Joint Effects of Physical Activity, Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio on the Risk of Heart Failure

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Background—Obesity increases heart failure (HF) risk; however, the independent effect of physical activity and the joint effect of physical activity and adiposity on HF risk are not established. We evaluated the single and joint associations of physical activity and different indicators of adiposity (body mass index, waist circumference, and waist-to-hip ratio) with HF risk.

Methods and Results—Study cohorts included 59,178 Finnish participants who were 25 to 74 years of age and free of HF at baseline. During a mean follow-up of 18.4 years, 1,921 men and 1,693 women developed HF. The multivariable-adjusted hazard ratios of HF associated with low, moderate, and high physical activity were 1.00, 0.79, and 0.69 (P_trend/H11021 0.001) for men and 1.00, 0.86, and 0.68 (P_trend/H11021 0.001) for women, respectively. The multivariable-adjusted hazard ratios of HF at different levels of body mass index (<25, 25 to 29.9, and ≥30 kg/m²) were 1.00, 1.25, and 1.99 (P_trend/H11021 0.001) for men and 1.00, 1.33, and 2.06 (P_trend/H11021 0.001) for women, respectively. Abdominal adiposity, measured by waist circumference or waist-to-hip ratio, was associated with a greater risk of HF among both men and women (all P_trend/H11021 <0.01). In joint analyses, the protective effect of physical activity was consistent in subjects at all levels of body mass index.

Conclusions—General overweight and general and abdominal obesity are independently associated with an increased risk of HF, whereas moderate or high levels of physical activity are associated with a reduced risk of HF. The protective effect of physical activity on HF risk is observed at all levels of body mass index. (Circulation. 2010;121:237-244.)

Key Words: epidemiology ■ exercise ■ heart failure ■ obesity

Heart failure (HF) has emerged as a major public health issue and is among the most significant causes of morbidity and mortality in older adults in the United States and other Western countries.1,2 According to the American Heart Association, 550,000 new cases occur in the United States each year,3 and >5 million Americans have HF.4 Hospital discharges for HF increased by 155% during the last 20 years, and HF is the most frequent cause of hospitalization in persons ≥65 years of age.5 In Europe, 10 million people have HF according to the estimate of the European Society of Cardiology (ESC).6 The prevalence of symptomatic HF is estimated to range from 0.4% to 2% in the general European population.2

Clinical Perspective on p 244

There is good evidence that regular physical activity has a protective effect against coronary heart disease and stroke;1 however, the association between regular physical activity and the risk of HF remains uncertain.4,5 Evidence from epidemiological studies has shown that overweight (body mass index [BMI], 25 to 29.9 kg/m²) or obesity (BMI ≥30 kg/m²) is a major established risk factor for coronary heart disease and ischemic stroke.6 Although an obese individual has an increased risk of HF, few studies have assessed whether an increased risk also exists in overweight individuals.4,5,7,8 It has been reported that greater abdominal (central) fatness is associated with an increased risk of coronary heart disease; however, only 2 recent studies have assessed its possible effect on the risk of HF.9,9 Furthermore, the interaction between physical activity and obesity on the risk of HF is not well understood.5 The aim of this study is to examine the single and joint associations of physical activity and 3 indicators of adiposity (BMI, waist circumference, and waist-to-hip ratio) with the risk of HF incidence.
Methods

Subjects

Seven independent cross-sectional population surveys were carried out in 6 geographic areas of Finland in 1972, 1977, 1982, 1987, 1992, 1997, and 2002.10 In 1972 and 1977, a randomly selected sample making up 6.6% of the population born between 1913 and 1947 was drawn. Beginning in 1982, the sample was stratified by area, sex, and 10-year age group according to the World Health Organization (WHO) Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) protocol.11 The participation rate varied by year from 65% to 88%.10 The subjects included in the 7 surveys were 25 to 64 years of age, and the 1997 and 2002 surveys also included subjects 65 to 74 years of age. Subjects who participated in >1 survey were included only in the first survey cohort. The total sample size of the 7 surveys was 62 013. The final sample comprised 28 843 men and 30 366 women after the exclusion of participants with a history of HF (n = 998) at baseline, participants who were underweight (BMI < 18.5 kg/m²) (n = 488), and the participants with incomplete data on any variables required for this analysis (n = 1349). Underweight participants were excluded because of the small number of participants and the potential for preexisting disease to cause weight loss. The excluded participants with incomplete data did not differ significantly from remaining participants in mean age and the sex distribution. The participants provided informed consent (verbal consent in 1972 to 1992, written consent in 1997 and 2002). These surveys were conducted according to the ethical rules of the National Public Health Institute, and the investigations were performed in accordance with the Declaration of Helsinki.

