Adiposity and incidence of heart failure hospitalization and mortality: a population-based prospective study

Levitan, Adiposity and incident heart failure

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Emily B. Levitan, ScD; Amy Z. Yang, BA; Alicja Wolk, DrMedSci; Murray A. Mittleman, MD, DrPH

Author affiliations: Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, Boston, MA, USA (Drs Levitan and Mittleman and Ms Yang) and Division of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden (Dr Wolk)

Correspondence: Emily B. Levitan, ScD, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 375 Longwood Avenue, MS-443, Boston, MA 02215, phone: (617) 632-7705, fax: (617) 632-7698, email: elevitan@bidmc.harvard.edu

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Abstract

*Background:* Obesity is associated with heart failure (HF) incidence. We examined the strength of the association of body mass index (BMI) with HF by age and joint associations of BMI and waist circumference (WC).

*Methods and Results:* Women aged 48-83 (n = 36,873) and men aged 45-79 (n = 43,487) self-reported height, weight, and WC. HF hospitalization or death (n = 382 women, 718 men) between January 1, 1998 and December 31, 2004 was determined through administrative registers. Hazard ratios (HR), from Cox proportional-hazards models, for an interquartile range higher BMI were 1.39 (95% confidence interval [CI] 1.15-1.68) at age 60 and 1.13 (95% CI 1.02-1.27) at 75 in women. In men, HR were 1.54 (95% CI 1.37-1.73) at 60 and 1.25 (95% CI 1.16-1.35) at 75. A 10 cm higher WC was associated with 15% (95% CI 2%-31%) and 18% (95% CI 4%-33%) higher HF rates among women with BMI 25 and 30 kg/m², respectively; HR for 1 kg/m² higher BMI were 1.00 (95% CI 0.96-1.04) and 1.01 (95% CI 0.98-1.04) for WC 70 and 100 cm, respectively. In men, a 10 cm higher WC was associated with 16% and 18% higher rates for BMI 25 and 30 kg/m², respectively; a 1 kg/m² higher BMI was associated with 4% higher HF rates regardless of WC.

*Conclusions:* Strength of the association between BMI and HF events declined with age. In women, higher WC was associated with HF at all levels of BMI. Both BMI and WC were predictors among men.
Key words: epidemiology, heart failure, obesity, aging
In the United States, heart failure (HF) is the leading cause of hospitalization among those ≥ 65 years old. The prevalence of HF rose between 1989 and 1999. In Sweden, treatment of HF consumes 2% of the healthcare budget. The world-wide increase in obesity may contribute to an increase in incidence of HF. Currently, 66% of adults in the United States are overweight or obese (body mass index (BMI) ≥ 25 kg/m²); by 2015 75% of the adult population are expected to be overweight or obese. The proportion of Swedish adults who are overweight or obese is lower, 51% of men and 42% of women, but also increasing.

Obesity and overweight have been associated with greater incidence of HF in several epidemiologic studies. In the Framingham Heart Study, risk of HF increased 5% (men) and 7% (women) per 1 kg/m² higher BMI, with obese participants (BMI ≥ 30.0 kg/m²) having double the risk of HF as those with normal BMI. In two studies, abdominal adiposity appeared to be a better predictor of HF incidence than overall obesity; in a third study, BMI and WC predicted HF to a similar extent. Joint effects of overall and abdominal adiposity have been less studied. Although HF is prevalent in elderly populations, little attention has been paid to whether the strength of the associations with anthropometric measures varies by age. Because older individuals tend to have more fat mass for a given BMI than younger individuals, we hypothesized that associations with anthropometrics would be weaker in older individuals.

We therefore examined the association between HF hospitalization or mortality and the anthropometric indices BMI, waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR) in a population of middle-aged to elderly women and men.
The large study population allowed us to examine whether the associations varied by age and to explore joint effects of overall adiposity and abdominal adiposity.

