Effects of Physical Activity and Sedentary Time on the Risk of Heart Failure

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Abstract

Background—Although the benefits of physical activity for risk of coronary heart disease are well established, less is known about its effects on heart failure (HF). The risk of prolonged sedentary behavior on HF is unknown.

Methods and Results—The study cohort included 82,695 men aged ≥45 years from the California Men’s Health Study without prevalent HF who were followed up for 10 years. Physical activity, sedentary time, and behavioral covariates were obtained from questionnaires, and clinical covariates were determined from electronic medical records. Incident HF was identified through International Classification of Diseases, Ninth Revision codes recorded in electronic records. During a mean follow-up of 7.8 years (646,989 person-years), 3473 men were diagnosed with HF. Controlling for sedentary time, sociodemographics, hypertension, diabetes mellitus, unfavorable lipid levels, body mass index, smoking, and diet, the hazard ratio (95% confidence interval [CI]) of HF in the lowest physical activity category compared with those in the highest category was 1.52 (95% CI, 1.39–1.68). Those in the medium physical activity category were also at increased risk (hazard ratio, 1.17 [95% CI, 1.06–1.29]). Controlling for the same covariates and physical activity, the hazard ratio (95% CI) of HF in the highest sedentary category compared with the lowest was 1.34 (95% CI, 1.21–1.48). Medium sedentary time also conveyed risk (hazard ratio, 1.13 [95% CI, 1.04–1.24]). Results showed similar trends across white and Hispanic subgroups, body mass index categories, baseline hypertension status, and prevalent coronary heart disease.

Conclusions—Both physical activity and sedentary time may be appropriate intervention targets for preventing HF.
Introduction

Heart failure (HF) is a major cardiovascular disease, affecting ≈5.7 million Americans with >600 000 yearly incident cases.\(^1\) Approximately 20% of adults will be diagnosed with HF during their lifetime.\(^2\) More than 8 million people may be living with HF by 2030, a 23% increase in prevalence.\(^3\) Total medical costs are projected to increase from $20.9 billion in 2010 to $53.1 billion by 2030.\(^3\) Blacks and Hispanics may have greater prevalence,\(^4\) and men have greater risk than women.\(^5\) The combination of its disease burden, racial/ethnic and sex disparities, and projections of increasing incidence suggest that we need to better understand lifestyle behaviors potentially associated with the development of HF.

Clinical Perspective on p \(27\)

Regular physical activity reduces risk of coronary heart disease (CHD),\(^6\)^\(^7\) myocardial infarction,\(^7\) hypertension,\(^8\) obesity,\(^9\) and diabetes mellitus\(^10\)—conditions associated with HF.\(^11\)\(^,\)\(^12\) However, few investigations have examined its effects on HF. Those that have indicate that regular physical activity may be protective.\(^12\)\(^,\)\(^16\) Of note, these studies included primarily white populations. Although evidence is accumulating that excessive sedentary behavior may increase risk for overall mortality and cardiovascular outcomes, independent of physical activity,\(^12\) the risk of sedentary behavior on HF has not been established.

The present study assessed the association between physical activity and HF incidence and sedentary behavior and HF incidence. With a large multiethnic cohort, the California Men’s Health Study (CMHS), we assessed the potential benefit of these behaviors in reducing HF incidence in a diverse population of middle-aged and older men.

Methods

Study Cohort

The CMHS was established in 2002 to 2003 and is a sociodemographically diverse cohort of >84 000 men who were members of Kaiser Permanente Southern or Northern California health plans.\(^18\) Men between the ages of 45 and 69 years in January 2000 were eligible if they had been members for ≥1 year. The institutional review boards of both organizations approved the study. Men provided informed consent.

