Increased Physical Activity Post–Myocardial Infarction Is Related to Reduced Mortality; Results From the SWEDEHEART Registry

Orjan Ekblom, PhD; Amanda Ek, MSc, RPT; Åsa Cider, PhD, RPT; Kristina Hambraeus, MD, PhD; Mats Börjesson, MD, PhD

Background—With increasing survival rates among patients with myocardial infarction (MI), more demands are placed on secondary prevention. While physical activity (PA) efforts to obtain a sufficient PA level are part of secondary preventive recommendations, it is still underutilized. Importantly, the effect of changes in PA after MI is largely unknown. Therefore, we sought to investigate the effect on survival from changes in PA level, post-MI.

Methods and Results—Data from Swedish national registries were combined, totaling 22 227 patients with MI. PA level was self-reported at 6 to 10 weeks post-MI and 10 to 12 months post-MI. Patients were classified as constantly inactive, increased activity, reduced activity, and constantly active. Proportional hazard ratios were calculated. During 100 502 person-years of follow-up (mean follow-up 4.2 years), a total of 1087 deaths were recorded. Controlling for important confounders (including left ventricular function, type of MI, medication, smoking, participation in cardiac rehabilitation program, quality of life, and estimated kidney function), we found lower mortality rates among constantly active (hazard ratio: 0.29, 95% confidence interval: 0.21–0.41), those with increased activity (0.41, 95% confidence interval: 0.31–0.55), and those with reduced activity (hazard ratio: 0.56, 95% confidence interval: 0.45–0.69) during the first year post-MI, compared with those being constantly inactive. Stratified analyses indicated strong effect of PA level among both sexes, across age, MI type, kidney function, medication, and smoking status.

Conclusions—The present article shows that increasing the PA level, compared with staying inactive the first year post-MI, was related to reduced mortality. (J Am Heart Assoc. 2018;7:e010108. DOI: 10.1161/JAHA.118.010108.)

Key Words: mortality • physical exercise • registry

Myocardial infarction (MI) remains one of the most feared complications of cardiovascular disease (CVD), being associated with substantial morbidity and mortality. However, because of the advancements in emergency care, including the widespread use of cardiac interventions as well as antithrombotic, antihypertensive, and dyslipidemia treatment, a larger proportion of patients now survive their first MI.1,2 This positive development has resulted in more focus being put on secondary prevention.

Physical activity (PA) is a well-recognized factor in the primary prevention of CVD.3,4 Also in patients with established CVD, structured physical activity (PA)5 as well as increases in PA6,7 have been shown to be associated with reduced cardiovascular mortality. These effects rest on multiple positive effects on traditional risk factors for CVD, including hypertension, dyslipidemia, obesity, and diabetes mellitus as well as on possible effects on atherosclerotic progression, endothelial dysfunction, autonomic control, and subsequent arrhythmia risk.8,9 Thus, a sufficiently high PA level is recommended as first-line treatment in primary and secondary prevention guidelines10 globally. However, the adherence to these PA recommendations, and the use of exercise as part of regular treatment in health care, vary to a great extent.11

Atherosclerosis is a progressing disease, and the disease itself, and its consequences, may affect the ability of the individual to be sufficiently physically active both before and after a cardiac event. One limitation of earlier studies on the association between the level of PA and survival post-MI is the risk of selection bias (ie, that the individuals with the most advanced disease are also the least active because of their
Mortality After Changing Physical Activity Post-MI

Ekblom et al

DOI: 10.1161/JAHA.118.010108
Journal of the American Heart Association

Clinical Perspective

What Is New?
- Patients who remained physically active over the first year post-myocardial infarction (MI) had the lowest risk of mortality, over a 4.2-year follow-up period.
- However, changes in physical activity level the first-year post-MI is important, lowering the risk of mortality in patients increasing their activity and increasing risk in those with decreased activity.
- It seems not to be too late to start being active post-MI, since the group with increased activity post-MI did not differ in survival from the constantly active group.

What Are the Clinical Implications?
- The shown relation to survival, in patients who maintain or increase their level of physical activity post-MI, reinforces the importance of the present guidelines and highlights the need for their implementation in secondary prevention.
- Being active post-MI seems to be equally important for different subgroups.

Methods

Data, analytical methods, and study materials will not be made available to other researchers by the authors for purpose of reproducing the results or replicating the procedure. The authors are not authorized to share SWEDHEART data.

