Physical Activity and Heart Failure Risk in a Prospective Study of Men

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ABSTRACT

OBJECTIVES This study investigated if total physical activity, as well as different types of physical activity, were associated with heart failure risk.

BACKGROUND Physical activity has shown to be associated with reduced risks of coronary heart disease and stroke. Studies have also suggested that physical activity is associated with heart failure development.

METHODS A study population of 33,012 men was followed from the beginning of 1998 until the end of 2012. First event of heart failure was ascertained through linkage to the Swedish National Patient Register and Cause of Death Register. The data were analyzed by using Cox proportional hazards regression and Laplace regression.

RESULTS During a mean follow-up of 13 years, we ascertained a total of 3,609 first events of heart failure. The average age at study baseline was 60 ± 9 years of age. When examining the entire study population, a U-shaped association between total physical activity and heart failure risk was detected, with both extremely high (57 metabolic equivalent [MET] h/day) and extremely low (38 MET h/day) levels of total physical activity associated with an increased risk of heart failure. When investigating different types of physical activity, we found that walking/bicycling at least 20 min/day was associated with 21% lower risk of heart failure (95% confidence interval: 0.72 to 0.87); corresponding to a median age at heart failure 8 months later for those who had actively walked or biked daily. When looking at long-term behavior of walking/bicycling, the results suggested a trend toward more recent active behavior being more related to heart failure protection than past physical activity levels.

CONCLUSIONS This study suggests that both low levels and high levels of total physical activity, in comparison with moderate levels, could increase heart failure risk in men and that certain types of physical activity are associated with a protective effect on heart failure in men. When examining different types of physical activity, walking/bicycling at least 20 min per day was associated with the largest risk reduction of heart failure. (J Am Coll Cardiol HF 2015;3:681–7)

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Heart failure (HF) is a large public health issue with a substantial effect on the disease burden in developed countries, particularly among the elderly (1). In the United States, more than 5.8 million people suffer from HF, and the number of HF sufferers worldwide is around 23 million (1). The lifetime risk for development of HF is around 20% (2).

Physical activity (PA) has been shown to be associated with reduced risks of coronary heart disease (3–5) and stroke (3,5–8). Studies have also suggested that PA is associated with HF development (9–14). To the best of our knowledge, no previous study has investigated the shape of association between total PA and HF modeling the exposure as a continuous variable using flexible spline modeling. Neither has long-term behavior regarding PA in relation to HF risk been investigated previously.

Moreover, previous studies have presented their results by relying only on relative measures of association. These popular risk measures that lack a time unit may be complemented by estimating differences in the percentiles of survival time, presenting results in the metric of time (i.e., days, months) (15).

We therefore examined how total PA and 5 different domains of PA are associated with the development of...
hf in a population-based prospective cohort study of men, examining both relative risks and survival percentiles. we also investigated if changes of pa at different time points were associated with hf risk.

methods

study population. the study participants belonged to the cohort of swedish men (cosm), a population-based cohort established between 1997 and 1998. all men born between 1914 and 1948 residing in örebro and västmanland counties in sweden were asked to complete an extensive questionnaire regarding pa, diet, anthropometric traits, and other lifestyle factors.

we excluded individuals with prevalent hf or myocardial infarction (n = 3,350) from the baseline population, based on linkage of the cohort to the swedish national patient register and the swedish cancer register. this effort was made because the previously mentioned diseases may affect both traditional hf risk factors and hf development. we also excluded individuals with missing information on total pa (n = 9,923) from the study sample. the final study population consisted of 33,012 men.

the questionnaire included information on participants’ educational attainment, smoking and alcohol consumption, presence of hypertension, family history of myocardial infarction, diagnosis of diabetes (which was complemented with information from the diabetes register and the swedish national patient register), weight, and height. information on history of stroke and angina was obtained from the swedish national patient register.

the study has been approved by the regional ethical review board at karolinska institutet.