Baseline Measurements

A self-administered questionnaire was mailed to the participants to be completed at home and returned to the survey site. The questionnaire included questions on medical history, socioeconomic factors, physical activity, smoking habits, and alcohol consumption. Education level, measured as the total number of school years, was divided into birth cohort–specific tertiles. On the basis of the responses, the participants were classified as never, ex-, and current smokers. Current smokers were categorized into those participants who smoked < 20 or ≥ 20 cigarettes per day. Because questions on alcohol consumption were different between the first 2 surveys (1972 and 1977) and the later surveys, participants were categorized into abstainers and alcohol users. Data on the history of myocardial infarction or diabetes mellitus at baseline were obtained from the questionnaire and collected by hospital discharge or drug register. Data on the history of valvular heart disease at baseline were collected by hospital discharge register.

Occupational, commuting, and leisure-time physical activity levels were assessed with a self-administered questionnaire. A detailed description of the questions has been presented elsewhere.12,13 The subjects reported their occupational physical activity according to the following 3 categories: low (work that is physically very easy such as sitting office work [eg, secretary]), moderate (work including standing and walking [eg, store assistant and light industrial worker]), and high (work including walking and lifting or heavy manual labor [eg, industrial or farm work]). Daily commuting return journey was divided into 3 categories: motorized transportation or no work (no walking or cycling), walking or bicycling 1 to 29 minutes per day, or walking or bicycling ≥ 30 minutes per day. Self-reported leisure-time physical activity was classified into 3 categories: low, defined as almost completely inactive such as reading, watching television, or doing some minor physical activity but not at a moderate or high level; moderate, defined as doing some physical activity ≥ 4 h/wk such as walking, cycling, or light gardening, excluding travel to work; and high, defined as performing vigorous physical activity ≥ 5 h/wk such as running, jogging, swimming, or heavy gardening or competitive sports several times a week. Because we found that moderate and high occupational, commuting, or leisure-time physical activity independently and significantly reduces risk of HF (data not shown), the groups were merged into 3 categories: low, which included those subjects who reported light levels of occupational, commuting (< 1 minute), and leisure-time physical activity; moderate, which included those subjects who reported only 1 of the all 3 types of moderate to high physical activity; and high, which included those subjects who reported 2 or 3 types of moderate to high physical activity. This method had been used to assess other outcomes such as incidence of diabetes mellitus and mortality in the same study samples.14,15

At the study center, specially trained nurses measured height, weight, and blood pressure using the standardized protocol according to the WHO MONICA project.11 Height and weight were measured without shoes and with light clothing. The measurements of height were rounded to the nearest centimeter; weight was rounded to the nearest 100 g. BMI was calculated by dividing weight in kilograms by the square of height in meters. Blood pressure was measured from the right arm after 5 minutes of sitting with a mercury sphygmomanometer in each survey. After blood pressure was measured, a venous blood specimen was taken. Total cholesterol was determined with the Lieberman Burchard method in 1972 and 1977 and by an enzymatic method (CHOD-PAP, Boehringer MANNEHEIM, Mannheim, Germany) since 1982. Because the enzymatic method gave 2.4% lower values than the Lieberman-Burchard method, the values measured in 1972 and 1977 were corrected by this percentage. All samples were analyzed in the same central laboratory at the National Public Health Institute.