We obtained data from the national SWEDHEART registry (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies17 including the initial care [subregistry RIKS-HIA] and all subsequent MI-related care [subregistry SEPHIA]). SWEDHEART has an uptake of >90% of all cardiology units in Sweden, and the cohort can be regarded as representative of the Swedish patients with MI. The SWEDHEART subregistry SEPHIA (Secondary Prevention after Heart Intensive Care Admissions)18 provided information from 2 follow-up visits, at 6 to 10 weeks and 12 months post-MI, which included data on secondary prevention treatments, lifestyle, and prevalence of risk factors. The primary outcome was mortality, which was obtained from the Swedish Census registry. Mortality data were extracted on October 7, 2014. Mean follow-up time (ie, between date for MI and date of death or end of study) was 1635 days or 4.2 years.

![Flow chart for inclusion in analyses. BMI indicates body mass index; EF, ejection fraction; eGFR, estimated glomerular filtration rate; EQ-5D, EuroQol-5 dimensions; PA, physical activity; STEMI, ST-segment-elevation myocardial infarction.](Image)

Figure 1. Flow chart for inclusion in analyses. BMI indicates body mass index; EF, ejection fraction; eGFR, estimated glomerular filtration rate; EQ-5D, EuroQol-5 dimensions; PA, physical activity; STEMI, ST-segment-elevation myocardial infarction.
We included all patients (n=22,227) between ages 18 and 75 years who were diagnosed with their first MI (International Classification of Diseases, Tenth revision [ICD-10] code I21) between December 28, 2004 and October 25, 2013 and who provided complete data in the SWEDEHEART registry (Figure 1).

From the SWEDEHEART registry, age, body mass index, serum creatinine, height, sex, type of MI, and left ventricular function were obtained. Type of MI was based on a cardiac assessment and patients were classified as having had a ST-segment–elevation MI (STEMI), or a non-ST-segment–elevation MI (NSTEMI). Left ventricular function was expressed as ejection fraction (EF) in percent, and was further divided into >50%, 49% to 40%, or ≤40%. The use of percutaneous cardiac interventions during treatment was also recorded in the SWEDEHEART and coded as yes or no. Estimated glomerular filtration rate (eGFR) was based on plasma creatinine values calculated according to the Cockcroft-Gault formula \[\text{eGFR} = (1.23 \times (140 - \text{age}) \times \text{body mass})/\text{serum creatinine} + (1.04 \times (140 - \text{age}) \times \text{body mass})/\text{serum creatinine}, \text{for women and men, respectively} \], which has previously been used in analyses of the SWEDEHEART registry.\(^{19} \) eGFR was dichotomized at 60 mL/min per 1.73 m\(^2\), to identify normal or mildly decreased GFR from moderately decreased or more pronouncedly decreased GFR.

PA was reported in the SEPHIA subregistry at both follow-up visits as self-reported number of PA sessions, 30 minutes or longer, during the last 7 days. Values between zero and 7 were accepted in the registry. Patients were classified as “inactive” if they reported none or 1 session of PA per week, only. Patients reporting 2 or more sessions per week were classified as “active.” Patients were further classified according to changes in activity level between the 2 secondary prevention visits (at 6–10 weeks and 12 months, respectively), as constantly being inactive, having reduced activity, increased activity, or being constantly active. Full pharmacological treatment was identified as being treated with angiotensin-converting enzyme inhibitors, β-blocking agent, statins, or other lipid-lowering agents and antithrombogenic agents (coded as yes or no). Smoking status (never-smoker, ex-smoker since >1 month or smoker) was recorded at the first rehabilitation visit, 6 to 10 weeks after discharge from the hospital. When data were missing on smoking (n=32), additional data were obtained from the second visit. Data on participation in exercise-based cardiac rehabilitation during the year following MI was obtained from the second rehabilitation visit. Data from the Euro-Qol 5 dimensions (EQ-5D) from the first visit was used to estimate health-related quality of life.\(^{20} \) The Regional Ethics Board in Stockholm, Sweden approved this study (2013/2067-31). No informed consent was required. The corresponding author had full access to all the data in the study and takes responsibility for its integrity and the data analysis.

**Statistics**

Descriptive demographic and clinical characteristics were analyzed using means (SDs) and percentage. Differences between survivors and fatal cases were tested using the t test and \(\chi^2\) test. Hazard ratios (HRs) and their 95% confidence interval were computed using Cox proportional hazard ratios using the SPSS Cox regression with time-dependent covariate module. Hazard ratios for the 4 PA strata (constantly active, reduced activity, increased activity, or constantly inactive) were computed unadjusted and controlled for potential confounders. In the fully adjusted models, age, sex, date for MI, body mass index, EQ-5D, EF, type of MI, the use of percutaneous cardiac interventions, eGFR, smoking, pharmacological treatment, and participation in cardiac rehabilitation training were included. We checked the proportionality assumption using scaled Schönenfeld residuals. All variables were checked for proportionality, including the separate measures from the first and second PA assessment. A weak and borderline significance was noted only for PA strata. Because of this, we included an interaction term for time × PA strata in all analyses. Formal interaction analyses for HRs between PA strata were performed as proposed by Bland and Altman.\(^{21} \) HRs was considered to be statistically significant if the 95% confidence interval did not include the value of 1. All statistics were performed in IBM SPSS (version 21).

