Body Mass Index and Vigorous Physical Activity and the Risk of Heart Failure Among Men

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Background—Elevated body mass index (BMI; weight in kilograms divided by height in meters squared) in the obese range (≥30 kg/m²) is associated with an excess risk of heart failure (HF). However, the impact of overweight or preobese (BMI, 25 to 29.9 kg/m²) status and physical activity on HF risk is unclear.

Methods and Results—In a prospective cohort of 21 094 men (mean age, 53 years) without known coronary heart disease at baseline in the Physicians’ Health Study, we examined the individual and combined effects of BMI and vigorous physical activity (exercise to the point of breaking a sweat) on HF incidence from 1982 to 2007. We evaluated BMI as both a continuous (per 1-kg/m² increment) and a categorical (lean, <25 kg/m²; overweight, 25 to 29.9 kg/m²; and obese, ≥30 kg/m²) variable; we evaluated vigorous physical activity primarily as a dichotomous variable (inactive [rarely/never] versus active [≥1 to 3 times a month]). During follow-up (mean, 20.5 years), 1109 participants developed new-onset HF. In multivariable analyses, every 1-kg/m² increase in BMI was associated with an 11% (95% confidence interval [CI], 9 to 13) increase in HF risk. Compared with lean participants, overweight participants had a 49% (95% CI, 32 to 69) and obese participants had a 180% (95% CI, 124 to 250) increase in HF risk. Vigorous physical activity conferred an 18% (95% CI, 4 to 30) decrease in HF risk. No interaction was found between BMI and vigorous physical activity and HF risk (P = 0.96). Lean active men had the lowest and obese inactive men had the highest risk of HF. Compared with lean active men, the hazard ratios were 1.19 (95% CI, 0.94 to 1.51), 1.49 (95% CI, 1.30 to 1.71), 1.78 (95% CI, 1.43 to 2.23), 2.68 (95% CI, 2.08 to 3.45), and 3.93 (95% CI, 2.60 to 5.96) in lean inactive, overweight active, overweight inactive, obese active, and obese inactive men, respectively.

Conclusions—In this cohort of men, elevated BMI, even in the preobese range, was associated with an increased risk of HF, and vigorous physical activity was associated with a decreased risk. Public health measures to curtail excess weight, to maintain optimal weight, and to promote physical activity may limit the scourge of HF. (Circulation. 2009;119:44-52.)

Key Words: exercise ▪ heart failure ▪ obesity ▪ overweight

Excess body weight, sedentary lifestyle, and heart failure (HF) are major public health problems in the United States and worldwide.1-3 In adult men and women living in the community, body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) is associated with the risk of HF.4-13 The Heart Failure Society of America recommends a BMI of <30 kg/m² as the target to prevent the development of HF.14

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Physical activity is a key determinant of body weight and an important component of weight reduction and weight maintenance.1,2,15 Numerous health benefits of physical activity have been reported,15 but its influence on the risk of HF, especially in men, remains uncertain.8 Furthermore, the interaction of BMI and physical activity with the risk of HF is not known. Therefore, we investigated the relation of individual and combined effects of BMI and physical activity with the risk of HF in a large prospective cohort of men in the Physicians’ Health Study (PHS).

Methods

Study Sample

The study design and methods of the PHS have been published previously.10,17 Briefly, the PHS was a randomized, double-blind, placebo-controlled trial that began in 1982 to evaluate the efficacy of low-dose aspirin and β-carotene according to a 2-by-2 factorial design among 22 071 US male physicians 40 to 84 years of age in the primary prevention of cardiovascular disease and cancer. At baseline, physicians with a personal history of myocardial infarction, stroke, transient ischemic attack, cancer (except nonmelanoma skin
cancer), liver or renal disease, peptic ulcer, goit, contraindications to aspirin consumption, and current use of aspirin, other platelet active drugs, nonsteroidal antiinflammatory agents, or a vitamin A supplement were excluded. For the present investigation, we excluded 977 participants (4.4%) with missing baseline information on height, weight, or physical activity (248 participants); missing information on other covariates (712 participants); and HF before baseline examination (17 participants). After these exclusions, 21 094 participants made up our baseline population. All participants provided written informed consent for enrollment in the PHS. The Institutional Review Board at the Brigham and Women’s Hospital (Boston, Mass) approved the research protocol for the present investigation.