Subgroup Measurements

More detailed data on alcohol consumption and measurement of waist and hip circumferences were included in the surveys of 1987, 1992, 1997, and 2002 (men, n = 13 696; women, n = 14 746). Ethanol consumption was categorized into 4 groups: 0, 1 to 34, 35 to 139, and ≥ 140 g/wk in men and 0, 1 to 34, 35 to 139, and ≥ 140 g/wk in women. Information on the use of hormone replacement therapy in women was obtained in the surveys of 1997 and 2002. Waist circumference was measured midway between the lower rib margin and iliac crest. Hip circumference was measured at the level of widest circumference over greater trochanters. The waist and hip measurements were rounded to the nearest half-centimeter. Waist-to-hip ratio was calculated as waist circumference divided by hip circumference.

Prospective Follow-Up

Follow-up information was obtained from the Finnish Hospital Discharge Register and the National Social Insurance Institution’s Register on special reimbursement for HF drugs for nonfatal outcomes and the Finnish Death Register for fatal outcomes by using social security numbers assigned to everyone in Finland. The International Classification of Diseases (ICD) codes 427.00 and 427.10 (ICD-8); 428, 4029B (hypertensive heart disease with HF), and 4148A-X (ischemic HF with chronic coronary heart disease) (ICD-9); and I 50, I11.0 (hypertensive heart disease with HF), I13.0, and I13.2 (hypertensive heart and renal disease with HF) (ICD-10) were used to identify cases in the above national databases. An HF diagnosis was made by the treating physicians and was based on clinical assessment, x-ray examination, and to various extents, echocardiography. Follow-up of each cohort member continued until the date of the diagnosis of HF from the Hospital Discharge Register, the National Social Insurance Institution’s Register, or mortality, death resulting from causes other than HF, or December 31, 2006. This diagnosed method has been used in other Scandinavian countries such as Sweden. The accuracy of the HF cases in the Swedish hospital discharge is found to exceed 80% on the basis of the ESC definition.8,16

Statistical Analyses

Survival data were analyzed with the Kaplan–Meier method, and survival curves were compared by use of the log-rank test in the univariate analysis. The Cox proportional-hazards model was used to estimate the single and joint associations of physical activity and the 3 indicators of adiposity with the risk of HF incidence. BMI was evaluated in the following 2 ways: as the 3 WHO weight categories

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those mediators in the multivariable analyses. To avoid the potential bias resulting from weight loss before death, additional analyses were carried out excluding subjects who died during the first 2 years of follow-up (n=407). All statistical analyses were performed with SPSS for Windows 17.0 (SPSS Inc, Chicago, Ill).

The authors had full access to the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Table 1. General Characteristics of Study Subjects *

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>1972</td>
<td>10 829</td>
<td>10 772</td>
</tr>
<tr>
<td>1977</td>
<td>9032</td>
<td>6038</td>
</tr>
<tr>
<td>1982</td>
<td>5902</td>
<td>8033</td>
</tr>
<tr>
<td>2002</td>
<td>8572</td>
<td>5972</td>
</tr>
</tbody>
</table>

*Values are given as mean (SD) when appropriate.
‡Included the surveys of 1997 and 2002.

(normal weight, <25 kg/m² [reference group]; overweight, 25 to 29.9 kg/m²; and obese, ≥30 kg/m²) and as a continuous variable. Waist circumference and waist-to-hip ratio were evaluated in 3 ways: as sex-specific quartiles; as the 2 categories of waist circumference (≥102 cm in men or ≥88 cm in women) or waist-to-hip ratio (≥0.9 in men or ≥0.85 in women) recommended by the AHA, National Heart, Lung, and Blood Institute (NHLBI),17 and WHO18; and as a continuous variable. Different levels of physical activity, BMI, waist circumference, and waist-to-hip ratio were included in the models as dummy and categorical variables, and the significance of the trend over different categories of physical activity, BMI, waist circumference, and waist-to-hip ratio was tested in the same models by giving an ordinal numeric value for each dummy variable. The significance of the trend over different categories of physical activity, BMI, waist circumference, and study year and then further for smoking, education, alcohol consumption, history of myocardial infarction, history of valvular heart disease, physical activity, BMI, and potential mediators of association of adiposity and HF (systolic blood pressure, total cholesterol, and history of diabetes mellitus) (multivariable model).