Methods

Research Participants

Participants came from two population-based prospective cohort studies, the Swedish Mammography Cohort and the Cohort of Swedish Men. The studies were approved by the Regional Ethical Review Board at Karolinska Institute, Stockholm, Sweden. Completion and return by mail of the self-administered questionnaires was considered to imply consent.

The Swedish Mammography Cohort is comprised of women born between 1914 and 1948 living in Västmanland and Uppsala counties in central Sweden. In late 1997, 39,227 women (70% of eligible women) responded to a mailed questionnaire on diet and demographic, behavioral, and anthropometric factors specifically designed for this population. The Cohort of Swedish Men is comprised of men 45-79 years of age living in Västmanland and Örebro counties in central Sweden who, in late 1997 and early 1998, responded to a questionnaire similar to the Swedish Mammography Cohort questionnaire (n = 48,850, 49% of eligible men). The study design and data collected have been previously described. Participants who did not provide or provided incorrect national identification numbers, reported implausible energy intakes (> 3 standard deviations from the natural logarithm-transformed mean), or had a previous diagnosis of cancer (other than non-melanoma skin cancer) were excluded (n = 792 women, 3,506 men). We excluded from these investigations participants with history of HF at baseline (n = 334...
women, 743 men) determined through the inpatient register. In addition, underweight participants (BMI < 18.5 kg/m\(^2\)) (n = 642 women, 232 men) were excluded because of concerns about accuracy of reporting, preexisting disease causing weight loss, and small numbers of participants. Because participants with undetected HF at baseline may experience a change in body size, we excluded participants who died or experienced HF hospitalization during the first two years of follow-up, leading to a final sample size of 36,873 women and 43,487 men.

**Anthropometric measures**

To estimate adiposity participants were asked “How tall are you (in cm)?”, “How much do you weigh (in kilos)?”, and “What are your measurements around your waist and around your hips at the widest part (in cm)?” Participants were not provided with tape measures or detailed instructions. BMI was calculated as weight (kg) divided by height squared (m\(^2\)), WHR as waist circumference (cm) divided by hip circumference (cm), and WHtR as waist circumference divided by height. Swedish women and men tend to overestimate height and underestimate weight,\(^{19}\) but the correlation between BMI based on self-report and measured values was high (r = 0.90).\(^{20}\) The correlations between self-reported and clinical measures of waist and hip circumference are reported to be high;\(^{21}\) however, they have not been validated in this population.
Assessment of other covariates

History of MI at baseline and incident MI during follow-up were assessed through the Swedish inpatient register. We considered participants to have diabetes if they self-reported diabetes on the questionnaire or had any diagnosis of diabetes recorded in the inpatient register. Total physical activity (MET-hrs/day) was estimated using information collected on the study questionnaires regarding occupational physical activity, exercise, and sedentary behavior.22 The questionnaire included questions on education (less than high school, high school, university), cigarette smoking (current, past, never), alcohol consumption (frequency of consumption of beer, wine, and spirits), family history of MI before age 60 (yes, no), history of hypertension (yes, no), and history of high cholesterol (yes, no). Marital status was only assessed in men, and post-menopausal hormone therapy and living alone were only assessed in women. Updated information on covariates other than incident MI was not available during follow-up.

Follow-up and event ascertainment

We followed study participants from January 1, 1998 until December 31, 2004 through linkage to the Swedish inpatient and cause-of-death registers. Participants contributed follow-up time from January 1, 1998 until the earliest of the following: December 31, 2004, death from causes other than HF, or HF hospitalization or mortality. Median follow-up was 7 years (range 2 days-7 years) in both women and men. HF events were defined as the composite endpoint of hospitalization for or death from HF, identified by codes 428 (International Classification of Disease-9), I50, or I11.0 (International Classification of Disease-10) as the primary diagnosis. In a study of the
inpatient register, 95% of people with these codes as primary diagnosis were found to have HF on medical record review using European Society of Cardiology criteria.\textsuperscript{23} We included only the first HF event recorded in the registers for each individual.