### Data Collection

Baseline information on self-reported demographic, medical history, and lifestyle variables was collected with a mailed questionnaire in 1982. Every 6 months for the first year and annually thereafter, participants provided information on compliance with randomized treatment assignments, various risk factors for chronic diseases, and newly diagnosed conditions in follow-up questionnaires. After the termination of the randomized aspirin16 and \-carotene17 components of the trial, participants continued to provide information on risk factors and relevant outcomes in yearly mailed questionnaires.

### Exposures and Covariates

On the baseline questionnaire, each physician reported his weight (in pounds) and height (in inches). The weight in kilograms was divided by the square of the height in meters to calculate BMI.1,2 The level of physical activity was ascertained at baseline with the single question, “How often do you exercise vigorously enough to work up a sweat?” Response options were rarely/never, 1 to 3 times a month, 1 time a week, 2 to 4 times a week, 5 to 6 times a week, and daily. Each physician also reported his age, parental history of myocardial infarction, cigarette smoking, frequency of alcohol consumption, and history of hypertension, diabetes mellitus, and hypercholesterolemia. On follow-up questionnaires, physicians reported the occurrence of myocardial infarction, which was confirmed on review of medical records by the PHS Endpoints Committee using the World Health Organization criteria.18

### Outcome Ascertainment

A diagnosis of HF was self-reported by physician participants on the yearly follow-up questionnaires. To validate the diagnosis of HF using established epidemiological criteria, we randomly selected 100 participants with a recent self-reported diagnosis of HF. Of these 100 participants, 8 had previously requested that they not be contacted for additional information, and 4 had died. The remaining 88 participants were mailed a questionnaire to collect information on symptoms, signs, and laboratory investigations at the time of first diagnosis of HF and a list of current medications for the treatment of HF. After 2 mailings followed by telephone contact, we collected and reviewed data from 76 of 88 (86%) to verify the diagnosis of HF. Among these 76 responders, 68 (89%) were on current treatment for HF and/or met the Framingham Heart Study criteria for HF at the time of first diagnosis.19 This extent of confirmation paralleled that reported by other investigators applying epidemiological criteria to the validation of the physician-determined diagnosis of HF.20,21

### Statistical Analysis

We performed all analyses using SAS software version 9.1.3 (SAS Institute, Cary, NC). We computed means (±SD) for continuous variables and proportions (expressed as percentage) for categorical variables according to various categories of BMI and levels of vigorous physical activity. We constructed cumulative incidence curves for HF according to exposure categories using the Kaplan–Meier estimation method.

We used Cox proportional-hazards regression models to examine the effects of BMI and vigorous physical activity on the risk of HF. We expressed these results as hazard ratios, 95% confidence intervals [CIs], and P values. We considered a 2-sided value of P<0.05 statistically significant. To examine the individual effects of exposure variables on the risk of HF, we considered BMI as both a continuous variable (per increment of 1 kg/m²) and a categorical variable (lean, <25.0 kg/m² [referent]; overweight, 25.0 to 29.9 kg/m²; and obese, ≥30 kg/m²)1,2 and categorized vigorous physical activity as both a dichotomous variable (inactive [rarely or never active, referent] and active [any vigorous activity ≥1 to 3 times a month]) and a 4-category variable (rarely/never [referent], 1 to 3 times a month, 1 to 4 times a week, and 5 to 7 times a week). To evaluate the combined effects of BMI and vigorous physical activity on the risk of HF, we used the aforementioned 3 categories of BMI (lean, overweight, and obese) and 2 levels of vigorous physical activity (inactive and active) and constructed 6 groups: lean and active [referent], lean and inactive, overweight and active, overweight and inactive, obese and active, and obese and inactive. Of note, because the underweight category included very few participants (n=46; BMI <18.5 kg/m²),2,2 we combined this category with the normal group (n=12 087; BMI, 18.5 to <25.0 kg/m²)1,2 and classified them as the lean group.