Because there were no significant differences in the multivariable models with and without the above potential mediators, we included those mediators in the multivariable analyses. To avoid the potential bias resulting from weight loss before death, additional analyses were carried out excluding subjects who died during the first 2 years of follow-up (n=407). All statistical analyses were performed with SPSS for Windows 17.0 (SPSS Inc, Chicago, Ill).

The authors had full access to the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Results

General characteristics of the study population at baseline are presented in Table 1. During a mean follow-up of 18.4 years, 1921 men and 1693 women developed HF.

On the basis of Kaplan–Meier estimates, the survival curves showing different patterns in HF were associated with different levels of physical activity (P<0.001, log-rank test), BMI (P<0.001, log-rank test), waist circumference (P<0.001, log-rank test), and waist-to-hip ratio (P<0.001, log-rank test) among both men and women. The multivariate-adjusted (age, study year, smoking, education, alcohol consumption, history of myocardial infarction, history of valvular heart disease, BMI, systolic blood pressure, total cholesterol, and history of diabetes mellitus) hazard ratios (HRs) of HF associated with light, moderate, and high physical activity were 1.00, 0.79, and 0.69 (P trend<0.001) in men and 1.00, 0.86, and 0.68 (P trend<0.001) in women, respectively (Table 2). The multivariable-adjusted HRs of HF among normal-weight (BMI <25 kg/m²), overweight (BMI, 25 to 29.9 kg/m²), and obese (BMI ≥30 kg/m²) subjects were
1.00 1.25, and 1.99 ($P_{\text{trend}}<0.001$) in men and 1.00 1.33, and 2.06 ($P_{\text{trend}}<0.001$) in women, respectively (Table 3). When BMI was examined as a continuous variable, multivariable-adjusted HRs of HF were 1.07 (95% confidence interval [CI], 1.06 to 1.08) in men and 1.07 (95% CI, 1.06 to 1.08) in women for each 1-unit increase. The HRs of HF showed almost no change in the multivariable analyses after additional adjustment for the use of hormone replacement therapy in women (data not shown).

When the analysis was restricted to surveys from 1987 to 2002 (men, n=13 696; women, n=14 746), the multivariable-adjusted HRs of HF across quartiles of waist circumference (quartile 2 as the reference group) were 1.06, 1.00, 1.21, and 1.85 ($P_{\text{trend}}<0.001$) in men and 0.48, 1.00, 1.18, and 1.64 ($P_{\text{trend}}<0.011$) in women, respectively (Table 4). Similarly, the multivariable-adjusted HRs of HF across quartiles of waist-to-hip ratio were 0.88, 1.00, 1.06, and 1.71 ($P_{\text{trend}}<0.001$) in men and 0.61, 1.00, 0.98, and 1.88 ($P_{\text{trend}}<0.001$) in women, respectively (Table 5).

The multivariable-adjusted HRs of HF were 1.03 (95% CI, 1.02 to 1.04) in men and 1.04 (95% CI, 1.03 to 1.05) in women for each 1-cm increase in waist circumference (as a continuous variable) and 1.48 (95% CI, 1.25 to 1.75) in men and 1.64 (95% CI, 1.31 to 2.04) in women for each 0.1-unit increase in waist-to-hip ratio (as a continuous variable). When the 2 categories of waist circumference (≥102 cm in men or ≥88 cm in women) or waist-to-hip ratio (≥0.9 in men or ≥0.85 in women) were used in the analyses, subjects with a high waist circumference or high waist-to-hip ratio had multivariable-adjusted HRs of HF of 1.75 (95% CI, 1.37 to 2.24) and 1.65 (95% CI, 1.18 to 2.31) in men and 1.66 (95% CI, 1.17 to 2.36) and 2.08 (95% CI, 1.46 to 2.97) in women, respectively.

After the exclusion of the participants with myocardial infarction (n=4663) and valvular heart disease (n=1009) at baseline or during follow-up, the inverse association between physical activity and HF risk (all $P_{\text{trend}}<0.001$) and the positive association between adiposity indicators and HF risk (all $P_{\text{trend}}<0.05$) did not change (data not shown). The exclusion of the subjects who died during the first 2 years of follow-up (n=407) did not affect the associations of physical activity or the adiposity indicators with the risk of HF (data not shown).