\textit{Statistical analysis}

Data were missing on BMI in 1.7% of the women, WC in 15.7%, WHR in 16.3%, WHtR in 20.9%, and physical activity in 23%. Among men, data were missing on BMI in 5.0%, WC in 18.9%, WHR in 20.6%, WHtR in 22.0%, and physical activity in 23%. We used Markov chain Monte Carlo (MCMC) multiple imputation to simulate complete datasets.\textsuperscript{24} Analysis was performed in each dataset, and the average value reported. Variability within each dataset and between different imputation data sets was combined to account for uncertainty in the imputed estimates. MCMC multiple imputation uses available information to model the multivariate distribution of all variables. For each imputed dataset a value is chosen from the distribution for the missing values. Under the assumption that the data are missing at random conditional on the observed data (eg the distribution of BMI among 53-year-old women with hypertension is the same in the women who reported height and weight and those who did not), MCMC multiple imputation has been shown to be less biased than complete case analysis.\textsuperscript{24} In this study, complete case analysis was similar to analysis using multiple imputation, though confidence intervals were wider.

We calculated means and standard deviations or percentages of adiposity measures and covariates by whether or not hospitalization or death from HF occurred during follow-up. To detect differences in continuous variables between groups, we used
t-tests or Wilcoxon rank-sum tests when there was evidence of deviation from normality. Chi-squared tests were used for categorical variables. We estimated age-adjusted partial correlation coefficients between anthropometric measures.

To examine the relationship between adiposity measures and HF events, we calculated hazard ratios using Cox proportional-hazards regression models stratified by sex with time to HF event or censoring as the outcome. An assumption of Cox proportional-hazards models is that the entire population would have the same underlying rate of disease if the entire population had the same exposure, termed the baseline hazard. To relax this assumption and to account for the strong effect of age on HF rates, we included age as a strata variable which allows the baseline hazard to vary by age.25 In the primary multivariable-adjusted model, we included covariates which were potential causes of HF but not caused by adiposity. The covariates, chosen based on previous literature, included education, cigarette smoking, alcohol consumption (modeled as the natural logarithm of ethanol consumption in g plus 0.1), total physical activity, family history of MI before age 60, postmenopausal hormone therapy (women only), living alone (women only), and marital status (men only). As a sensitivity analysis, we created models additionally adjusted for covariates which could be caused by adiposity (potential mediators of the association between adiposity and HF chosen based on previous literature) including history of MI at baseline, incident MI within the past year, and more distant history of MI, and baseline history of hypertension, high cholesterol, and diabetes.

To explore the shape of the association between the anthropometric measures and HF we used fractional polynomial terms in the multivariable-adjusted Cox proportional-hazards models described above. Fractional polynomials are a family of polynomials of
the form $X^p + X^q$ where $X$ is the variable of interest, in this case one of the anthropometric measures. The powers $p$ and $q$ were chosen from the set $-2, -1, -0.5, \log, 0.5, 1, 2, 3$ based on the best fit to the data. Fractional polynomials allow for a wide variety of dose-response shapes and for approximate likelihood ratio tests for nonlinearity comparing the model in which the anthropometric measure was expressed as a polynomial to the model in which it was expressed as a linear term.

Because recommended clinical cutpoints for BMI, WC, and WHR do not necessarily represent the same degree of adiposity and there are no well-established clinical cutpoints for WHtR, we calculated the hazard ratio for an interquartile range increase (a comparison between the 25th and 75th percentile) with the anthropometric measures modeled as continuous terms based on the best fitting model. This allowed us to compare the strength of the associations on a consistent scale when considering the distribution in this population.

To examine the joint association of BMI and WC with HF hospitalization or mortality, we included BMI, WC, and a BMI-WC interaction term in Cox models. We centered BMI and WC before calculating the interaction term to avoid unnecessary collinearity. We calculated variance inflation factors to assess the effect of correlation between BMI and WC; all variance inflation factors were $\leq 2.1$ which is considered acceptable.