The cohort consists of men who completed a screener and baseline questionnaire. Follow-up is passive, with use and diagnostic outcomes obtained from the Kaiser Permanente electronic medical record systems. Race/ethnicity, educational attainment, marital status, and body mass index (BMI; kg/m\(^2\)) are comparable with similarly aged men living in California in 2001.\(^18\)

Determination of HF
HF was identified from electronic records using the criteria described by Goyal et al., including ≥1 hospitalization with an ICD-9 diagnosis code of HF (codes 402.X1, 404.X1, 404.X3, and 428.XX) or ≥2 outpatient diagnoses of HF. Validity of an inpatient discharge diagnosis of HF was assessed from 200 randomly selected hospital charts to determine the extent to which Framingham criteria for HF were met; results indicated a positive predictive value of 97%. Outpatient diagnosis codes may be less accurate; hence, we required ≥2 separate outpatient diagnoses. In a systematic review of validated methods for identifying HF using administrative data, Saczynski et al. recommended, including outpatient codes, to maximize sensitivity because many patients with HF are identified and managed in the outpatient setting. Incident cases were defined as receiving a diagnosis from baseline to May 1, 2012. Prevalent cases were defined from 3 years before the baseline date.

Analysis

Cohort characteristics were described using percentages. Characteristics were compared across physical activity and sedentary time categories using the χ² test.

Kaplan–Meier curves, time-dependent analyses, and Schoenfeld residuals were used to assess the proportionality of variables to be included in models. The Cox proportional hazards model was used to assess the effects of physical activity and sedentary activity on HF, controlling for baseline age, education, income, BMI category, smoking status, race/ethnicity, hypertension and diabetes mellitus status, high-density lipoprotein cholesterol, triglycerides, fasting glucose, daily percent of calories from fat, daily fruit servings, daily vegetable servings, and alcohol intake.

To assess multiplicative interaction, we used a fully adjusted model that included the physical activity by sedentary time interaction term. It was not significant and not included in the final models. To assess additive interaction, we used Poisson regression to calculate adjusted rates for each combination of physical activity and sedentary time. We then calculated the relative excess risk due to interaction score in the original Cox proportional hazards model.

To examine whether the associations among physical activity, sedentary time, and HF risk would vary by race/ethnicity, BMI category, hypertension, and prevalent CHD, additional Cox proportional hazard models stratifying by these variables were completed including the same covariates as for the main models.

All analyses were performed using SAS version 9.2 (SAS Institute, Inc, Cary, NC). Significance level was set at 0.05 for a 2-sided test.

Results

A total of 84 170 men were enrolled in the cohort. Prevalent HF cases (n=1201) were excluded, as were men without follow-up information (n=274), leaving 82 695 participants.

At baseline, the mean age was 58±7 years. Mean BMI was 27.9±4.7 kg/m². Median moderate-to-vigorous physical activity was 1102 MET-minutes per week (75% interquartile
The racial/ethnic distribution was 63% non-Hispanic white, 14% Hispanic, 11% Asian, 7% black, and 5% other. Almost half the sample had at least a college degree. Baseline characteristics across physical activity and sedentary time categories are displayed in Table 1. High physical activity was associated with low sedentary category, older age, non-Hispanic white race/ethnicity, college completion, higher income, lower BMI, favorable cardiovascular risk factors, and favorable dietary intake. Low sedentary time was associated with younger age, Asian or Hispanic race/ethnicity, higher education and income, lower BMI, and favorable cardiovascular risk factors and dietary intake. Prevalent CHD was found in 13.2% of the participants before an HF diagnosis.

Baseline Characteristics of California Men’s Health Study Participants by Physical Activity and Sedentary Time Categories

During a mean follow-up of 7.8 years (646,989 person-years), there were 3,473 incident HF diagnoses. HF incidence decreased across physical activity level: 7.8, 4.9, and 3.8 per 1000 person-years for low, medium, and high categories, respectively. Compared with the high physical activity category, adjusted hazard ratios (HR) were 1.52 (95% confidence interval [CI], 1.39–1.68) for the low and 1.17 (95% CI, 1.06–1.29) for the medium category (Table 2). HF risk was higher in the low physical activity category compared with the medium category (HR, 1.30 [95% CI, 1.20–1.42]). The test for trend was significant (P<0.0001). Including CHD in the model only slightly attenuated results.