assessment of physical activity. study participants were asked to report how their level of activity at work, home/housework, walking/bicycling, and exercise, had been in the year before study enrollment and at 30 years of age. questions regarding inactivity (watching television or reading) and an open question about hours per day of sleeping and sitting or lying down were also included in the questionnaire. each type of pa was assigned an intensity score defined as metabolic equivalent (met) hours per day, deriving the intensity score from the compendium of physical activities (16). the mean met values assigned for the different types of pas were as follows: walking/bicycling ~3.6 met; exercise ~5.0 met; work occupation ~1.3 met for mostly sitting down to 3.9 for heavy manual work; home/household work ~2.5 met; watching tv/reading ~1.2 met; sleep ~0.9 met. total daily physical activity (tpa) score was then estimated by multiplying the intensity score of each type of pa for its reported duration and then adding all specific activities together. the intensity of an activity was based on the rate of the work and did not take into account the physiological capacity of an individual. implausible self-reported 24 h were corrected either by adding missing hours or subtracting over-reported hours. the correction time was multiplied by an intensity of 2.0 met, which corresponded to the average of walking at home (2.5 met) and sitting (eating, transportation, etc., 1.5 met).

the questions on tpa in cosm have been validated by a previous study on a subpopulation of cosm. the study found that the correlation comparing self-reported tpa with records (7 days of pa diaries) was 0.56 (17), which suggests reasonable validity.

ascertainment of hf events. dates of incident hf hospitalization as well as dates of deaths from hf were ascertained from january 1, 1998, to december 31, 2012, through linkage to the swedish national patient register and the causes of death register. the swedish national patient register represents the inpatient register, which includes all hospital admissions that entailed at least 1 overnight stay, and the outpatient register, which covers diagnoses registered during outpatient care. hf events were identified by using international classification of diseases-10 codes 150 (hf) and i11.0 (hypertensive heart disease with hf). we included the first hf event recorded in the registers listed as either the primary or secondary diagnosis of hospitalization or death.

statistical analyses. data handling and generation of descriptive statistics were performed in sas (version 9.2, sas institute, inc., cary, north carolina). stata software version 12.1 (statacorp lp, college station, texas) was used to fit cox proportional hazards regression and laplace regression. hazard ratios (hr) and 95% confidence intervals (ci) were estimated using cox proportional hazards regression models with attained age as the underlying time scale. start of follow-up was january 1, 1998, and follow-up was censored at the date of first event of hf, death, or december 31, 2012, whichever occurred first. tpa was modeled as a continuous variable by means of restricted cubic splines with 3 knots of the distribution (at 36, 41, and 48 met h/day) using the median level of 41 met h/day as the reference value. we examined the linearity of the dose-response by testing the null hypothesis that the coefficient of the second spline...
was equal to zero. The top 1% and bottom 1% of TPA levels were removed to diminish influence from potential outliers. We then graphed the dose-response association between TPA and HF incidence.

Additionally, we evaluated the different domains of TPA: exercise, walking/bicycling, work occupation, home/household work, and physical inactivity. To examine if the results were influenced by reverse causality, we conducted a sensitivity analysis in which study participants who developed HF during the first 3 years of follow-up time were excluded.

Laplace regression was next used to evaluate HF-free survival according to levels of PA and adjusting for potential confounders (15,18,19). We focused on the 50th percentile of attained age at first HF event; attained age being also used as the underlying time scale in the Cox regression models, and estimated multivariable-adjusted differences in the median age at first HF event between men who were active and inactive on the different domains of PA (walking/bicycling, exercise, work occupation, household work, and reading/watching TV).

We also investigated the relationship between long-term behavior regarding walking/bicycling and the incidence of HF. This was done by combining information on levels of walking/bicycling (≥20 min/day vs. <20 min/day) at 30 years of age and in 1997, examining if the level of walking/bicycling changed or remained the same. Walking/bicycling less than 20 min/day both at age 30 and in 1997 served as the reference category.

Covariates included in the multivariable-adjusted model were age at study entry, educational attainment (primary school, high school, university), smoking (never/past/current [≤10, >10 cigarettes/day]), alcohol consumption (never/past/current [<5, ≥5 g/day]), family history of myocardial infarction before 50 years of age, history of stroke, history of angina, hypertension, diabetes, and body mass index (<18.5, 18.5 to 24.9, 25 to 29.9, ≥30 kg/m²). The proportional hazards assumption was examined by investigating Schoenfeld’s residuals.

