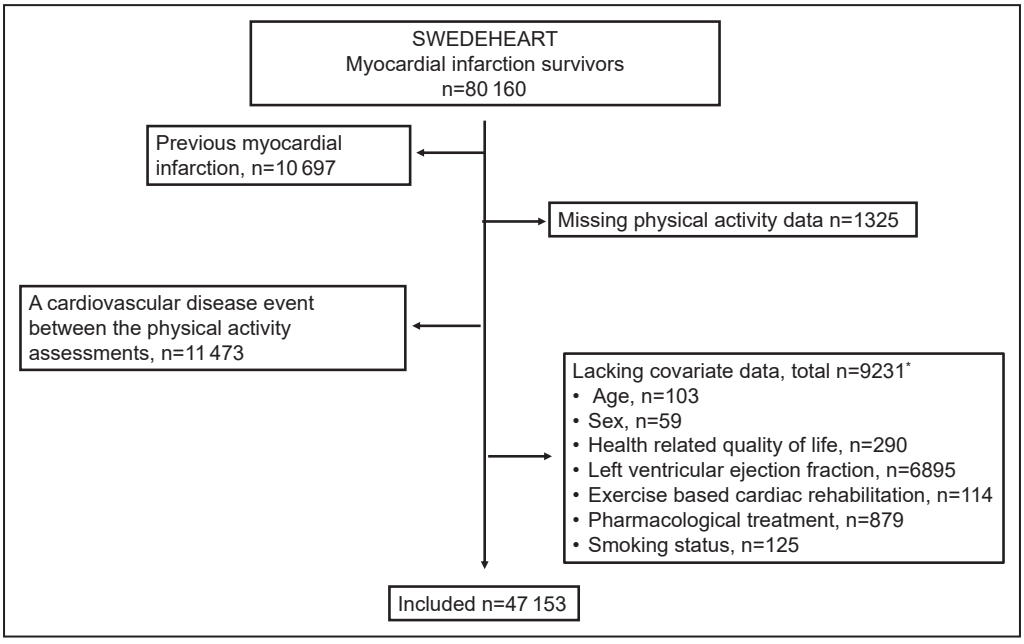

Figure 2. Flowchart of recruitment of study population.
*Excluded because of 1 or several missing covariates. SWEDEHEART indicates Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies-Cardiac Rehabilitation.

Table 1. Patient Characteristics by Different Physical Activity Categories

Characteristic	Remaining inactive (n=4944)	Increase (n=4352)	Decrease (n=6970)	Remaining active (n=31 067)	*P* value
Sex, men	3194 (65%)	3004 (69%)	5047 (74%)	23 595 (76%)	<0.0001
Age, y, median (IQR)	66 (13)	65 (13)	62 (14)	64 (12)	<0.0001
Smoking status					<0.0001
Nonsmoker	1264 (26%)	1364 (31%)	2045 (30%)	12 075 (39%)	
Former smoker	2728 (55%)	2393 (55%)	3885 (57%)	16 730 (54%)	
Persistent smoker	952 (19%)	595 (14%)	860 (13%)	2262 (7%)	
Left ventricular ejection fraction					<0.0001
>50	3152 (64%)	2883 (66%)	4553 (67%)	21 720 (70%)	
40–49	1020 (21%)	899 (21%)	1436 (21%)	6116 (20%)	
<39	772 (16%)	570 (13%)	801 (12%)	3231 (10%)	
Participate in exCR	1266 (26%)	1653 (38%)	2935 (43%)	15 350 (49%)	<0.0001
Health-related quality of life, EQ-5D, median (IQR)	0.74 (0.20)	0.79 (0.30)	0.80 (0.26)	1.00 (0.21)	<0.0001
eGFR >60 mL/min per 1.73 m^2	4054 (82%)	3717 (85%)	6919 (89%)	27 487 (89%)	<0.0001
Full pharmacological treatment	3325 (67%)	2889 (66%)	4692 (69%)	20 921 (67%)	0.012
Deaths during follow-up	1107 (22%)	536 (12%)	904 (13%)	2724 (9%)	<0.0001

eGFR indicates estimated glomerular filtration rate; EQ-5D, EuroQol-5D; exCR, exercise-based cardiac rehabilitation; and IQR, interquartile range.

no meaningful differences in the risk of MI, ischemic stroke, or vascular dementia among individuals with at least 5 years follow-up compared with the total group. However, for total CVD events, the lower risk only remained among individuals categorized as active at both time points (Table 2). The same pattern was seen when adjusting for all-cause mortality, as presented in Table S2.