Number of Heart Failure Cases, Person-Years, Cases Per 1000 Person-Years, and Hazard Ratios by Physical Activity and Sedentary Time Categories

There were 3.8 cases per 1000 person-years for the low sedentary time category, 5.6 for medium sedentary time, and 8.8 for high sedentary time (Table 2). Compared with low sedentary time, adjusted HRs were 1.13 (95% CI, 1.04–1.24) and 1.34 (95% CI, 1.21–1.48) for the medium and high sedentary time categories, respectively. The test for trend was significant (P<0.0001). The model including CHD produced similar HRs.

We evaluated the extent to which the physical activity and sedentary time constructs overlapped using the Gamma statistic. The value was −0.10, a small correlation. The Figure illustrates the adjusted HRs across joint physical activity and sedentary time categories. Men in the low physical activity and high sedentary time category had 2.2× (95% CI, 1.84–2.53) the risk of HF compared with men in the high physical activity and low sedentary time category. There was a slight additive interaction (relative excess risk due to interaction=0.08; 95% CI, 0.03–0.14), evidenced by examining the absolute unadjusted and adjusted event rates in the Figure footnote.
Hazard ratios for heart failure by physical activity and sedentary time adjusted for baseline age, race/ethnicity, education, income, body mass index, smoking status, hypertension and diabetes mellitus status, antihypertensive medications, high-density lipoprotein cholesterol, fasting glucose, triglycerides, daily percent calories from fat, daily fruit servings, daily vegetable servings, and alcohol intake.

Sensitivity analyses were performed excluding men with <3 months of follow-up (n=1161) and excluding HF cases diagnosed within the first year of follow-up (n=408). Results indicated that the HRs for HF only slightly changed.

The adjusted HRs for HF by physical activity and sedentary time categories across racial/ethnicity groups are presented in Table 3. For the Asian, Hispanic, white non-Hispanic, and other subgroups, the HRs were higher for the low compared with the high physical activity category. High sedentary time conferred increased HF risk for the Hispanic (HR, 1.78 [95% CI, 1.35–2.36]) and white non-Hispanic men (HR, 1.29 [95% CI, 1.13–1.47]).

Hazard Ratios for Heart Failure by Physical Activity and Sedentary Time Categories Across Baseline Race/Ethnicity, Body Mass Index Categories, Hypertension, and Coronary Heart Disease Status

Compared with those with high physical activity, the low physical activity category conferred higher HF risk among normal weight, overweight, and obese men (Table 3). Obese men with high sedentary time and normal weight and overweight men with both medium and high sedentary time had increased risk compared with men with low sedentary time.
Low physical activity had a 53% greater risk among men with and without hypertension (Table 3). HF risk increased for the medium and high sedentary time categories for men without hypertension and for the high sedentary time with hypertension.

Low physical activity increased HF risk for those with and without CHD, with the risk twice as great for men without CHD (32% versus 70%, respectively; Table 3). High sedentary time had an increased HF risk only for those without CHD.

**Discussion**

In this diverse cohort of middle-aged and older men, low physical activity and high sedentary time each contributed to increased HR risk. These associations had independent contributions beyond each other and known sociodemographic, clinical, and lifestyle risk factors. The trends were consistent across most race/ethnicities, BMI categories, and hypertension status.

Others have found that prolonged sedentary behavior increases risk for cardiovascular disease incidence \[31,32\] and mortality \[33–35\] after controlling for physical activity. Some studies included HF in their definition of cardiovascular events \[31,32\] but none specifically examined HF. With our large sample size and during 10 years of follow-up, we had >600 000 person-years to examine this cardiovascular event. Our results strengthen the developing position that too much sitting is detrimental to cardiovascular health, independent of regular physical activity.