To graphically represent the joint association, we plotted the association between BMI and HF events for 4 values of WC: 70, 80, 90, and 100 cm.

Because fat mass tends to be higher in older individuals than younger individuals with the same value of the anthropometric measures, we tested whether the effect of the anthropometric measures varied by age by entering the product of age and the
anthropometric measures in multivariable-adjusted Cox proportional-hazards models which also contained a term for the main effect of the anthropometric measure and allowed the baseline hazard to vary with age (the main effect of age). We present estimates of the effects of those measures at age 60, 65, 70, and 75.

To test the assumption of proportional hazards we entered the product of the anthropometric measures and the natural logarithm of time in the model. We did not find evidence for deviation from this assumption.

Analysis was performed using SAS version 9.1 (Cary, NC) and Stata version 10.0 (College Station, TX). Two-sided p-value < 0.05 were considered statistically significant.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

During follow-up of 36,873 women and 43,487 men, we recorded 382 first HF events among women (357 hospital admissions and 25 deaths) and 718 first HF events among men (679 hospital admissions and 39 deaths). Thirty-four percent of women and 46% of men were overweight (BMI 25.0-29.9 kg/m²); 11% of women and 10% of men were obese (BMI ≥ 30.0 kg/m²). Participants who experienced HF events during follow-up tended to be older and had a higher prevalence of diabetes, hypertension, high cholesterol, and personal and family history of MI (Table 1). They also tended to have lower educational attainment and to be less likely to be married or living with a partner. Mean BMI, WC, WHR, and WHtR were higher in those with HF events than those without HF events. Age-adjusted partial correlations between BMI, WC, and WHtR
ranged between 0.72 and 0.96; WHR was least correlated with the other measures with correlations ranging between 0.21 and 0.62.

For all of the anthropometric measures, linear models fit as well as fractional polynomial models (p > 0.05 for likelihood ratio tests comparing fractional polynomial to linear models). A 1 kg/m² higher BMI was associated with a 3% higher rate of HF events (95% CI 1%-5%) in women and 7% higher in rate (95% CI 5%-8%) in men in multivariable-adjusted models. A 10 cm higher waist circumference was associated with a 19% higher rate of HF events (95% CI 8%-31%) in women and a 30% higher rate (95% CI 21%-38%) in men. For an interquartile range increase (comparing the 75th to the 25th percentile), the HR of HF events associated with BMI was 1.16 (95% CI 1.05-1.29) in women and 1.31 (95% CI 1.23-1.39) in men, the HR associated with WC was 1.26 (95% CI 1.12-1.43) in women and 1.36 (95% CI 1.25-1.47) in men, the HR associated with WHR was 1.05 (95% CI 0.95-1.15) in women and 1.10 (95% CI 1.03-1.18) in men, and the HR associated with WHtR was 1.21 (95% CI 1.06-1.38) in women and 1.35 (95% CI 1.25-1.46) in men (Figure 1).

After further adjustment for potential mediators of the association between adiposity and HF, including history of MI, hypertension, high cholesterol, and diabetes, the HRs were 1.12 (95% CI 1.00-1.24) in women and 1.27 (95% CI 1.19-1.36) in men for an interquartile range difference in BMI, 1.20 (95% CI 1.05-1.36) in women and 1.31 (95% CI 1.21-1.42) in men for an interquartile range difference in WC, 1.02 (95% CI 0.93-1.12) in women and 1.08 (95% CI 1.00-1.17) in men for an interquartile range difference in WHR, and 1.14 (95% CI 1.00-1.31) in women and 1.28 (95% CI 1.18-1.39) in men for an interquartile range difference in WHtR.
Joint associations of BMI and WC with HF events are shown in Figure 2. Among women, BMI, WC, and their interaction were jointly significant predictors of HF events (p < 0.001). At all levels of BMI, higher WC was associated with a higher rate of HF events. For example, a 10 cm higher WC was associated with 15% (95% CI 2%-31%, p = 0.03) and 18% (95% CI 4%-33%, p = 0.01) higher HF rates among women with BMI 25 and 30 kg/m², respectively. BMI did not appear to be associated with HF events at moderate WC, but there was a suggestion that BMI may be associated with HF events at higher WC. A 1 kg/m² higher BMI was associated with HR of 1.00 (corresponding to a 0% higher rate, 95% CI 0.96-1.04, p = 0.93) and 1.01 (corresponding to a 1% higher rate, 95% CI 0.98-1.04, p = 0.52) for women with WC 70 and 100 cm, respectively.