### Table 2. HRs for HF According to Different Levels of Physical Activity

<table>
<thead>
<tr>
<th>Physical Activity</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
<th>$P_{\text{trend}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>2269</td>
<td>8745</td>
<td>17 828</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>30 897</td>
<td>133 765</td>
<td>348 891</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year</td>
<td>1.00</td>
<td>0.68 (0.59–0.79)</td>
<td>0.52 (0.45–0.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>0.79 (0.68–0.92)</td>
<td>0.69 (0.60–0.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>2900</td>
<td>9226</td>
<td>18 210</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>346</td>
<td>597</td>
<td>750</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year</td>
<td>1.00</td>
<td>0.75 (0.66–0.86)</td>
<td>0.54 (0.47–0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>0.86 (0.75–0.99)</td>
<td>0.68 (0.59–0.78)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Multivariate models included age, study year, education, smoking, alcohol consumption, history of myocardial infarction, valvular heart disease, and diabetes mellitus, systolic blood pressure, total cholesterol, and BMI.

### Table 3. HRs for HF According to Different Levels of BMI

<table>
<thead>
<tr>
<th>BMI, kg/m²</th>
<th>&lt;25</th>
<th>25–29.9</th>
<th>≥30</th>
<th>$P_{\text{trend}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>10 984</td>
<td>13 375</td>
<td>4483</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>560</td>
<td>913</td>
<td>448</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year</td>
<td>1.00</td>
<td>1.23 (1.11–1.37)</td>
<td>2.18 (1.93–2.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>1.25 (1.12–1.39)</td>
<td>1.99 (1.74–2.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>14 254</td>
<td>10 357</td>
<td>5725</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>359</td>
<td>648</td>
<td>686</td>
<td></td>
</tr>
<tr>
<td>Adjustment for age and study year</td>
<td>1.00</td>
<td>1.38 (1.21–1.57)</td>
<td>2.43 (2.13–2.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multivariate adjustment*</td>
<td>1.00</td>
<td>1.33 (1.16–1.51)</td>
<td>2.06 (1.80–2.37)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Multivariate models included age, study year, education, smoking, alcohol consumption, history of myocardial infarction, valvular heart disease, and diabetes mellitus, systolic blood pressure, total cholesterol, and physical activity.
We also found a positive association between the 3 indicators of adiposity (BMI, waist circumference, and waist-to-hip ratio) and the risk of HF in both nonsmokers and smokers (data not shown).

Figures 1 and 2 show the cumulative incidence curves of HF based on the joint effects of physical activity and the 3 indicators of adiposity. We used 3 categories of physical activity (low, moderate, and high), 3 categories of BMI (lean, overweight, and obese), and 2 categories of waist circumference (≥86.5 cm in men or ≥73.0 cm in women) or waist-to-hip ratio (≥0.9 in men or ≥0.85 in women) recommended by the AHA, NHLBI, and WHO in the joint analyses. Because the interactions between sex and any one of physical activity, BMI, waist circumference, and waist-to-hip ratio on the risk of HF were not statistically significant, data for men and women were combined in joint analyses. In joint analyses of physical activity and BMI on HF risk, the protective effect of physical activity was consistent in subjects with any levels of BMI (all \( P_{\text{trend}}<0.05 \)). Similarly, the positive association of BMI with HF risk was consistent in subjects with any levels of physical activity (all \( P_{\text{trend}}<0.05 \)). The joint associations of physical activity and waist circumference or waist-to-hip ratio with the risk of HF were inconsistent. The protective effect of physical activity was found in subjects with low waist circumference (all \( P_{\text{trend}}<0.05 \)) and subjects with high waist-to-hip ratio (all \( P_{\text{trend}}<0.05 \)). The positive association of waist-to-hip ratio with HF risk was consistent in subjects at all levels of physical activity (all \( P_{\text{trend}}<0.001 \)); however, the positive association of waist circumference with HF risk was found only in subjects with a moderate (\( P<0.001 \)) or high (\( P<0.01 \)) level of physical activity. There were significant interactions of physical activity and BMI with the risk of HF among both men and women (all \( P<0.01 \)). However, there were no statistically significant interactions between physical ac-