**Results**

Subject inclusion is described in Figure 1. The included and nonincluded patients differ in some aspects. Those with PA data, compared with those without, were less likely to be smokers (11.0% versus 13.6%), and have a low eGFR (8.2% versus 10.1%). Also their survival was lower (90.0% versus 94.2%). When comparing those included with PA data and those with PA data but lacking other variables, the latter group was less likely to have full medication (64.2% versus 69.6%), have had a STEMI (37.7% versus 41.1%), and more likely to be female (28.7% versus 26.1%). Also their survival was lower (92.0% versus 95.1%).

Subject characteristics, for the 22,227 included MI patients, are given in Table 1. All the examined variables differed across PA strata, except for pharmacological treatment, where no difference could be seen between PA groups. Some differences were small, albeit statistically significant (age, body mass index). Women and current smokers were overrepresented in the constantly inactive strata, as were patients with NSTEMI. Constantly active participants also participated in exercise-based cardiac rehabilitation to a higher degree (40.9% versus 21.6%) compared with the constantly inactive group.
Patients reporting being active at both 6 to 10 weeks, and 1-year post-MI, had higher EQ-5D, less prevalence of low eGFR, more often underwent percutaneous cardiac interventions, and had a higher EF post-MI (Table 1).

In uncontrolled analyses, mortality (cases per 1000 person-years with 95% confidence interval) in the 4 PA strata was 28.5 (25.3–32.0) among the constantly inactive, 12.7 (11.0–14.6) among those who reduced their activity, 11.5 (9.4–14.0) among those who increased their activity, and 7.5 (6.9–8.2) among the constantly active patients. In the fully controlled model, HRs for mortality were lower for those being constantly active, and for those with increased and decreased activity strata compared with those in the constantly inactive strata. However, HR for patients who increased and patients who decreased their PA did not differ. Constantly active patients had lower HR compared with individuals decreasing their PA level. HR for patients who increased their PA level did not differ from those being constantly active (Table 2, Figure 2).

No interactions were found for any of the variables in the full model, indicating similar differences between PA strata and mortality between age, sex, STT changes, the use of

<table>
<thead>
<tr>
<th>Table 1. Subject Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Number of deaths (total 1087)</td>
</tr>
<tr>
<td>Person-y at risk (total 100 502 person-y)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>STEMI</td>
</tr>
<tr>
<td>Ejection fraction</td>
</tr>
<tr>
<td>&gt;50</td>
</tr>
<tr>
<td>40–49</td>
</tr>
<tr>
<td>&lt;39</td>
</tr>
<tr>
<td>Participation in cardiac rehabilitation training (≥12 mo)</td>
</tr>
<tr>
<td>PCI during treatment</td>
</tr>
<tr>
<td>Smoking status (@6–10 wks)</td>
</tr>
<tr>
<td>Never-smoker</td>
</tr>
<tr>
<td>Ex-smoker</td>
</tr>
<tr>
<td>Smoker</td>
</tr>
<tr>
<td>eGFR &lt;60 mL/min per 1.73 m²</td>
</tr>
<tr>
<td>Full pharmacological treatment</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age distribution</td>
</tr>
<tr>
<td>Under 40 y, n</td>
</tr>
<tr>
<td>40–49, n</td>
</tr>
<tr>
<td>50–59, n</td>
</tr>
<tr>
<td>60–69, n</td>
</tr>
<tr>
<td>≥70, n</td>
</tr>
<tr>
<td>EQ-5D score (SD)</td>
</tr>
<tr>
<td>BMI, kg/m² (SD)</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; eGFR, estimated glomerular filtration rate; EQ-5D, EuroQol-5 dimensions; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction.
Table 2. HR (95% CI) for the PA Strata in Age- and Sex-Adjusted and Fully Adjusted Models