In multivariable analyses evaluating BMI and the risk of HF, we adjusted for (1) age only; (2) age, cigarette smoking (never [referent], past only, and current), alcohol consumption (rarely/never, monthly, weekly, and daily [referent]), parental history of myocardial infarction, and random assignment to aspirin or \-carotene (baseline variables not likely in the causal pathway); (3) the aforementioned baseline covariates and vigorous physical activity (rarely/never [referent] versus ≥1 to 3 times a month); (4) all of the above covariates and the presence or absence of history of hypertension, diabetes mellitus, and hypercholesterolemia (baseline variables likely on the causal pathway); and (5) all of the above baseline variables plus myocardial infarction (likely in the causal pathway) during follow-up as a time-dependent variable. We considered variables as likely or not likely in the causal pathway on the basis of prior epidemiological evidence and biological plausibility.22 We used the same model building approach in the evaluation of physical activity and the risk of HF (except that BMI was considered a variable possibly in the causal pathway between vigorous physical activity and the risk of HF). We constructed trend models to assess for a gradient of risk across multicycle exposure variables for the risk of HF.

In multivariable models including all baseline covariates, we examined for effect modification between baseline covariates and BMI (per 1-kg/m² increment) and between baseline covariates and vigorous physical activity (inactive versus any vigorous activity) on the risk of HF by introducing appropriate interaction terms. In the presence of statistically significant interactions (defined as P<0.05), we conducted stratified analyses according to various levels of the baseline covariate.

Of note, in statistical models adjusting for history of hypercholesterolemia, we introduced a dummy variable for missing information on this variable that made up ~12% of study participants. Finally, in secondary analyses, to account for the competing risk of death that may alter the probability of experiencing HF (the event of interest), we evaluated the individual effects of BMI and vigorous physical activity on the risk of composite death or HF.

Dr Kenchaiah had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors have read and agree to the manuscript as written.

### Results

#### Baseline Characteristics

About 40% of physicians in our sample were overweight, and ~5% were obese at baseline. As anticipated, a greater proportion of obese individuals exercised less and had a history of hypertension and diabetes mellitus (Table 1). However, a marginally greater proportion of obese individuals were current smokers. Physicians who rarely or never exercised vigorously were older, had a higher BMI, smoked cigarettes more often, and had a greater prevalence of hypertension and diabetes mellitus. By design, randomized
aspirin and \( \beta \)-carotene treatment was similar across all categories of BMI and physical activity.

**BMI and the Risk of HF**

During a mean±SD follow-up of 20.5±5.4 years (maximum, 24.8 years; 431 654 total person-years), 1109 men developed new-onset HF. The cumulative incidence of HF increased with increasing categories of BMI (Figure 1A).

In models adjusting for variables probably not in the causal pathway between BMI and HF (age, smoking, alcohol consumption, parental history of myocardial infarction), each 1-kg/m\(^2\) increase in BMI was associated with a 13% increase in the risk of HF (Table 2). Compared with lean men, overweight men showed a 62%-increased risk of HF and obese men a 240%-increased risk. Increasing categories of BMI were associated with a stepwise increase in the risk of HF (\( P \) for trend<0.0001).

Including vigorous physical activity as a covariate in multivariable analyses did not materially alter the excess risk of HF associated with elevated BMI. Additional adjustment for baseline variables possibly in the causal pathway between elevated BMI and HF (hypertension, diabetes mellitus, and hypercholesterolemia) resulted in a decline of the hazard ratio from 1.62 to 1.49 in overweight and obese men, respectively.

During follow-up, 764 (6.3%) in the lean, 702 (8.7%) in the overweight, and 117 (12.6%) in the obese group developed myocardial infarction. Interim myocardial infarction preceded the onset of HF in 77 (15.9%), 87 (16.5%), and 14 (14.4%) lean, overweight, and obese participants with HF, respectively. The association between BMI and HF remained robust after adjustment for all baseline covariates and interim myocardial infarc-

