Healthy Lifestyle and Decreasing Risk of Heart Failure in Women

The Women’s Health Initiative Observational Study

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ABSTRACT

BACKGROUND The impact of a healthy lifestyle on risk of heart failure (HF) is not well known.

OBJECTIVES The objectives of this study were to evaluate the effect of a combination of lifestyle factors on incident HF and to further investigate whether weighting each lifestyle factor has additional impact.

METHODS Participants were 84,537 post-menopausal women from the WHI (Women’s Health Initiative) observational study, free of self-reported HF at baseline. A healthy lifestyle score (HL score) was created wherein women received 1 point for each healthy criterion met: high-scoring Alternative Healthy Eating Index, physically active, healthy body mass index, and currently not smoking. A weighted score (wHL score) was also created in which each lifestyle factor was weighted according to its independent magnitude of effect on HF. The incidence of hospitalized HF was determined by trained adjudicators using standardized methodology.

RESULTS There were 1,826 HF cases over a mean follow-up of 11 years. HL score was strongly associated with risk of HF (multivariable-adjusted hazard ratio [HR] [95% confidence interval (CI)] 0.49 [95% CI: 0.38 to 0.62], 0.36 [95% CI: 0.28 to 0.46], 0.24 [95% CI: 0.19 to 0.31], and 0.23 [95% CI: 0.17 to 0.30] for HL score of 1, 2, 3, and 4 vs. 0, respectively). The HL score and wHL score were similarly associated with HF risk (HR: 0.46 [95% CI: 0.41 to 0.52] for HL score; HR: 0.48 [95% CI: 0.42 to 0.55] for wHL score, comparing the highest tertile to the lowest). The HL score was also strongly associated with HF risk among women without antecedent coronary heart disease, diabetes, or hypertension.

CONCLUSIONS An increasingly healthy lifestyle was associated with decreasing HF risk among post-menopausal women, even in the absence of antecedent coronary heart disease, hypertension, and diabetes. Weighting the lifestyle factors had minimal impact. (J Am Coll Cardiol 2014;64:1777–85) © 2014 by the American College of Cardiology Foundation.
Heart failure (HF) is a major public health concern, characterized by a high prevalence, poor clinical outcomes, and significant healthcare costs (1). HF primary prevention through lifestyle approaches may be more effective and less costly than secondary or tertiary prevention efforts. A healthy lifestyle, often characterized by a combination of prudent diet, regular exercise, healthy weight, and not smoking, is related to a lower risk of atherosclerotic cardiovascular diseases, such as coronary heart disease (CHD) (2) and stroke (3). Few studies, however, have focused on a healthy lifestyle in relation to HF. Healthy lifestyle factors were individually and collectively associated with a lower risk of HF among white males in the Physician’s Health Study I (4) and among men and women from a large and homogenous Finnish sample (5).

See page 1786

Post-menopausal women and African Americans experience a greater burden of HF (6–8), and they are predicted to make up a greater proportion of future HF cases in the United States (9,10). Therefore, examination of the impact of a healthy lifestyle on HF risk in these groups is of particular interest. In addition, it has been proposed that the association of healthy lifestyle factors with HF risk may largely be accounted for by the development of interim CHD (4,11), as well as interim hypertension and diabetes (11–13). However, we were particularly interested in whether an association between healthy lifestyle and HF risk would be present among women without development of any of these conditions before HF development. For example, HF in women is less associated with CHD than in men (14); thus, other mechanisms are of interest. Lastly, most prior studies investigating a combination of lifestyle factors weighted each lifestyle factor equally (2–5,15). This approach assumes that each lifestyle factor has the same magnitude of effect on the outcome, and this may lead to misclassification when lifestyle factors are combined.

Accordingly, we examined whether a healthy lifestyle, as captured by a combination of high dietary quality, physical activity, healthy body mass index (BMI), and not currently smoking, is associated with risk of HF in a diverse prospective cohort of post-menopausal women from the WHI (Women’s Health Initiative) observational study, and we further assessed the additional impact of weighting each lifestyle factor according to its independent magnitude of effect on HF. We further examined the association of healthy lifestyle with HF in women with versus without antecedent CHD, in African American versus non-Hispanic white women, and among women without antecedent CHD, hypertension, or diabetes.