<table>
<thead>
<tr>
<th></th>
<th>Constantly Inactive</th>
<th>Reduced Activity</th>
<th>Increased Activity</th>
<th>Constantly Active</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full sample</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1087 deaths</td>
<td>1 (ref)</td>
<td>0.43 (0.35–0.53)</td>
<td>0.32 (0.24–0.43)</td>
<td>0.19 (0.14–0.26)</td>
</tr>
<tr>
<td>100 502 person-y</td>
<td></td>
<td>1 (ref)</td>
<td>0.83 (0.62–1.12)</td>
<td>0.54 (0.37–0.80)</td>
</tr>
<tr>
<td><strong>Fully adjusted</strong></td>
<td></td>
<td>1 (ref)</td>
<td>0.82 (0.49–1.37)</td>
<td></td>
</tr>
</tbody>
</table>

Fully adjusted for age, sex, date of myocardial infarction, body mass index, estimated glomerular filtration rate, EuroQol-5 dimensions, ejection fraction, ST-elevation myocardial infarction, percutaneous coronary intervention, smoking status, pharmacological treatment, participation in cardiac rehabilitation training, and an interaction term for time × physical activity strata. CI indicates confidence interval; HR, hazard ratio; PA, physical activity.

Discussion

The main result of this study, based on a national registry of unselected patients with MI, is that the mortality among inactive patients, who increase their PA level during the first year following a MI, was much lower, over a 4.2-year follow-up period, compared with those who remained inactive. The lowest risk was seen in patients who remained physically active over the first year, post-MI. Results for the group increasing their PA level is interesting, since the results indicate that patients who were initially inactive (which previous single-assessment-based studies have indicated to be at high risk) can reduce the risk by increasing activity. HRs in the group with increasing activity post-MI did not differ from the constantly active group at follow-up. The previous studies have also concluded that this group may be more affected by unmeasured factors or residual confounding, which in turn worsen the prognosis. Although this might well be present in this study, results from the group increasing their activity level post-MI clearly show that mortality is lower in this group compared with the constantly inactive group, controlled for a large number of covariates.

Similarly, results from the group decreasing their PA level indicate that those who were active 6 to 10 weeks after MI but reduced PA have a worse prognosis, as compared with those remaining physically active. Again, even if unmeasured and uncontrolled factors may differ between active and inactive patients at 6 to 10 weeks after MI, changes in PA level over 1 year were still related to mortality. Patients potentially having a more severe disease still benefit from PA increase to a similar extent as those with less severe disease. The exception was between patients with EF between 40% and 50% and EF <40%, where HRs differed between PA strata. Results indicated that patients with a low EF (<40%), compared with a moderately reduced EF 40% to 50%, showed an even stronger risk reduction among constantly active patients and patients increasing their PA level.

When analyzing the 2 assessments separately, we found smaller risk reductions among active patients as compared with those being constantly active. One possible explanation for this is that the inactive group at a single assessment will include participants with either a more active future or being more active in the past, which would dilute the contrast. This stresses the importance of studying PA level at more than 1 time point. Also, these results add to previous studies, by showing that these relations seem independent of cardiac rehabilitation participation in major subgroups post-MI. Also, the similarity of the HRs found at the 2 assessments (6–10 weeks and 10–20 months post-MI) when analyzed separately can be taken as an argument against a possible competing hypothesis that the type or intensity of the PA performed at the 2 time points differ.

Presently, the association between higher levels of PA and lower risk of events in those with cardiovascular disease is well established. We were able to confirm this association and also expand on the previous findings by Stefens-Batey16 and Gorczyca2 by identifying a lower risk in those patients with MI who increased their activity and an increased risk in those decreasing their activity, during the first year post-MI. The present study, however, includes >22 000 patients with MI, and allowed for adjusting for multiple possible confounders.
which was not possible in the previous studies. We could also show that this was true for several important subgroups, including older patients, those having heart failure, those with decreased kidney function, smokers, and for both sexes. Importantly, our study included the sum of all self-reported PA and exercise, and not only exercise-based cardiac rehabilitation, which has earlier been found to be related to lower mortality post-MI.\textsuperscript{12,13} Indeed, our results were independent of participation or nonparticipation in cardiac rehabilitation. Exercise-based cardiac rehabilitation performed at home or at the hospital have both been related to CVD reduction in patients with MI.\textsuperscript{23} However, far from all patients are offered cardiac rehabilitation for different reasons, often related to severity of the MI or other health-related factors, including older age. Of those offered hospital-based cardiac rehabilitation, not all choose to participate, perhaps because of practical reasons (such as living a long distance from the hospital or lack of interest). Thus, those investigated in studies of hospital or home-based cardiac rehabilitation may constitute a selected subgroup. In addition, when entering a physical training program, such as cardiac rehabilitation, other parts of the activity pattern, such as everyday activity or hobbies, may be compensatorily decreased, leading to a status quo regarding total PA.\textsuperscript{24} Similarly, sedentary activity may increase again after the end of cardiac rehabilitation.\textsuperscript{25} Unfortunately, Hansen et al showed that the cardiovascular disease risk profile worsened significantly during long-term follow-up after cardiac rehabilitation.\textsuperscript{26} Therefore, focusing on all PA, regardless of context, may offer an important target for improved clinical secondary prevention post-MI.