We found increased risk across BMI categories for low and medium physical activity compared with the high-activity group. These results are consistent with others who found that higher physical activity lowered HF risk within BMI levels, with the greatest HF risk for the obese with low physical activity.\[15,16\]

Low physical activity conferred increased HF risk for men with and without CHD. However, high sedentary time increased risk only for those without CHD. With the relatively few men with CHD in this sample, it may be premature to conclude that high sedentary time increases HF risk only for those without CHD. Future studies with greater power are needed to examine sedentary time on HF risk for those with CHD.

It was notable that the combinations of low physical activity with high sedentary time and high physical activity with low sedentary time, respectively, yielded similar HRs when the analyses were stratified by baseline hypertensive status. In contrast, Djoussé et al \[36\] found that the lifetime HF risk for normal weight, nonsmoking, regularly exercising men was greater for those with hypertension than those without hypertension. Rather than creating a lifestyle risk score as Djoussé et al, \[36\] we controlled for other lifestyle factors that may explain the differing results.

We conducted stratified analyses by race/ethnicity and found that the associations were generally consistent. However, we had limited power to detect significant associations among the black and Asian men. Bell et al, \[37\] examining physical activity and cardiovascular disease among blacks in the Atherosclerotic Risk In Communities (ARIC) study, reported
similar HRs for HF incidence among blacks and whites after 21 years of follow-up. There are several key differences between ARIC and CMHS cohorts. During follow-up, 9.4% of the blacks in their cohort developed HF as opposed to 6.3% in our cohort, possibly increasing their power to detect associations. Also, most of the blacks in ARIC were recruited from Jackson, MS, a region vastly different from our predominantly urban regions.

The possible biological mechanisms through which either low physical activity or prolonged sedentary time may cause HF are not well established, but scant evidence suggests that the pathways may be different. Low physical activity is associated with higher blood pressure and unfavorable lipoprotein profile, glucose metabolism, and weight status. These increase the risk of CHD, thereby increasing the risk of HF. In addition, regular physical activity improves myocardial structure and function. Physical activity may prevent cardiac injury and neurohormonal activation and thereby decrease the risk of HF. Excessive sedentary behavior is also associated with unfavorable cardiovascular risk factors. Animal and prolonged human bed rest studies suggest that inadequate muscle contraction may suppress skeletal muscle lipoprotein lipase. This may elevate triglycerides and blood glucose and lower high-density lipoprotein cholesterol production, which can accelerate the development of CHD and eventual HF. This mechanism seems to be specific to prolonged sedentary time and not lack of regular physical activity.

There are study limitations. Our cohort consisted of only men. However, an NHANES (National Health and Nutrition Examination Survey) I follow-up study on HF risk factors found relative risks of low physical activity at 1.14 for men and 1.31 for women, suggesting that similar biological mechanisms may apply. Our exposures were determined by self-report. The physical activity instrument may have resulted in over-reporting in absolute terms, although we used it to determine relative ranking. The sedentary behavior questions only included the nonwork domain, and thus, our data cannot be applied to overall sedentary time. The condition of HF was identified from diagnosis codes, which can result in misclassification, although any misclassification was likely nondifferential and would attenuate toward the null. Men who are unhealthy, have underlying symptoms, or a newly diagnosed disease may have decreased their physical activity or increased their sedentary time before obtaining an HF diagnosis. We attempted to reduce this bias by adjusting for prevalent hypertension, diabetes mellitus, CHD, BMI, and lipids. We conducted stratified analyses by BMI category and hypertension and CHD status and performed sensitivity analyses to examine this potential bias. Finally, participants were members of health plans that provide comprehensive care; results may not generalize to men lacking health insurance.

In conclusion, the results from this large, prospective study of a racially/ethnically diverse population bolster the accumulating evidence of the importance of a physically active and nonsedentary lifestyle for reducing the risk of HF.