Methods

Study sample. The WHI observational study recruited women from 40 U.S. clinical centers from 1993 to 1998. The WHI observational study comprised a sample of post-menopausal women (ages 50 to 79 years at baseline) who were in overall good health and were either unwilling or ineligible to be WHI clinical trial participants (16–18). This study was approved by each center’s institutional review board, and the subjects provided informed consent. Women were excluded from the current analyses if they reported a history of HF at baseline (n = 897); were missing information on lifestyle factors (n = 3,110); had energy intake <600 or >5,000 kcal/day (n = 3,571); or were underweight (BMI ≤18.5 kg/m²) at baseline (because of the potential for preclinical disease; n = 1,050). Those excluded were more likely (p < 0.05) to be nonwhite, from the South, and divorced, separated, or widowed; to have a history of hypertension or CHD at baseline; and to have lower levels of education.

Measures. We considered 4 lifestyle variables: Diet quality as measured by the Alternative Healthy Eating Index (AHEI), physical activity, BMI, and smoking. Data used to generate the AHEI were derived from the semiquantitative WHI food frequency questionnaire (19). The AHEI is a composite numerical measure of dietary quality, based on foods and nutrients predictive of chronic disease risk (20,21) and consisting of 11 dietary components, with each scored based on a 10-point scale (0 points, least healthy; 10 points, most healthy) (12). Women also reported on their physical activity. For analyses, physical activity was categorized as inactive (e.g., no report of moderate or vigorous physical activity); somewhat active (i.e., less active than recommendations [22]: <150 min/week of moderate physical activity, or <75 min/week of vigorous physical activity, or equivalent combination); and active (e.g., meeting physical activity recommendations [22]: ≥150 min of moderate physical activity per week or ≥75 min of vigorous physical activity or an equivalent combination). Smoking status was categorized as a current, former, or never smoker. BMI was calculated from weight and height measures obtained at clinical examinations with a calibrated stadiometer and categorized as normal weight (18.5 ≤ BMI ≤ 25 kg/m²), overweight (25 ≤ BMI <30 kg/m²), and obese (BMI ≥30 kg/m²).
At baseline, women reported on sociodemographic factors and medical history, including CHD (included cardiac arrest, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, angina, and myocardial infarction), diabetes, and hypertension. Race/ethnicity was self-reported as American Indian or Alaskan Native, Asian or Pacific Islander, black or African American, Hispanic/Latino, white (not of Hispanic origin), or other.

Incident hospitalized HF was ascertained yearly in WHI by medical record review of self-reported hospitalizations and classified by trained adjudicators using standardized methodology. Specifically, HF that required and/or occurred during hospitalization required physician diagnosis of new-onset or worsened congestive HF on the reported hospital admission and 1 or more of the following 4 criteria: HF diagnosed by a physician and receiving medical treatment for HF; symptoms plus documentation in the current medical record of a history of an imaging procedure that showed impaired left ventricular systolic or diastolic function, pulmonary edema/congestion on chest radiograph in the current admission, dilated ventricle(s) or “poor” left ventricular or right ventricular function by echocardiography, radionuclide ventriculography, or other contrast ventriculography; or evidence of left ventricular diastolic dysfunction. This method was found to have a high (79%) agreement rate (kappa) comparing central adjudicated HF to local adjudication (23, 24).

**STATISTICAL ANALYSES.** To create a healthy lifestyles score (HL score) for the present analyses, each lifestyle factor was dichotomized as healthy versus unhealthy as follows: high-scoring AHEI (quintiles 4 and 5) versus low-scoring AHEI (quintiles 1, 2, 3), physically active versus somewhat active or inactive, normal BMI ($18.5 \leq \text{BMI} < 25 \text{ kg/m}^2$) versus overweight or obese (BMI $\geq 25 \text{ kg/m}^2$), and not a current smoker versus current smoker. Women then received 1 point for every healthy criterion met, and points were summed to obtain an HL score that ranged from 0 (least healthy) to 4 (most healthy).

A weighted HL score (wHL score) was also created, in which each dichotomous lifestyle factor was first weighted according to its independent magnitude of effect (e.g., beta coefficient adjusted for the other dichotomous lifestyle factors) on HF risk. Weighted points attained by each individual were summed to obtain a wHL score, which ranged from 0 (least healthy) to 1.55 (most healthy). To compare the HL scores with the wHL scores, both were analyzed as tertiles given that the scores could only take on a certain number of values (e.g., 0, 1, 2, 3, or 4 for the HL score), they could not be partitioned into quintiles.