In addition to PA in the fully adjusted model, sex, older age, lower HQoL, lower LVEF, and lower eGFR were associated with higher risk for all CVD outcomes. For additional results of association between covariates and recurrent MI, stroke, and vascular dementia in the fully adjusted model, see Table S3.

In analyses stratified by sex, age, LVEF, and eGFR and controlled for variables of the fully adjusted model, there were differences between sex (*P*=0.021) and LVEF (*P*=0.032) for CVD, as well as sex (*P*=0.032) and age (*P*=0.009) for MI. For the remaining stratified analyses, there were no differences (Table 3).

DISCUSSION

The main result of this national cohort study was that remaining physically active or change in PA levels during the first year after an MI was associated with a lower risk of recurrent nonfatal CVD events compared with remaining physically inactive. The same results were found for recurrent MI and ischemic stroke, whereas for vascular dementia, individuals who remained active had a lower risk than individuals remaining inactive at both time points.

Recurrent Cardiovascular Events

The results of this study are important, because CVD accounts for the greatest proportion of the burden of disease worldwide.[1] Additionally, a large cohort study of the general population in Sweden concluded that 42% of those 50 to 64 years of age show signs of underlying subclinical coronary heart disease on computed tomography angiography.[28] In our study cohort, the incidence of total recurrent nonfatal CVD events was 28.3 per 1000 person-years, with a pronounced higher incidence among those remaining inactive compared with remaining active (40.8 and 25.7, respectively, per 1000 person-years). A high incidence of recurrent CVD events among MI survivors has been shown by Ergatoudes et al, with ≈47% having an event within 2 years.[29] The higher CVD incidence among MI survivors is also supported in large case–control studies with matched controls.[7,8] Thus, a large group in society who harbor clinical and subclinical coronary heart disease have an increased risk of CVD events, highlighting the need to implement cost-effective secondary prevention interventions.[1,11] Interestingly, a study focusing on secondary prevention found that 77% to 97% of patients fulfilled the recommendation for pharmacological treatment, whereas only 18% achieved the preventive goals of low-density lipoprotein cholesterol levels and 57% for systolic blood pressure.[29]

Table 2. Follow-Up, Number of Events, Incidence, and Hazard Ratio (95% CI) for the Physical Activity Categories in Adjusted Models

Change in physical activity level	Follow-up time, median (IQR)	No. of events	Incidence per 1000 person-years	Age and sex adjusted	Fully adjusted*	Fully adjusted ≥5 years†
Cardiovascular disease	5.9 (7.9)	6534	28.3			
Remaining inactive		849	40.8	1 (reference)	1 (reference)	1 (reference)
Increase		608	30.8	0.75 (0.67–0.83)	0.78 (0.70–0.87)	0.86 (0.69–1.06)
Decrease		1033	30.9	0.75 (0.68–0.83)	0.81 (0.73–0.90)	0.83 (0.63–1.10)
Remaining active		4044	25.7	0.60 (0.54–0.66)	0.67 (0.60–0.75)	0.64 (0.44–0.93)
Myocardial infarction	6.5 (8.3)	3249	13.2			
Remaining inactive		450	19.9	1 (reference)	1 (reference)	1 (reference)
Increase		326	15.5	0.75 (0.65–0.87)	0.80 (0.69–0.92)	0.73 (0.57–0.95)
Decrease		527	14.7	0.69 (0.60–0.80)	0.76 (0.66–0.88)	0.67 (0.49–0.91)
Remaining active		1946	11.6	0.51 (0.44–0.60)	0.59 (0.51–0.69)	0.50 (0.33–0.75)
Ischemic stroke	6.8 (8.5)	1392	5.5			
Remaining inactive		233	10.0	1 (reference)	1 (reference)	1 (reference)
Increase		136	6.2	0.60 (0.48–0.75)	0.65 (0.52–0.80)	0.68 (0.48–0.95)
Decrease		224	6.0	0.59 (0.47–0.73)	0.66 (0.53–0.82)	0.53 (0.34–0.81)
Remaining active		799	4.6	0.39 (0.31–0.49)	0.48 (0.37–0.60)	0.27 (0.15–0.48)
Vascular dementia	7.4 (4.9)	160	0.6			
Remaining inactive		30	1.3	1 (reference)	1 (reference)	1 (reference)
Increase		27	1.2	0.80 (0.46–1.40)	0.88 (0.50–1.52)	1.02 (0.51–2.05)
Decrease		32	0.8	0.49 (0.26–0.94)	0.57 (0.30–1.11)	0.52 (0.21–1.26)
Remaining active		71	0.4	0.15 (0.07–0.34)‡	0.20 (0.08–0.44)‡	0.23 (0.07–0.67)

IQR indicates interquartile range.