**RESULTS**

During a mean follow-up of 13 years (450,523 person-years), we ascertained a total of 3,609 HF events including 3,190 first events of HF hospitalizations and 419 HF deaths. The average age at study entry among study participants was 60 years of age. Baseline characteristics of the cohort according to quartiles of TPA are presented in Table 1.

**TOTAL PHYSICAL ACTIVITY.** We modeled TPA as a continuous predictor using restricted cubic splines. We found evidence of non-linearity (p < 0.001). Compared with participants with the median TPA level (41 MET h/day), lower levels of TPA (beginning from 40 MET h/day) were progressively associated with higher HF risk, with up to 44% higher risk for participants with the lowest TPA (HR: 1.44; 95% CI: 1.24 to 1.68). High levels of TPA (starting from 47 MET h/day) were also associated with increased risk of HF, and men who had the highest level of TPA (57 MET h/day) had an increased risk of HF (HR: 1.25; 95% CI: 1.03 to 1.53) compared with men with the median TPA level (Figure 1).

**SPECIFIC TYPES OF PHYSICAL ACTIVITY.** When examining the different domains of activities that constituted TPA, we found certain types of PA to be associated with a reduced risk of HF (Table 2). Walking/bicycling than 20 min/day was associated with an HR of 0.79 (95% CI: 0.72 to 0.87). Exercising more than 1 h/week was associated with HF risk reduction with an HR of 0.86 (95% CI: 0.79 to 0.94) in the multivariable-adjusted model. Work occupation, household work, and physical inactivity were not significantly associated with HF development.

Table 2 also shows the absolute differences in the median age at first HF event between groups of moderate to high versus low levels of different types of PA estimated with Laplace regression. Moderate to high levels of walking/bicycling and exercise were significantly associated with longer HF-free survival.
compared to low levels of the corresponding PA types. The largest difference was detected for walking/bicycling. By looking at the median age at HF event, HF cases who had engaged at least 20 min/day in this activity had the HF event 8 months later than HF cases who had engaged in this activity less than 20 min/day (50th percentile difference = 230 days; 95% CI: 144 to 317 days).

We further investigated if age at study entry or educational level differed significantly between men walking/bicycling at least 20 min/day versus men walking/bicycling less than 20 min/day. We did not find any significant difference on age or level of education between the 2 groups (data not shown).

SENSITIVITY ANALYSIS. In the sensitivity analysis, in which we excluded study participants who developed HF in the 3 first years of follow-up (n = 104), to account for potential reverse causality, the results remained similar to the main analysis. The association between walking/bicycling at least 20 min/day and HF risk was comparable with the results from the main model (HR: 0.77; 95% CI: 0.69 to 0.86) in the sensitivity analysis.

LONG-TERM WALKING/BICYCLING. We also examined the relationship between long-term behaviors in walking/bicycling with incidence of HF (Table 3). Compared with men who had been inactive at both time points the HR was lower for men who had gone from being inactive in this PA domain at age 30 to active in 1997 (HR: 0.77; 95% CI: 0.58 to 1.02) and also for men who had been active at both time points (HR: 0.84; 95% CI: 0.69 to 1.03). The results, however, did not reach statistical significance (Table 3).

DISCUSSION

In this prospective population-based study, we found moderate levels of TPA to be associated with a lower risk of future HF. Compared with the median level of TPA, both extremely low and extremely high levels of TPA were associated with an increased risk of HF. However, the association was larger for lower levels of TPA. When investigating which domains of TPA were associated with a reduced risk of HF, we found that engaging in walking or biking at least 20 min per day and exercising during leisure time at least 1 h per week were associated with reduced HF risk.

When examining long-term behavior regarding walking or biking and HF risk, the results suggested that more recent active behavior in this PA domain may be more important for HF protection than past
PA levels. Being active at age 30 but turning inactive in 1997 was not found to be associated with decreased risk of HF.

Previous studies have shown that low levels of PA increase the risk of HF (20). One former study investigating the effect of different types of PA on HF risk in a Finnish population found leisure time PA to have the largest inverse association with HF (13). A previous study by Lee et al. (21) showed that running from 5 to 10 min per day at low speed was associated with a markedly HF risk reduction. In our study, we observed the largest inverse association with moderate levels of walking/bicycling and leisure time exercise. Hence our results are in line with the results from the previous studies.