We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Person-time was calculated from baseline interview until development of HF, death, or date of last contact. The proportional hazards assumption, assessed with models that included log(time)-by-covariate interaction terms, was not violated.

Analyses were initially adjusted for age and race/ethnicity, with further adjustment for education, marital status, U.S. region, and antecedent CHD, hypertension, and diabetes (“antecedent” referring to occurrence at any point before the time of censoring, whether reported at baseline or developed during follow-up). Additional analyses were stratified on absence versus presence of antecedent CHD and African-American women versus non-Hispanic white women, as well as with restriction of analyses to the subgroup of women without antecedent CHD, hypertension, or diabetes.

Partial population attributable risk (PAR) calculations (25) estimated the proportion of HF that would hypothetically be prevented if all women were in the healthiest category of the lifestyle factors or the HL score. All statistical analyses were conducted with SAS software version 9 (SAS Institute Inc., Cary, North Carolina).

**RESULTS**

The final analytic sample included 84,537 women, with a mean age of $63.5 \pm 7.3$ years at baseline. General baseline characteristics are presented in Table 1. Approximately 41% of participants had

<table>
<thead>
<tr>
<th>TABLE 1 Baseline Characteristics According to the Healthy Lifestyle Score, the WHI Observational Study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy Lifestyle Score</strong></td>
</tr>
<tr>
<td><strong>Age, yrs</strong></td>
</tr>
<tr>
<td><strong>African American</strong></td>
</tr>
<tr>
<td><strong>Hispanic/Latino</strong></td>
</tr>
<tr>
<td><strong>Non-Hispanic white</strong></td>
</tr>
<tr>
<td><strong>Less than high school</strong></td>
</tr>
<tr>
<td><strong>Never married</strong></td>
</tr>
<tr>
<td><strong>Divorced/separated</strong></td>
</tr>
<tr>
<td><strong>History of diabetes</strong></td>
</tr>
<tr>
<td><strong>History of hypertension</strong></td>
</tr>
<tr>
<td><strong>History of CHD</strong></td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
</tr>
<tr>
<td><strong>AHEI score</strong></td>
</tr>
</tbody>
</table>

Values are mean ± SD or %. Categories of a given variable (e.g., race) may not necessarily add up to 100%, given that not all categories were included. "Self-reported CHD includes cardiac arrest, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, angina, and myocardial infarction.

AHEI = Alternative Healthy Eating Index; BMI = body mass index; CHD = coronary heart disease.
normal BMI, 44% were physically active, 94% were current nonsmokers, and 40% had a high-scoring AHEI. Approximately 14% of women met all 4 of these healthy lifestyle criteria. There were 1,826 documented HF cases during a mean follow-up of 11 years.

After multivariable adjustment, each individual lifestyle factor was independently associated with risk of HF in an inverse and graded manner (Table 2), with the strongest associations observed for BMI and smoking. The percentage of partial PAR was highest for AHEI (27%; 95% CI: 15% to 39%), followed by BMI (20%; 95% CI: 10% to 29%), cigarette smoking (16%; 95% CI: 10% to 23%), and physical activity (12%; 95% CI: 4% to 20%).

A strong inverse and graded association was observed between the HL score and HF risk (Table 3). According to PAR% calculations, 35% (95% CI: 28% to 43%) of HF could theoretically be prevented if all women met all 4 healthy lifestyle criteria. When we compared the HL score and the wHL score, differences between the 2 were minimal (Figure 1). Comparing the highest versus lowest tertile, a multivariable adjusted HR of 0.46 (95% CI: 0.41 to 0.52) was observed for the regular HL score and 0.48 (95% CI: 0.42 to 0.55) for the wHL score. Results were very similar when time-dependent lifestyle factors were used to create the HL score and the wHL score.