*Adjusted for sex, age, left ventricular ejection fraction, estimated glomerular filtration rate, health-related quality of life, smoking, participation in exercise-based cardiac rehabilitation, and full pharmacological treatment.

†Follow-up for ≥5 years (n=25 897).

‡Differed from increase and decrease.

Additionally, only 46% of the study population achieved the recommended levels of PA. To lower the risk of recurrent CVD events, improved interventions focusing on lifestyle-related factors such as PA are needed, because these affect mediating risk factors, such as lipid level and blood pressure,[30,31] as well as have a direct effect on endothelial function, arrhythmias, and atherosclerosis progression.[11]

Relation Between PA and Recurrent Cardiovascular Events

The findings of the present study are supported by studies focusing on mortality and emphasize the importance of increasing cardiorespiratory fitness,[17] remaining physically active, or increasing PA level after a coronary event to decrease the risk of all-cause and CVD mortality.[16–18] A systematic review concluded that there was a graded lower risk across PA categories for fatal CVD events (ie, 51% lower risk for remaining active and 37% lower risk among increasers compared with remaining inactive).[18] Studies focusing on recurrent nonfatal events are based on PA at 1 time point, with conflicting results. A large national Swedish study (n=22 049) found a 25% lower risk of 1-year CVD readmission among patients with MI who remained active compared with those remaining inactive.[32] However, this was not supported by a study (n=15 486) by Stewart et al, who found no difference in the risk of recurrent MI or stroke among patients remaining active compared with those remaining inactive during a median follow-up of 3.7 years.[33] Our results, with repeated assessments of PA level, add to current knowledge by showing that in fully adjusted analyses of nonfatal events, there was a 33% lower risk among individuals remaining active, 22% lower for individuals increasing, and 19% lower risk for individuals decreasing their PA level compared with remaining inactive. The importance of maintaining PA or increasing PA level is of clinical relevance, emphasizing that the health care sector should support patients to be regularly physically active. However, interestingly, there might be some type of legacy effect of prior PA level, because patients decreasing their activity level at 12 months post-MI have a lower risk compared with those remaining inactive. The same pattern has been shown for CVD risk factors[34] and all-cause mortality[16] in recent publications. To our knowledge, there are no other studies exploring changes in PA levels post-MI

Table 3. Subgroup Analyses (Sex, Age, LVEF, and eGFR) of Fully Adjusted Models* Hazard Ratio (95% CI)