### Table 4. HRs for HF Based on Waist Circumference as Quartile*

<table>
<thead>
<tr>
<th>Waist Circumference Quartile</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>( P_{\text{trend}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n</td>
<td>3422</td>
<td>3471</td>
<td>3379</td>
<td>3424</td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>36</td>
<td>48</td>
<td>68</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>39 975</td>
<td>38 241</td>
<td>35 896</td>
<td>33 771</td>
<td></td>
</tr>
</tbody>
</table>
| Adjustment for age and study year & 1.02 (0.66–1.58) & 1.00 & 1.24 (0.85–1.79) & 2.24 (1.60–3.13) & <0.001 &
| Multivariate adjustment† & 1.06 (0.69–1.64) & 1.00 & 1.21 (0.84–1.76) & 1.85 (1.32–2.61) & <0.001 &
| Women, n                    | 3608    | 3752    | 3682    | 3704    |                      |
| Cases, n                    | 7       | 25      | 40      | 70      |                      |
| Person-y                    | 43 789  | 43 680  | 40 397  | 37 090  |                      |
| Adjustment for age and study year & 0.49 (0.21–1.13) & 1.00 & 1.30 (0.79–2.15) & 2.16 (1.36–3.42) & <0.001 &
| Multivariate adjustment† & 0.48 (0.21–1.13) & 1.00 & 1.18 (0.71–1.96) & 1.64 (1.02–2.64) & 0.011 &

*This analysis only included the surveys of 1987, 1992, 1997, and 2002. Cut points for quartile of waist circumference were 86.5, 94.0, and 101.5 cm in men and 73.0, 80.0, and 89.0 cm in women.

†Multivariate models included age, study year, education, smoking, alcohol consumption, history of myocardial infarction, valvular heart disease, and diabetes mellitus, systolic blood pressure, total cholesterol, and physical activity.

### Table 5. HRs for HF Based on Waist-to-Hip Ratio as Quartile*

<table>
<thead>
<tr>
<th>Waist-to-Hip Ratio Quartile</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>( P_{\text{trend}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>3405</td>
<td>3421</td>
<td>3440</td>
<td>3430</td>
<td></td>
</tr>
<tr>
<td>Cases, n</td>
<td>40</td>
<td>61</td>
<td>67</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td>Person-y</td>
<td>45 202</td>
<td>39 532</td>
<td>34 187</td>
<td>28 962</td>
<td></td>
</tr>
</tbody>
</table>
| Adjustment for age and study year & 0.83 (0.56–1.24) & 1.00 & 1.10 (0.77–1.56) & 2.08 (1.51–2.87) & <0.001 &
| Multivariate adjustment† & 0.88 (0.58–1.31) & 1.00 & 1.06 (0.74–1.50) & 1.71 (1.23–2.37) & 0.001 &
| Women                       | 3605    | 3569    | 3840    | 3732    |                      |
| Cases, n                    | 13      | 27      | 36      | 66      |                      |
| Person-y                    | 49 051  | 42 195  | 40 189  | 33 520  |                      |
| Adjustment for age and study year & 0.59 (0.30–1.15) & 1.00 & 1.12 (0.68–1.85) & 2.53 (1.60–3.98) & <0.001 &
| Multivariate adjustment† & 0.61 (0.31–1.19) & 1.00 & 0.98 (0.59–1.63) & 1.88 (1.17–3.01) & <0.001 &

*This analysis only included the surveys of 1987, 1992, 1997, and 2002. Cut points for quartile of waist-to-hip ratio were 0.88, 0.93, and 0.98 in men, and 0.76, 0.80 and 0.85 in women.

†Multivariate models included age, study year, education, smoking, alcohol consumption, history of myocardial infarction, valvular heart disease, and diabetes mellitus, systolic blood pressure, total cholesterol, and physical activity.
activity and waist circumference or waist-to-hip ratio with the risk of HF (all \( P > 0.25 \)).

**Discussion**

In this large prospective study, moderate or high levels of physical activity were associated with a reduced risk of HF among both men and women. General overweight or obesity, measured by BMI, and abdominal adiposity, measured by waist circumference or waist-to-hip ratio, were significantly and independently associated with an increased risk of HF among both men and women. The favorable association of physical activity with HF risk was observed regardless of levels of BMI.