In stratified analyses, the HL score was strongly related to HF risk in a graded manner in both women with and without antecedent CHD (Figure 2), and this was similarly observed among the subgroup of women without antecedent CHD, hypertension, and diabetes (Figure 3). Associations of HL score with HF

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**Table 2** Risk of Heart Failure in Relation to Individual Lifestyle Factors, The WHI Observational Study

<table>
<thead>
<tr>
<th>Lifestyle Factor</th>
<th>Quintile 1</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Quintile 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Cases</td>
<td>499</td>
<td>411</td>
<td>350</td>
<td>321</td>
<td>245</td>
</tr>
<tr>
<td>Person-Years</td>
<td>178,032</td>
<td>183,884</td>
<td>188,254</td>
<td>191,496</td>
<td>194,954</td>
</tr>
<tr>
<td>Crude Incidence Rate</td>
<td>2.80</td>
<td>2.24</td>
<td>1.86</td>
<td>1.68</td>
<td>1.26</td>
</tr>
<tr>
<td>per 1,000 Person-Years</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Model 1 HR (95% CI)</td>
<td>Referent</td>
<td>0.83 (0.73-0.95)</td>
<td>0.76 (0.66-0.87)</td>
<td>0.72 (0.62-0.83)</td>
<td>0.60 (0.51-0.70)</td>
</tr>
<tr>
<td>p Value for Trend</td>
<td>Referent</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.06</td>
</tr>
<tr>
<td>Model 2 HR (95% CI)</td>
<td>Referent</td>
<td>0.85 (0.74-0.97)</td>
<td>0.81 (0.70-0.93)</td>
<td>0.76 (0.65-0.88)</td>
<td>0.61 (0.52-0.73)</td>
</tr>
</tbody>
</table>

**Table 3** Risk of Heart Failure in Relation to the Healthy Lifestyle Score, The WHI Observational Study

<table>
<thead>
<tr>
<th>Healthy Lifestyle Score</th>
<th>No. of Cases</th>
<th>Person-Years</th>
<th>Crude Incidence Rate/1,000 Person-Years</th>
<th>Age- and Race-Adjusted HR (95% CI)</th>
<th>Multivariable-Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>74</td>
<td>15,099</td>
<td>4.90</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>1</td>
<td>614</td>
<td>204,287</td>
<td>3.01</td>
<td>0.45 (0.35-0.57)</td>
<td>0.49 (0.38-0.62)</td>
</tr>
<tr>
<td>2</td>
<td>620</td>
<td>300,462</td>
<td>2.06</td>
<td>0.30 (0.24-0.38)</td>
<td>0.36 (0.28-0.46)</td>
</tr>
<tr>
<td>3</td>
<td>365</td>
<td>276,654</td>
<td>1.32</td>
<td>0.19 (0.15-0.25)</td>
<td>0.24 (0.19-0.31)</td>
</tr>
<tr>
<td>4</td>
<td>153</td>
<td>140,121</td>
<td>1.09</td>
<td>0.17 (0.13-0.22)</td>
<td>0.23 (0.17-0.30)</td>
</tr>
</tbody>
</table>

*p value for trend <0.001. Model 1 adjusted for age, race/ethnicity, and all other healthy lifestyle factors. Model 2 adjusted for model 1 covariates, marital status, education, U.S. region, and antecedent coronary heart disease, diabetes, and hypertension. Test for linear trend. CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.
risk were similar when we compared African Americans and non-Hispanic whites (Figure 4).

**DISCUSSION**

In this large and diverse prospective study of postmenopausal women, an increasingly healthy lifestyle was associated with a progressively decreasing HF risk. Weighting each lifestyle factor according to its magnitude of effect on HF did not have a notable impact on the associations observed. Associations of healthy lifestyle with HF risk were also strong and graded among women without antecedent CHD, hypertension, or diabetes (Central Illustration), and similarly so among African Americans.

Smoking is currently well known as a strong and independent risk factor for HF (26). BMI also has been shown to be strongly and independently related to HF incidence in women (11,27). Excess weight gain may increase risk of HF through increased blood pressure (28,29), insulin resistance (30,31), and elevated cholesterol levels (32) or through mechanisms that involve inflammation (33,34), sleep apnea (35–37), or kidney disease (38–40).

Fewer studies have focused on dietary pattern in relation to HF. The AHEI recently was shown to be...
strongly related to HF (41) and overall cardiovascular disease risk (21), more so than other dietary indexes (20,21). The AHEI-2010 explicitly emphasizes high intakes of whole grains, polyunsaturated fatty acids, nuts, and legumes and low intakes of sugar-sweetened beverages, red and processed meats, and trans fats (12). High levels of physical activity also have been related to reduced risk of HF in previous studies and may act through beneficial effects on body weight, hypertension, diabetes, and CHD (42–45).