Change in physical activity level	Men, n=34 840	Women, n=12 313	Age, <64 years n=24 480	Age, ≥64 years, n=22 673	LVEF ≤49%, n=14 845	LVEF ≥50%, n=32 308	eGFR, ≤60 mL/min per 1.73 m^2, n=5876	eGFR, >60 mL/min per 1.73 m^2, n=41 277
Cardiovascular disease, events=8075								
Remaining inactive	1.00†	1.0	1.0	1.0	1.0†	1.0	1.0	1.0
Increase	0.82 (0.72–0.93)	0.73 (0.60–0.88)	0.80 (0.68–0.93)	0.76 (0.66–0.88)	0.79 (0.69–0.90)	0.74 (0.64–0.91)	0.79 (0.62–1.01)	0.78 (0.69–0.87)
Decrease	0.87 (0.77–0.99)	0.72 (0.59–0.86)	0.83 (0.71–0.96)	0.81 (0.70–0.94)	0.83 (0.73–0.94)	0.79 (0.67–0.95)	0.87 (0.68–1.11)	0.80 (0.71–0.90)
Remaining active	0.72 (0.64–0.83)	0.59 (0.49–0.72)	0.75 (0.64–0.88)	0.61 (0.52–0.70)	0.66 (0.58–0.76)	0.70 (0.58–0.84)	0.70 (0.55–0.90)	0.66 (0.59–0.75)
Myocardial infarction, events=4081								
Remaining inactive	1.00†	1.00	1.00†	1.0	1.0	1.0	1.0	1.0
Increase	0.78 (0.65–0.93)	0.86 (0.67–1.10)	0.83 (0.67–1.03)	0.79 (0.65–0.96)	0.88 (0.73–1.05)	0.66 (0.51–0.86)	0.80 (0.58–1.11)	0.80 (0.68–0.94)
Decrease	0.81 (0.68–0.97)	0.68 (0.52–0.88)	0.79 (0.64–0.98)	0.77 (0.63–0.95)	0.76 (0.63–0.91)	0.79 (0.62–1.01)	0.82 (0.58–1.14)	0.76 (0.64–0.89)
Remaining active	0.64 (0.53–0.77	0.50 (0.38–0.66)	0.66 (0.52–0.83)	0.56 (0.46–0.69)	0.57 (0.47–0.69)	0.66 (0.51–0.85)	0.59 (0.42–0.84)	0.59 (0.50–0.71)
Ischemic stroke, events=1693								
Remaining inactive	1.00	1.00	1.00	1.0	1.0	1.0	1.0	1.0
Increase	0.73 (0.55–0.96)	0.55 (0.38–0.79)	0.79 (0.55–1.15)	0.58 (0.44–0.76)	0.65 (0.49–0.86)	0.63 (0.45–0.90)	0.61 (0.40–0.94)	0.67 (0.52–0.86)
Decrease	0.70 (0.53–0.92)	0.65 (0.46–0.93)	0.70 (0.47–1.02)	0.66 (0.50–0.86)	0.66 (0.50–0.88)	0.66 (0.47–0.94)	0.76 (0.48–1.19)	0.66 (0.51–0.84)
Remaining active	0.55 (0.40–0.74)	0.40 (0.26–0.58)	0.60 (0.39–0.92)	0.42 (0.32–0.57)	0.46 (0.34–0.63)	0.50 (0.34–0.74)	0.49 (0.30–0.80)	0.49 (0.37–0.64)
Vascular dementia, events=198								
Remaining inactive	1.00	1.00	1.0	1.0	1.0	1.0	1.0	1.0
Increase	0.54 (0.25–1.15)	1.56 (0.64–3.76)	0.94 (0.21–4.27)	0.84 (0.46–1.53)	0.85 (0.42–1.73)	0.91 (0.38–2.21)	0.98 (0.38–2.51)	0.90 (0.45–1.82)
Decrease	0.60 (0.28–1.29)	0.43 (0.11–1.60)	0.28 (0.03–2.41)	0.64 (0.32–1.27)	0.53 (0.23–1.22)	0.62 (0.21–1.81)	0.88 (0.28–2.76)	0.58 (0.25–1.31)
Remaining active	0.17 (0.07–0.45)	0.19 (0.04–1.05)	0.15 (0.01–2.77)	0.19 (0.08–0.46)	0.21 (0.07–0.58)	0.16 (0.04–0.65)	0.15 (0.03–0.74)	0.24 (0.09–0.68)

eGFR indicates estimated glomerular filtration rate; and LVEF, left ventricular ejection fraction.

*Adjusted for sex, age, left ventricular ejection fraction, eGFR, health-related quality of life, smoking, participation in exercise-based cardiac rehabilitation, and full pharmacological treatment.

†$P<0.05$.

and the risk of recurrent nonfatal events. Increasing PA could be an important strategy to decrease the general burden of disease and cost for the society.[1,5]

In analyses of recurrent MI and ischemic stroke, the association between PA strata could be divided into 3 PA categories (remaining inactive, change, or remaining active). Meanwhile for vascular dementia, differences in PA levels could be categorized into 2 groups (remaining inactive or active). This would indicate that a change was more valuable for preventing recurrent MI or ischemic stroke, whereas no significant differences were seen between individuals who increased PA and those who remained inactive for risk of vascular dementia. Vascular dementia can occur after stroke or manifest as a progressive or stepwise cognitive decline without a history of stroke, with prevalence increasing with age. Mild cognitive impairment and impairment of cognitive function may precede the diagnosis and influence the ability of the patient to engage in PA. Because this study only reflects readmissions for vascular dementia, the diagnosis may be present at the index event but only registered in an outpatient setting.[35,36] However, the consistent results for the different CVD outcomes emphasize the positive effect of regular PA on the total cardiovascular system at various locations.[37]

Importantly, the lower risk for different nonfatal CVD events among individuals who changed or were regularly physically active was consistent in subgroups such as sex, age, LVEF, and eGFR, indicating a similar

association between PA categories and recurrent CVD events. However, because there were some differences in association with PA and risk of nonfatal CVD events for sex and LVEF, and this population mainly consists of men with a preserved LVEF, it would have been of interest to explore the association among women and patients with a lower LVEF more specifically.