### Table 1. Baseline Characteristics According to BMI and Vigorous Physical Activity Categories in the PHS*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BMI Categories</th>
<th>Vigorous Physical Activity Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lean (n=12 133)</td>
<td>Overweight (n=8 032)</td>
</tr>
<tr>
<td>Age, y</td>
<td>52.9±9.7</td>
<td>53.6±9.1</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>23.0±3.8</td>
<td>26.6±1.3</td>
</tr>
<tr>
<td>Lean, %</td>
<td>100</td>
<td>· · ·</td>
</tr>
<tr>
<td>Overweight, %</td>
<td>· · ·</td>
<td>100</td>
</tr>
<tr>
<td>Obese, %</td>
<td>· · ·</td>
<td>· · ·</td>
</tr>
<tr>
<td>Vigorous physical activity, %</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inactive (rarely/never)</td>
<td>12.1</td>
<td>14.9</td>
</tr>
<tr>
<td>Low active (1–3 times/mo)</td>
<td>12.6</td>
<td>16.1</td>
</tr>
<tr>
<td>Medium active (1–4 times/wk)</td>
<td>56.0</td>
<td>56.3</td>
</tr>
<tr>
<td>Highly active (5–7 times/wk)</td>
<td>19.3</td>
<td>12.7</td>
</tr>
<tr>
<td>Parental history of myocardial infarction, %</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cigarette smokers, %</td>
<td>51.7</td>
<td>47.1</td>
</tr>
<tr>
<td>Past</td>
<td>38.1</td>
<td>41.0</td>
</tr>
<tr>
<td>Current</td>
<td>10.2</td>
<td>11.9</td>
</tr>
<tr>
<td>Alcohol consumption, %</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rarely</td>
<td>14.4</td>
<td>15.2</td>
</tr>
<tr>
<td>Monthly</td>
<td>10.7</td>
<td>11.2</td>
</tr>
<tr>
<td>Weekly</td>
<td>49.1</td>
<td>49.5</td>
</tr>
<tr>
<td>Daily</td>
<td>25.8</td>
<td>24.1</td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>18.9</td>
<td>28.8</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic</td>
<td>124.3±11.4</td>
<td>128.1±11.7</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77.7±7.4</td>
<td>80.0±7.3</td>
</tr>
<tr>
<td>History of diabetes mellitus, %</td>
<td>2.2</td>
<td>3.2</td>
</tr>
<tr>
<td>History of hypercholesterolemia, %</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Present</td>
<td>9.8</td>
<td>11.6</td>
</tr>
<tr>
<td>Missing</td>
<td>11.4</td>
<td>12.2</td>
</tr>
<tr>
<td>Study medications, %</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>50.3</td>
<td>49.5</td>
</tr>
<tr>
<td>( \beta )-Carotene</td>
<td>49.9</td>
<td>50.0</td>
</tr>
</tbody>
</table>

*BMI is weight in kilograms divided by the square of the height in meters. The BMI was ~25 kg/m\(^2\) in lean participants, 25 to 29.9 kg/m\(^2\) in overweight participants, and ~30 kg/m\(^2\) in obese participants. Data on blood pressure were available for 10 755 participants in the lean group, 7124 participants in the overweight group, 818 participants in the obese group, 2457 participants in the inactive group, and 16 240 participants in the active group. Values are mean±SD when appropriate.
tion as a time-dependent variable. In these models, every 1-kg/m² increase in BMI was associated with a hazard ratio of 1.11 (95% CI, 1.09 to 1.12). Compared with lean participants, the hazard ratios were 1.46 (95% CI, 1.29 to 1.66) and 2.65 (95% CI, 2.12 to 3.31) in overweight and obese participants, respectively.

### Vigorous Physical Activity and the Risk of HF

Compared with participants in the inactive group, those in the active group had a lower cumulative incidence of HF (Figure 1B). The divergence of these curves was apparent within 5 years of follow-up.

In models adjusting for lifestyle and other variables not likely in the causal pathway, vigorous physical activity at least 1 to 3 times a month was associated with a significant 26% reduction in the risk of HF (Table 2). Compared with men who rarely or never vigorously exercised, a 23%, 20%, and 36% reduction in the risk of

HF was found among men who vigorously exercised for 1 to 3 times a month, 1 to 4 times a week, and 5 to 7 times a week respectively (P for trend across categories <0.001). Inclusion of BMI as an additional covariate in multivariable analyses resulted in a minor change in the effect of vigorous physical activity on the risk of HF. After adjustment for known baseline variables presumably in the causal pathway (BMI, hypertension, diabetes mellitus, and hypercholesterolemia), the risk reduction of HF conferred by vigorous physical activity changed from 24% to 18%, thereby accounting for ~25% of the decreased risk. In these analyses, a statistically significant trend toward decreasing HF risk was found with increasing levels of vigorous physical activity (P for trend=0.016).

During follow-up, interim myocardial infarction occurred in a greater proportion of inactive (278 events, 9.8%) compared with active (1305 events, 7.2%) participants. Myocardial infarction preceded the onset of HF in a similar proportion of inactive (47 events, 22.8%) and active (206 events, 22.8%) participants who
developed HF. In models adjusting for all covariates at baseline and myocardial infarction during follow-up as a time-dependent variable, the association between vigorous physical activity and HF remained significant. Compared with inactive participants, the hazard ratio for incident HF among active participants was 0.85 (95% CI, 0.73 to 0.99).