BMI, WC, and their interaction were also jointly significant predictors of HF events among men (p < 0.001). Higher WC was associated with higher rates of HF at all levels of BMI. A 10 cm higher WC was associated with 16% (95% CI 6%-27%, p = 0.001) and 18% (95% CI 8%-28%, p <0.001) higher rates among men with BMI 25 and 30 kg/m², respectively. Unlike the results seen in women, BMI was also associated with higher rates of HF events at all levels of WC. A 1 kg/m² higher BMI was associated with 4% (95% CI 0%-7%, p = 0.04) and 4% (95% CI 2%-7%, p < 0.001) higher HF rates for men with WC 70 and 100 cm, respectively.

The strength of the association between the anthropometric measures and HF events appeared to decline with age (Table 2). For example, an interquartile range increase in BMI was associated with a HR of 1.39 (95% CI 1.15-1.68) in 60 year old women and a HR of 1.13 (95% CI 1.02-1.27) in 75 year old women. Similarly, an interquartile range increase in BMI was associated with a HR of 1.54 (95% CI 1.37-1.73)
in 60 year old men and a HR of 1.25 (95% CI 1.16-1.35) in 75 year old men. The interactions with age were statistically significant for BMI, WC, and WHtR among women and BMI among men.

Discussion

In this population of middle-aged and older Swedish women and men, BMI, WC, WHR, and WHtR all were associated with HF hospitalization or mortality; WHR had the weakest association. The magnitude of the associations between all of the anthropometric measures and HF was somewhat greater in men than women. We found that WC was predictive of HF events regardless of BMI, but there was a suggestion of an association with BMI only at high WC among women. In contrast, both abdominal and overall adiposity appeared to be associated with HF events among men. For all participants, strength of the association between adiposity and HF events appeared to weaken with age.

The associations between the anthropometric measures and HF events are consistent with previous studies. Several studies have presented the associations between adiposity measures and HF separately in women and in men. In the Framingham Heart Study and the NHANES I Epidemiologic Follow-up Study, BMI was a stronger predictor of HF in women than in men. In contrast, the Renfrew-Paisley study and our study showed stronger association among men.

Abdominal adiposity, often measured using WC, WHR, or more recently WHtR, has frequently been cited as a stronger predictor of cardiovascular risk than total adiposity and has been identified as a powerful predictor of cardiovascular risk factors.
including hypertension, dyslipidemia, and diabetes mellitus.\textsuperscript{16,28,29} In one study of men and women aged 70-79, abdominal body fat distribution as measured by WC was more strongly associated with onset of HF than overall obesity as measured by BMI.\textsuperscript{14} In another study of elderly individuals with a history of CHD, WC, but not BMI, was a risk factor for HF incidence.\textsuperscript{13} However, in a study of Swedish men, BMI and WC appeared to be equally strong predictors.\textsuperscript{11} In our study, BMI, WC, WHR, and WHtR were all predictive of HF, but when we examined the effects of an interquartile range increase, WHR was a weaker predictor than the other measures.