Finally, in this cohort, individuals who remained active or made a change (both increase and decrease) did participate in exCR to a higher degree compared with individuals who remained inactive, underlining the importance to further implement and develop the use of exCR in clinical practice to support patients to maintain or increase PA levels over time.[38] This could potentially decrease the risk of recurrent nonfatal CVD events and thereby ease the total burden of disease.

Strengths and Limitations

A major strength of this study is that data of exposure and covariates were collected from most cardiac departments in Sweden between 2005 and 2019, providing data for the course of natural disease over time with high agreement (>95%) with medical record data.[22] Therefore, including most patients suffering an MI in Sweden during this period increases the generalizability of the results. The included patients had to have complete data of covariates, and explanatory and outcome variables, thereby excluding a large number of patients. There were statistical differences in baseline characteristics between included and nonincluded patients, with included individuals being younger, having better LVEF, eGFR, and HQoL, but these differences do not seem to be considered as clinically relevant due to the small absolute differences and high statistical power. Additionally, this inclusion strategy decreases the risk of type II error and increases internal validity. A limitation is the lack of data on family history of coronary artery disease, sociodemographic factors, and dietary habits, which are all associated with the risk of CVD.[12,39,40] Another limitation is the missing information of previous PA level. However, a case–control study concluded that most individuals with a CVD event did not change their lifestyle habits from before a CVD event. Small changes in individuals with a CVD event seem to improve their PA level over time compared with a matched control.[41]

Another strength is the size of the study cohort, which enabled us to explore the association with different CVD outcomes (recurrent MI, ischemic stroke, and vascular dementia), with adjustments for multiple potential confounders and subgroup analyses.

A limitation is that the exposure variable of change in PA level was based on subjective (self-rated) data. Subjective PA data contain a component of recall bias due to difficulties in estimating PA duration and intensity, how questions are interpreted, as well as social desirability.[42] Previous studies have shown that cardiorespiratory fitness is a strong predictor of mortality.[17] However, assessing cardiorespiratory fitness in clinical practice is more extensive and time consuming. Thus, it is important to explore if a single-item PA question can be used as an easy tool to predict future CVD events. The convergent validity of this question is moderate (r=0.3) in an MI cohort, showing similar agreement and correlation to device-measured PA and other PA questions.[23] Although the moderate convergent validity, the question seems to have a good predictive validity for all-cause mortality and hospital readmission.[16,32] Another shortcoming of the PA assessment is that the question is not validated to explore change in PA level over time. Using the same question at both time points to explore the change in PA levels is, however, an added strength. A limitation is dichotomizing the PA data to inactive (0–1 sessions) and active (2–7 sessions). It would have been interesting with a more high-resolution description of change in PA level. Schnor et al found a U-shaped association between duration in sport activities assessed at 1 time point and risk of mortality,[43] although we concluded in a previous publication that the greatest differences in risk were seen among individuals reporting 2 to 4 sessions compared with 0 to 1 session.[32] However, in the future it would be interesting to explore changes in more specific PA levels rather than reducing the number of PA response categories to remaining active and inactive. Finally, another limitation with assessing self-rated PA at 2 time points is that PA may fluctuate, and the PA level may not be representative of the total PA level over the year. Despite these limitations, it was still possible to predict risk of CVD morbidity.

The outcome measurements (ie, all CVD events, recurrent MI, ischemic stroke, and vascular dementia) were all collected from the national patient registry. This is an advantage, due to difficulties in reporting health care use.[44] However, because vascular dementia is a slowly progressive disease not necessarily diagnosed in an in-hospital setting, the prevalence may be underestimated. To further explore the burden of disease, it would be interesting to explore outpatient visits, duration of inpatient hospital stays, and calculations of health economics.

Finally, the study is a prospective cohort study exploring association over time but does not give information about causality between change in PA levels and recurrent CVD events. There is a risk of reversed causality due to individuals with better health status having higher levels of PA. To adjust for reversed causality, we repeated the analysis excluding patients with shorter follow-up times than 5 years and saw only minor differences for all nonfatal CVD compared with

the total study cohort. This may suggest that the effect of reverse causation was limited.

CONCLUSIONS

This study of a nationwide representative cohort of patients with MI demonstrates that remaining physically active or change (both increase and decrease) in PA levels during the first year post-MI is associated with a lower risk of nonfatal CVD events during a median follow-up of 6 years. These findings remained after excluding cases within the first 5 years post-MI. These results emphasize the importance of adhering to the international guidelines of cardiovascular prevention[11] that stipulate supporting patients' physical activity habits in clinical practice.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S3

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