Combined Effect of BMI and Vigorous Physical Activity on the Risk of HF
In models evaluating BMI as a continuous variable (per 1-kg/m² increase) and vigorous physical activity as a dichotomous variable (inactive versus active), no significant interaction (P=0.96) between BMI and vigorous physical activity and the risk of HF was found. After adjustment for all baseline covariates, compared with participants who were lean and active, the risk of HF increased progressively by 19% (albeit statistically nonsignificant) in the lean and inactive, 49% in the overweight and active, 78% in the overweight and inactive, 168% in the obese and active, and 293% in the obese and inactive groups (Figure 2).

Effect Modification by Other Baseline Covariates
Elevated BMI was associated with a relatively greater risk of HF among younger compared with older participants (P for interaction = 0.020) and among nondiabetic compared with diabetic participants (P for interaction < 0.0001) (Table 3). Other baseline covariates, including parental history of myocardial infarction, cigarette smoking, alcohol consumption, history of hypertension, diabetes mellitus, and hypercholesterolemia (baseline covariates likely not in the causal pathway).

Secondary Analyses
During follow-up, 3159 (26.0%) in the lean group, 2473 (30.8%) in the overweight group, and 399 (42.9%) in the
obese group died or developed HF. In analyses adjusting for all baseline covariates, each 1-kg/m² increment in BMI was associated with a hazard ratio of 1.06 (95% CI, 1.05 to 1.06) for the risk of death or HF. Compared with participants in the lean group, hazard ratios were 1.12 (95% CI, 1.06 to 1.18) for overweight participants and 1.97 (95% CI, 1.77 to 2.19) for obese participants (P for trend <0.0001).

The composite outcome of death or HF occurred in a lesser proportion of active men (4897 events, 26.8%) compared with inactive men (1134 events, 39.9%). In multivariable analyses adjusting for all baseline covariates, vigorous physical activity was associated with a lower risk of death or HF (hazard ratio, 0.81; 95% CI, 0.76 to 0.87). In analyses of vigorous physical activity as a 4-level categorical variable, the hazard ratios were 0.80 (95% CI, 0.73 to 0.88) for vigorously exercising 1 to 3 times a month, 0.81 (95% CI, 0.76 to 0.87) for 1 to 4 times a week, and 0.84 (95% CI, 0.77 to 0.91) for 5 to 7 times a week (P for trend <0.0001).

Table 3. Results of Cox Proportional-Hazards Regression Models Evaluating the Association of BMI and Vigorous Physical Activity and the Risk of HF Stratified According to Various Levels of Baseline Covariates

<table>
<thead>
<tr>
<th>Model 1: BMI as a continuous variable (per 1-kg/m² increment)</th>
<th>Events/Persons at Risk, n (%)</th>
<th>Follow-Up, Person-y (Rate per 10 000 Person-y)</th>
<th>Multivariable Hazard Ratio (95% CI)*</th>
<th>P for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>126/8704 (1.4)</td>
<td>194 427 (6.5)</td>
<td>1.15 (1.10–1.20)</td>
<td>0.020</td>
</tr>
<tr>
<td>50–59.9</td>
<td>405/7147 (5.7)</td>
<td>150 136 (27.0)</td>
<td>1.09 (1.06–1.12)</td>
<td>…</td>
</tr>
<tr>
<td>≥60</td>
<td>578/5243 (11.0)</td>
<td>87 271 (66.2)</td>
<td>1.09 (1.06–1.12)</td>
<td>…</td>
</tr>
<tr>
<td>B. Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1012/20 505 (4.9)</td>
<td>422 477 (24.0)</td>
<td>1.11 (1.09–1.13)</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>97/589 (16.5)</td>
<td>9178 (108.9)</td>
<td>1.07 (1.02–1.12)</td>
<td>…</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Model 2: vigorous physical activity as a dichotomous variable</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Diabetes Mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Inactive (rarely/never)</td>
<td>183/2675 (6.8)</td>
<td>51 334 (35.6)</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Active (≥1–3 times/mo)</td>
<td>829/17 830 (4.6)</td>
<td>371 143 (22.3)</td>
<td>0.80 (0.68–0.94)</td>
<td>…</td>
</tr>
<tr>
<td>Yes</td>
<td>Inactive (rarely/never)</td>
<td>23/166 (13.9)</td>
<td>2380 (96.6)</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Active (≥1–3 times/mo)</td>
<td>74/423 (17.5)</td>
<td>6798 (108.9)</td>
<td>1.02 (0.63–1.64)</td>
<td>…</td>
</tr>
</tbody>
</table>