Several studies have indicated that general obesity (BMI \( \geq 30 \)) was associated with an increased risk of HF.\(^4\)\(^5\)\(^7\)\(^20\) However, the results of the previous studies were contradictory in that overweight (BMI, 25 to 29.9 kg/m\(^2\)) was found to be a strong risk factor for HF in some studies\(^5\)\(^8\) but not in others.\(^7\)\(^20\) In the present study, overweight and obesity among both men and women predicted HF risk. The smaller sample size of the previous studies\(^7\)\(^20\) may have caused in the differences with our study. The prospective data of the effects of abdominal obesity on the HF incidence are still scant. A recent Swedish study indicated that higher waist circumference was associated with HF at all levels of BMI in women, and both BMI and waist circumference were predictors among men.\(^8\) In the Uppsala Longitudinal Study of Adult Men cohort, a 1-SD increase in waist circumference was associated with a 36% (95% CI, 10 to 69) increased risk of HF.\(^9\) The Multi-Ethnic Study of Atherosclerosis study found that abdominal obesity was associated with an increased risk of HF.\(^21\) In the present study, we found that elevated waist circumference or waist-to-hip ratio was associated with a greater risk of HF in both men and women.

Obesity has been found to be a strong risk factor for hypertension,\(^22\) diabetes mellitus,\(^14\) and high serum cholesterol\(^6\) and was an important component of the metabolic syndrome.\(^17\) All of these factors were associated with an increased risk of HF and were considered mediating factors for the physiological effects of adiposity on HF risk. In our study, adjustment for systolic blood pressure, total cholesterol, and history of diabetes mellitus attenuated the association between the 3 indicators of adiposity and HF risk, but all 3 indicators of adiposity remained statistically significant predictors of HF in the multivariable model. The failure to control for smoking also may have distorted the association between adiposity and HF risk. In our study, smoking status was considered a confounding factor in the multivariable model, and a positive association between all 3 indicators of adiposity and the risk of HF was found in both nonsmokers and smokers.

The present study is, to the best of our knowledge, the first large prospective study to determine that moderate or high levels of physical activity were associated with a decreased risk of HF in both men and women. Only 2 assessed the association of physical activity with HF risk, and the results were inconsistent.\(^4\)\(^5\) In the First National Health and Nutrition Examination Survey, the significant inverse association between leisure-time physical activity and HF risk was found only in women. In a recent analysis from the Physicians’ Health Study, vigorous physical activity was associated with a decreased risk of HF.\(^5\) The larger sample size of both men

![Figure 1](image1.png)

**Figure 1.** Cumulative incidence curve of HF based on joint effects of physical activity (PA) and BMI. Adjusted for age, study year, education, smoking, alcohol consumption, history of myocardial infarction, history of valvular heart disease, history of diabetes mellitus, systolic blood pressure, and total cholesterol.

![Figure 2](image2.png)

**Figure 2.** Cumulative incidence curve of HF based on joint effects of physical activity (PA) and waist circumference (A) and physical activity and waist-to-hip ratio (B). Adjusted for age, study year, education, smoking, alcohol consumption, history of myocardial infarction, history of valvular heart disease, history of diabetes mellitus, systolic blood pressure, and total cholesterol. High WC was defined as waist circumference \( \geq 102 \) cm in men or \( \geq 88 \) cm in women. High waist-to-hip ratio was defined as waist-to-hip ratio \( \geq 0.9 \) in men or \( \geq 0.85 \) in women.
and women and the inclusion of physical activity during occupation, commuting, and leisure time in our study may partially explain the differences between our study and the previous studies.4,5

Until now, only the Physicians’ Health Study has evaluated the joint associations of physical activity and BMI with HF risk. That study found that overweight and obesity were associated with a greater risk of HF and that vigorous physical activity was associated with a reduced risk of HF.3 BMI and vigorous physical activity did not modify each other’s individual effect on HF risk. Lean and active individuals had the lowest risk of HF; obese and inactive individuals had the highest risk.5 However, this study used self-reported height and weight and had no data on waist and hip circumference. Our study supports the above findings3 and expands the favorable association of physical activity with HF risk among subjects with different levels of BMI, waist circumference, and waist-to-hip ratio.