Given that certain lifestyle factors show stronger associations with risk of disease than others, simply adding the lifestyle factors when combining them may lead to misclassification due to heterogeneous people having the same HL score. However, we found that the relative weighting of lifestyle factors did not have any impact on associations of healthy lifestyle with HF risk, which suggests that the adoption of an overall healthy lifestyle in which these healthy lifestyle habits are integrated is optimal.

A large proportion of HF incidence is accounted for by antecedent CHD (46,47), and lifestyle factors are thought to increase risk of HF largely through development of CHD as an intermediate endpoint (4,11). In our analyses, however, the association between healthy lifestyle and HF risk was strong and graded, even among women without antecedent CHD. These findings are consistent with previous studies showing that smoking, BMI, and physical activity are strongly associated with HF risk independent of the presence or absence of CHD or other atherogenic risk factors for HF (11,13,26). Thus, healthy lifestyle factors may act on HF through other mechanisms. For example, obesity may impact HF risk through renal insufficiency (38–40). In addition, HF in the elderly, and particularly among elderly women, is more commonly characterized by impaired diastolic function but preserved left
ventricular systolic function, and the vast majority of HF patients with preserved systolic function do not have a defined myocardial disease but rather a clinically significant impairment of diastolic function (47,48). Even in HF characterized by left ventricular systolic dysfunction, one-third of cases are not defined by underlying CHD but rather by nonischemic causes (48). Similarly, the association of healthy lifestyle with risk of HF risk remained strong even after further exclusion of women with antecedent hypertension and diabetes. Finally, a healthy lifestyle was strongly related to risk of HF among both African Americans and non-Hispanic whites.

PRIOR LITERATURE. Two prior studies examined a combination of lifestyle factors in relation to HF. Normal body weight, not smoking, regular exercise, moderate alcohol intake, and consumption of fruits, vegetables, and breakfast cereals were individually and collectively associated with lower lifetime risk of HF among male physicians. Lifetime risk of HF was 21% and 10% in men with 0 versus ≥4 healthy lifestyle factors, respectively (4). Smoking, BMI, physical activity, and vegetable intake also were individually and collectively associated with risk of HF in both men and women from a large, homogeneous Finnish sample (5), with an inverse association observed between number of healthy lifestyle factors and HF risk.

STRENGTHS AND LIMITATIONS. Strengths of this study include the large sample size, prospective design, and the racial, socioeconomic, and geographic diversity within the WHI. Our investigation was the first, to the best of our knowledge, to report on the association of healthy lifestyle with risk of HF among a diverse group of U.S. women. In addition, we took into account the relative magnitude of impact of each lifestyle factor. Finally, a thorough follow-up of HF cases using comprehensive criteria and standardized methodology used in WHI ensures satisfactory case ascertainment (23).

Several limitations should also be noted. The ascertainment of HF was based on initial self-report, and this may have led to some HF cases being missed. Similarly, hospitalization was used to identify incident HF, and exclusion of outpatient diagnoses of HF may have underestimated mild or transient cases of HF.

CONCLUSIONS

HF remains a costly disease, with approximately two-thirds of costs reported to come from hospitalizations (9). Despite improved medical and surgical management, mortality after onset of HF remains high (49,50).

In parallel, the prevalence of healthy habits (with the exception of smoking abstinence) is generally low among middle-aged and older women in the United States (51). We observed that an overall healthy lifestyle was strongly protective against HF among post-menopausal women, even in the absence of antecedent CHD, hypertension, and diabetes. This suggests that a healthy lifestyle is beneficial for protection against HF over and above its benefits in lowering risk for these clinical intermediates. Evidence from randomized trials suggests that multi-component lifestyle interventions, in which several healthy lifestyle habits are promoted simultaneously, are successful in increasing healthful habits and decreasing cardiovascular disease risk (52–55), in some cases even more so than clinical treatment (56). Therefore, prevention strategies that place a higher emphasis on the combination and integration of healthy lifestyle habits may be of most benefit.

Healthy Lifestyle in Women and HF Risk

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