Adjusted for cigarette smoking (never [referent], past only, and current), alcohol consumption (rarely/never, monthly, weekly, and daily [referent]), parental history of myocardial infarction, random assignment to aspirin or β-carotene, and presence or absence of history of hypertension and hypercholesterolemia in all models, and additionally for diabetes mellitus and vigorous physical activity (rarely/never [referent], ≥1–3 times a month) in model 1A, age (per year increment) and vigorous physical activity in model 1B, and age and BMI (per 1 kg/m²) in model 2A.
Discussion

Principal Findings

In men, we found that higher BMI was associated with a greater risk of HF. This increased risk occurred in a linear fashion without evidence of a threshold and was evident not only in obese (BMI ≥30 kg/m²) but also in overweight or preobese (BMI, 25 to 29.9 kg/m²) men. Vigorous physical activity was associated with a reduced risk of HF, and increasing levels of vigorous physical activity were associated with a graded reduction in the risk of HF. 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. The statistically significant association of elevated BMI with an increased risk of the composite of death or HF and vigorous physical activity with a decreased risk of this combined outcome suggests that death as a competing event is an unlikely reason for the observed association between BMI and vigorous physical activity with the risk of HF.

Elevated BMI was associated with a greater risk of HF in all subgroups, although its effect was stronger in younger compared with older participants and in nondiabetic compared with diabetic participants. The beneficial impact of vigorous physical activity was evident in all categories of baseline covariates except among diabetics, in whom no association was noted, likely because of the small sample size of this subgroup.

Comparison With Previous Studies

The increased risk of HF among obese individuals noted in our investigation is consistent with that found in previously published studies.7–11 However, a statistically nonsignificant association between overweight but not obese (preobese) status and the risk of HF has been reported among men in a nested case-control analyses from the United Kingdom–based General Practice Research Database (589 cases versus 2500 age-matched controls; relative risk, 0.9; 95% CI, 0.7 to 1.3) and a prospective cohort analyses from the Framingham Heart Study (2704 men, 252 events; mean follow-up, 14 years; hazard ratio, 1.20; 95% CI, 0.87 to 1.64).11 The observed nonsignificant association may have been due to the smaller number of men and HF end points evaluated in these studies. In the present investigation, we noted a statistically significant 49% increase in the risk of HF among overweight men, suggesting a continuous gradient of HF risk across increasing categories of BMI (lean to overweight to obese).

In multivariable analyses of 5545 men in the First National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-Up Study, compared with low levels of recreational physical activity (determined with the question, “Do you get much exercise in things you do for recreation [sports, or hiking, or anything like that], or hardly any exercise, or in between?”), medium to high levels of recreational physical activity were associated with a statistically nonsignificant 12% (95% CI, −6 to 28) decline in the risk of HF.8 In contrast, in our cohort of 21,094 men, vigorous physical activity (defined as exercise to the point of breaking a sweat) for at least 1 to 3 times a month conferred a significant 18% reduction in the risk of HF. The larger sample size of men investigated in our study and difference in the definition of physical activity may partially explain the significant association between vigorous physical activity and the reduced risk of HF in our investigation.

Mechanisms

Several mechanisms by which elevated BMI increases the risk of HF have been proposed. These include promotion of atherogenic risk factors such as hypertension,23,24 insulin resistance,25,26 diabetes mellitus,27–29 and dyslipidemia30 that enhance the risk of myocardial infarction,30,33 These factors may mediate or independently increase the risk of HF.7,8,10,12,30 Excess weight may alter cardiac structure and function,33–35 activate neuroendocrine pathways,36–38 predispose to sleep-disordered breathing,39–41 and promote chronic kidney disease42–45 that may subsequently manifest as overt HF.32 Increased BMI is an anthropometric surrogate of surplus total body fat,46 and evidence from animal models suggests direct myocardial lipotoxicity in the pathogenesis of cardiomyopathy.37–49

Greater levels of physical activity promote weight loss,50 improve lipoprotein profile,51 and reduce the risk of hypertension,52 diabetes mellitus,53,54 and coronary artery disease.55,56 These favorable influences on cardiovascular risk profile may, in turn, reduce the likelihood of HF.