The relative intensity of the performed activities in the present study is unknown. The intensity of the PA performed may be of importance, since aerobic fitness has been shown to be an important predictor of survival, also post-MI,\textsuperscript{27} and cardiac rehabilitation has been shown to increase aerobic fitness.\textsuperscript{28} However, both high-intensity exercise and less-intense continuous exercise have been shown to reduce CVD risk in cardiac patients,\textsuperscript{29} while Williams et al showed that walking had equal CVD-risk-reducing effects as running did in patients at high cardiac risk.\textsuperscript{22} Regarding frequency of PA, we showed that two 30-minute sessions/wk of physical exercise, or an increase to that level within the first year post-MI, were related to lowered mortality post-MI, while 0 to 1 sessions/wk seems to be too little. The lowered mortality related to activity may be even smaller, as self-reported PA generally is higher than the levels found by more objective measures, such as accelerometry.\textsuperscript{30} Interestingly, these findings are consistent with the findings of Hansen et al, showing that a smaller exercise volume during phase II rehabilitation generated equal long-term clinical benefits, compared with a greater exercise volume.\textsuperscript{26} Such findings may be associated with a lower compliance of greater exercise volumes and higher-intensity activity.

Thus, the findings of the present study may have important clinical implications, since although universally recommended,\textsuperscript{10} PA is still underutilized as part of preventive and treatment strategies in health care. This is troublesome, since other commonly used components in secondary prevention, such as patient education, have been shown to be less efficient.\textsuperscript{15} The shown relation to survival, in patients who maintain or increase their level of PA post-MI, reinforces the importance of the present guidelines and highlights the need for improved secondary prevention including the implementation of PA advice as part of regular postinfarction treatment. At present not enough is known regarding how to
设计有效的咨询服务，以增加MI后患者的生活水平，尽管存在许多研究。制定倡议和方法，例如处方PA（PAP）和运动是医学（EiM），已被证明可以增加PA，\(^{31,32}\)并可能获得较大的推动，作为研究的当前发现，但需要进行进一步的研究，以确定MI患者在MI前可以被建议为PA的基础康复。其他干预措施包括不同形式的自动反馈，可以利用可穿戴电子设备。一个这样的系统在随机临床试验中被测试，报告了活动水平的变化，\(^{33}\)尽管存在矛盾的数据。 \(^{34}\)患者应接受PA的咨询服务，如果在患有MI后，这可以作为一选项，或者作为替代的，心脏康复，当这一建议不可行时。

一个明显的优势是，目前的研究的样本量大，其代表性的整个瑞典MI人群超过10年。这个大样本量允许我们进行子群分析，对重要的子群，如前所述。在2000年代，随着医学的进步，MI患者的生存率有所提高。因此，这项研究是在现代MI治疗的时代进行的，包括高接受程度的预防措施，进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要变量进行初步的治疗，包括高接受程度的预防措施，对重要的参与者的代表性的来自整个瑞典MI人群。该研究的样本量足够大，可以对重要的子群进行子群分析，如前所述。我们在结果部分讨论了这一发现。包括和非包括的患者在几个方面有所不同，如在结果部分所述。包括的患者一般较少吸烟，有较好的eGFR，较少可能患有STEMI，且有较高的生存率。研究一个被偏倚的患者可能更具健康，可能会导致对PA变化效应的低估。然而，虽然PA的变化在全模型和PA strata中表明，能否被被显著地不依赖于PA strata（即，类似的结果在高/低eGFR，STEMI/NSTEMI等条件下），与EF。因此，假定该偏差有限。如在结果部分所述，PA strata在几个方面有所不同。它可能表明，虽然PA的保健作用在所有strata中相似，存在重要的相互作用，从而限制了PA的使用。

在结论中，PA的第一年出现在后MI与较低的死亡风险有关。这是一个研究，以评估在后MI PA的变化的影响在新近的MI治疗时代进行的，对一个较大的代表性的队列。该研究的目前的研究将对secodary预防措施对MI后。希望我们现在能

**Acknowledgments**

此工作在瑞典学校于运动和健康科学完成。

**Sources of Funding**

Ekblom与Ek由ICA Sweden资助。除此之外，没有其他具体的资助来自任何资助机构。

**Disclosures**

无。

**References**

Mortality After Changing Physical Activity Post-MI