Our study has several strengths and limitations. First, a large number of both men and women from a homogeneous population participated in the study. Second, the mean follow-up was long enough to ascertain a large number of HF end-point events. Third, we had data on standardized measurement of 3 different indicators of adiposity and a large number of other adiposity-related risk factors, which may modify the association of adiposity with HF risk. A limitation of our study is the self-report of physical activity and the fact that physical activity was recorded only once at baseline. Although no specific assessment of repeatability or validity of our questionnaire for physical activity has been carried out, similar questionnaires have been used in a large number of studies in Finland and other Nordic countries12,13,23 where the patterns of physical activity are relatively similar. The method has worked in a large number of studies that can be considered validation in practice. We have no data on possible changes in physical activity during follow-up. Misclassification, particularly overreporting of the amount of physical activity at baseline and changes in the activity during follow-up, probably underestimated the association between physical activity and outcome. Because our data allowed only a dichotomized measure of alcohol consumption in the whole sample, we may not be able to fully control for the effect of this variable on the risk of HF. To evaluate the impact of this shortcoming, we performed separate subgroup analyses (surveys of 1987, 1992, 1997, and 2002) in the multivariable-adjusted model of a dichotomized measure of alcohol consumption compared with another multivariable-adjusted model of 4 categories of alcohol consumption. In general, the associations of physical activity and adiposity with HF risk were not influenced substantially or systematically. Ascertainment of HF status was based on the National Hospital Discharge Registry, the National Social Insurance Institution’s Register on special reimbursement for HF drugs, and the Causes of Death Register. This diagnosis method has been used in other Scandinavian countries such as Sweden. The accuracy of the HF cases in the Swedish hospital discharge is found to exceed 80% on the basis of the ESC definition.8,16 Although accuracy of clinical HF diagnosis in our cohort is likely to be high, some diagnostic errors are inevitable.

However, the misdiagnosis is most likely to be independent of the exposure status and therefore tends to attenuate the underlying associations rather than cause spurious associations. We cannot completely exclude the effects of residual confounding resulting from measurement error in the assessment of confounding factors or some unmeasured dietary factors.

Conclusions

Our study confirms that general overweight and general and abdominal obesity are independently associated with an increased risk of HF, whereas physical activity is associated with a reduced risk of HF among both men and women. The protective effect of physical activity on HF risk is observed at all levels of BMI.

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Disclosures

None.

References


CLINICAL PERSPECTIVE

In a prospective cohort of 59,178 Finnish participants who were 25 to 74 years of age and free of heart failure (HF) at baseline, we evaluated the single and joint associations of physical activity and different indicators of adiposity (body mass index, waist circumference, and waist-to-hip ratio) with HF risk. During a mean follow-up of 18.4 years, 1921 men and 1693 women developed HF. The multivariable-adjusted hazard ratios of HF associated with low, moderate, and high physical activity were 1.00, 0.79, and 0.69 (P_trend<0.001) for men and 1.00, 0.86, and 0.68 (P_trend<0.001) for women, respectively. The multivariable-adjusted hazard ratios of HF at different levels of body mass index (<25, 25 to 29.9, and ≥30) were 1.00, 1.25, and 1.99 (P_trend<0.001) for men, and 1.00, 1.33, and 2.06 (P_trend<0.001) for women, respectively. Abdominal adiposity, measured by waist circumference or waist-to-hip ratio, was associated with a greater risk of HF among both men and women (all P_trend<0.01). In joint analyses, the protective effect of physical activity was consistent in subjects at all levels of body mass index. Our study confirms that general overweight and general and abdominal obesity are independently associated with an increased risk of HF, whereas moderate or high levels of physical activity are associated with a reduced risk of HF. To combat the epidemic of overweight/obesity and to improve cardiovascular health at a population level, it is important to develop strategies to increase habitual physical activity and to prevent obesity in collaboration with communities.
Joint Effects of Physical Activity, Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio on the Risk of Heart Failure
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