Study Strengths and Limitations

The large sample size, prospective nature of the analyses, long duration of follow-up, adequate adjustment for confounding variables (including interim myocardial infarction), and evaluation of composite of HF and all-cause death as an end point to account for competing risk of death are particular strengths of our study. Several limitations also are relevant. First, although the mean age of PHS participants was similar to that in other published cohorts from the general population,7–11 the incidence rate of HF was lower in the PHS. This is likely explained by the fact that the PHS is made up of physicians who were generally healthier in terms of coronary risk factors, presumably had better access to health care, and as a group belonged to a higher socioeconomic status. Second, measures of weight and height and frequency of vigorous physical activity were self-reported. This is likely to result in modest nondifferential misclassification that may underestimate the true hazard ratios of HF. Third, the small sample size (n=46) precluded evaluation of the impact of underweight status (BMI <18.5 kg/m²) on the risk of HF. Fourth, our study assessed the impact of vigorous physical activity, and its frequency was ascertained at 1 point in time. The intensity and frequency of activity may change over time, which conceivably underestimates the magnitude of the true association between vigorous physical activity and HF.

Finally, data on left ventricular function at the time of onset of HF were not available to assess the influence of excess weight and vigorous physical activity on the risk of HF with preserved versus impaired left ventricular ejection fraction. Finally, our study population consisted of men, and the results of our investigation cannot be generalized to women.
Future Implications
It is intriguing to note that exercising to the point of breaking a sweat even at a frequency as low as 1 to 3 times a month was associated with a reduced risk of HF. This finding may imply that any vigorous physical activity is an indicator of healthier lifestyle in men at risk of developing HF. Whether specific domains (at work, for transport, in domestic duties, or in leisure time),

9 modes (aerobic versus muscle strengthening and intentional versus usual activities), types (eg, walking, jogging, swimming, bicycling, or stair climbing), duration (short versus long bouts of activity), or amount (total energy expenditure) of physical activity have different degrees of beneficial impact on the risk of HF needs further evaluation.

Our findings indicate that both overweight (preobese) and obese men have an increased risk of HF and that men with higher levels of vigorous physical activity have a reduced risk of HF. Additional research is warranted to ascertain whether intentional weight reduction to optimal levels in overweight (preobese) women and men, respectively, perhaps a BMI <25 kg/m² represents an optimal goal for the primary prevention of HF. Clinical trials targeting improvements in BMI and physical activity levels will be critically important in determining whether our observational data bear clinical relevance.

In the United States, 37% are overweight (preobese), 25% are obese, 38% do not achieve the recommended amount of physical activity, and 14% are inactive. Recent global estimates also reveal a comparable high prevalence of excess weight and physical inactivity. Concurrently, HF continues to impose substantial morbidity, mortality, and financial costs. Hence, public health approaches to curtail excess weight, to maintain optimal weight, and to promote regular physical activity have the potential to limit the scourge of HF.

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Disclosures
None.

References
in a prospective cohort of 21,094 men (mean age, 53 years) without known coronary heart disease at baseline in the Physicians’ Health Study, we examined the individual and combined effects of body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), an anthropometric surrogate of surplus body fat) and vigorous physical activity (defined as exercise to the point of breaking a sweat) on the incidence of heart failure (HF) from 1982 to 2007. During a mean follow-up of 20.5 years, 1,109 participants developed new-onset HF. After adjustment for established risk factors for HF, every 1-kg/m² increase in BMI was associated with an 11% increase in the risk of HF. Compared with lean participants (BMI <25 kg/m²), overweight or preobese participants (BMI, 25 to 29.9 kg/m²) had a 49% and obese participants (BMI ≥30 kg/m²) had a 180% increase in HF risk. Vigorous physical activity (at least 1 to 3 times a month) conferred an 18% decrease in HF risk. Lean active men had the lowest and obese inactive men had the highest (290%) risk of HF. Our findings support the existence of causal links between excess body weight and HF and sedentary lifestyle and HF. Therefore, given the high prevalence of these 2 modifiable risk factors in the general population, together with the substantial morbidity, mortality, and financial costs imposed by HF, public health measures to curtail excess weight, to maintain optimal weight, and to promote physical activity may limit the scourge of HF.

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