The biological link between PA and cardiovascular disease is not fully understood. Several biological explanations for potential cardioprotective effects exerted by PA have been suggested. For example, it has been suggested that the beneficial effects could be mediated through reductions in inflammatory and hemostatic biomarkers, and to some extent blood pressure, lipids, and body mass index (22). In a recent study, it was shown that moderate levels of PA were associated with lower levels of sensitive troponin T and N-terminal pro-B-type natriuretic peptide and also lower risk of HF (23).

In contrast to other studies, we also found extremely high levels of TPA to be associated with an increased risk of HF. It is important to bear in mind that TPA was a construct encompassing various types of PAs, with work occupation being the biggest contributor. Some studies have suggested that heavy physical exercise, such as intense long-distance running, is associated with adverse cardiovascular outcomes (24,25). It is possible that substantial increase of pumping of blood by the heart could damage the cardiac muscle fibers, causing damage in the myocardium. Moreover, adverse cardiovascular outcomes could potentially be attributed to increased oxidative stress, arterial stiffness, and coronary artery calcification (25). Moreover, it is possible that very heavy manual work causes a great deal of stress, which in turn has adverse effects on cardiovascular health. Another potential explanation could be that extremely heavy manual work occupations are correlated with unhealthy lifestyle factors that exert increased risk of HF, factors which were not accounted for in this study.

It is also interesting to note that a recent study investigating the relationship between TPA and HF in women, using the same TPA construct, did not detect an increased risk of HF with very high levels of TPA (26). Hence, the effects of PA might be different for men and women. A randomized controlled study examining the effects of exercise training on mortality and hospitalization reported that exercise training in individuals with HF was associated with a larger risk reduction of all-cause mortality and hospital stay in women compared with men (27).

**STUDY STRENGTHS AND LIMITATIONS.** To the best of our knowledge, the majority of previous studies have not investigated the dose-response association between PA and HF by using flexible tools such as splines. We also had information on long-term PA behavior and could show that more recent PA behaviors, associated with lower levels of sensitive troponin T and N-terminal pro-B-type natriuretic peptide and also lower risk of HF (23).

### Table 2

<table>
<thead>
<tr>
<th>Type of Physical Activity</th>
<th>Hazard Ratio (95% CI)*</th>
<th>Hazard Ratio (95% CI)+</th>
<th>50th PD (95% CI), days†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking/bicycling, ≥20 min/day vs. &lt;20 min/day</td>
<td>0.75 (0.68 to 0.82)</td>
<td>0.79 (0.72 to 0.87)</td>
<td>230 (144 to 317)</td>
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<tr>
<td>Exercise, ≥1 h/week vs. &lt;1 h/week</td>
<td>0.80 (0.74 to 0.87)</td>
<td>0.86 (0.79 to 0.94)</td>
<td>125 (51 to 200)</td>
</tr>
<tr>
<td>Work occupation, active vs. mostly sitting</td>
<td>0.88 (0.81 to 0.96)</td>
<td>0.93 (0.85 to 1.01)</td>
<td>49 (27 to 126)</td>
</tr>
<tr>
<td>Home/household work, ≥1 h/day vs. &lt;1 h/day</td>
<td>0.97 (0.91 to 1.04)</td>
<td>0.95 (0.89 to 1.02)</td>
<td>3 (56 to 61)</td>
</tr>
<tr>
<td>Inactivity (watching television/reading), &lt;3 h/day vs. ≥3 h/day</td>
<td>1.01 (0.89 to 1.15)</td>
<td>0.99 (0.87 to 1.12)</td>
<td>33 (1.79 to 146)</td>
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*Hazard ratios adjusted for educational attainment (primary school, high school, university), smoking (never, past, current [10, >10 cigarettes/day]), alcohol consumption (never/past/current [5, >5 g/day]), family history of myocardial infarction, history of stroke, history of angina, hypertension, diabetes, and body mass index (18.5, 18.5 to 24.9, 25 to 29.9, >30 kg/m²). †Hazard ratios additionally mutually adjusted for all types of physical activity. Estimates were obtained by fitting a Laplace regression model on the 50th percentile of age at heart failure (HF) event, and adjusted for age at baseline, educational attainment (primary school, high school, university), smoking (never, past, current [10, >10 cigarettes/day]), alcohol consumption (never/past/current [5, >5 g/day]), family history of myocardial infarction, history of stroke, history of angina, hypertension, diabetes, and body mass index (18.5, 18.5 to 24.9, 25 to 29.9, >30 kg/m²). All types of physical activity were mutually adjusted for. CI = confidence interval; HF = heart failure; PD = percentile difference.

### Table 3

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>Walking/bicycling at 30 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive (&lt;20 min/day)</td>
<td>1.00 reference</td>
</tr>
<tr>
<td>Active (≥20 min/day)</td>
<td>1.01 (0.92-1.32)</td>
</tr>
<tr>
<td>Inactive (&lt;20 min/day)</td>
<td>0.77 (0.58-1.02)</td>
</tr>
<tr>
<td>Active (≥20 min/day)</td>
<td>0.84 (0.69-1.03)</td>
</tr>
</tbody>
</table>

Multivariable-adjusted hazard ratio (95% confidence interval [CI]) adjusted for age at baseline, educational attainment (primary school, high school, university), smoking (never, past, current [10, >10 cigarettes/day]), alcohol consumption (never/past/current [5, >5 g/day]), family history of myocardial infarction, history of stroke, history of angina, hypertension, diabetes, body mass index (18.5, 18.5 to 24.9, 25 to 29.9, >30 kg/m²), and other types of physical activity. Abbreviations as in Table 2.
activity levels is associated with decreased risk of HF compared with past PA levels.

Furthermore, we complemented our main results by reporting the association between PA domains and HF risk in terms of time differences, by estimating survival percentiles. This approach allows for an easier interpretation of the results and might facilitate the presentation of scientific results to the general public (15). Laplace regression, the method we used for this analysis, directly estimates differences in survival percentiles and enables adjustment for potential confounders (18).

It is important to note that we cannot infer on causality based on our study results. It is possible that the association between PA and risk of future HF could have been due to unmeasured confounders or residual confounding both at baseline and during the follow-up period. Education level varied according to level of TPA in a strong negative fashion and it is thus possible that residual confounding of education was present. It could also be that educational level is correlated with income level/socioeconomic status and therefore with better health care services. These potential limitations could be particularly pertinent to the positive association observed between very high levels of TPA at baseline and HF risk, as there was an inverse association between TPA and education. Moreover, we did not have information on medication use and objective measurements of risk factors such as blood pressure, variables that could have exerted confounding effects. We also lacked information on whether PA levels among the study participants changed during the course of the follow-up period.

We used self-reported PA data, and therefore it is possible that PA levels were misclassified. It would have been desirable to include objective measures of PA, such as accelerometer data. However, our study was a prospective cohort study and such, recall bias is not expected to be an issue. Potential misclassification of PA should be independent of the outcome status and could have attenuated the association between PA and HF risk.

The generalizability of this study might also be limited. This study population comprised middle-aged and elderly white men, so that we might not be able to extrapolate our findings to other ethnicities, younger age groups, or women.

**CONCLUSIONS**

This study shows that certain types of PA are associated with a protective effect on HF in men. Walking or biking at least 20 min each day and leisure time PA were in particular found to be associated with a risk reduction of HF. In addition, this study suggests that both extremely low and extremely high levels of TPA could elevate the risk of developing HF in men. Public awareness of specific types of PA as well as sufficient amount and duration of PA required for HF protection could potentially reduce the HF burden in society. Further studies unraveling the duration of PA and specific types of PA that are most beneficial for HF protection are therefore needed.

**REFERENCES**


**PERSPECTIVES**

**COMPETENCY IN MEDICAL KNOWLEDGE:**
Among men, both high and low extremes of total physical activity were associated with an increased risk of heart failure. The domain of total physical activity that was associated with the largest risk reduction in heart failure was walking/bicycling at least 20 min/day.

**TRANSLATIONAL OUTLOOK:** Prospective studies should carefully study nonlinear relationships between total physical activity and heart failure risk in men, as well as look deeper into what types of physical activity actually have a protective effect on heart failure. Certain types of physical activity, such as walking or biking 20 min daily, can be promoted in heart failure risk prevention strategies.

KEY WORDS epidemiology, heart failure, physical activity