Although several studies have examined the associations between BMI and HF adjusted for WC and WC and HF adjusted for BMI,\textsuperscript{13,14} joint effects of BMI and WC allowing for synergy between the two aspects of adiposity are less studied. In the current study, both WC and BMI were predictors of HF events in men, but BMI only appeared to be a predictor in women with high WC. This observation is consistent with studies suggesting that both BMI and WC were risk factors for coronary heart disease in men, but that central adiposity was more important in women.\textsuperscript{30,31}

On average, an elderly person will have more body fat than a young person for a given BMI.\textsuperscript{16} Although previous studies of HF have not examined whether the predictive power of anthropometric measures varies by age, a decrease in risk of mortality associated with adiposity has been seen in some studies, though evidence is mixed.\textsuperscript{32,33}

In addition to the adverse effects of obesity on established cardiovascular risk factors such as blood lipids, blood pressure, and diabetes, obesity is linked to increased blood volume, increased cardiac work load, diastolic dysfunction, hypertrophy and dilation of the left ventricle, and fat deposits in the heart which may lead to HF.\textsuperscript{34}
Increased aortic stiffness, another precursor of HF, has been consistently associated with obesity in adults,\(^35\) particularly those with high levels of abdominal adiposity.\(^{35-37}\) Obesity may increase sympathetic neural activity, which can exacerbate the condition of the failing heart; increased muscle sympathetic nerve activity has been associated with increased body fat, particularly abdominal fat.\(^{38}\)

A strength of this study is that it is population-based; 70% of eligible women and 48% of eligible men participated in this study which suggests that it is not a highly selected population. However, there are several important limitations. First, we did not have detailed clinical data on the study population. The diagnosis of HF using ICD codes has, however, been shown to be accurate in Sweden\(^{23}\) as well as the US.\(^2\) The inpatient and case-of-death registers only recorded cases of HF that resulted in hospitalization or death. Consequently, our results may not be generalizable to HF treated exclusively on an outpatient basis. We were not able to determine HF etiology or differentiate between HF with impaired or preserved systolic function. In addition, HF may be overdiagnosed in obese people because of dyspnea and edema related to obesity.\(^{34}\)

Self-reported height, weight, hip circumference, and WC are inherently less accurate than clinically measured anthropometrics. Swedish women were shown to underreport weight by an average of 1.8 kg and overreport height by 0.4 cm; corresponding figures for men were 1.6 kg and 0.3 cm.\(^{19}\) However, in this population correlations between BMI calculated using self-reported data correlated well with BMI calculated using measured data, and we expect that the measurement error will not be related to HF hospitalization or mortality.\(^{20}\) Finally, we can not rule out residual or unmeasured confounding.
In summary, we found that measures of both overall and abdominal adiposity were associated with HF hospitalization or mortality in this middle-aged and older population. In women, higher WC was associated with HF at all levels of BMI, but BMI appeared to predict HF only among those with high WC. Both BMI and WC were predictors among men. The associations between adiposity and HF events weakened with age.
**Funding sources:** Grants from the Swedish Research Council/Committee for infrastructure contributed to the maintenance of the two cohorts. Dr. Levitan was supported by a grant from the Swedish Foundation for International Cooperation in Research and Higher Education (STINT) and NIH grant F32HL091683.

**Disclosures**

None.
References


Figure 1 legend

Association of anthropometric measures with heart failure hospitalization or mortality. Body mass index (BMI), waist circumference (WC), waist-hip ratio (WHR), and waist-height ratio (WHtR) were modeled as continuous linear exposures. Circles represent the hazard ratio for an interquartile range increase among women and diamonds represent the hazard ratio for an interquartile range increase among men. Bars represent the 95% confidence intervals. Hazard ratios were adjusted for age, education, smoking, alcohol consumption, total physical activity, postmenopausal hormone therapy (women only), living alone (women only), and marital status (men only) and family history of myocardial infarction.
Figure 2 legend

Joint association of body mass index and waist circumference with heart failure hospitalization or mortality. Lines represent the hazard ratios associated with body mass index at waist circumferences of 70 cm, 80 cm, 90 cm, and 100 cm. Hazard ratios were calculated using Cox proportional hazards models which include terms for body mass index, waist circumference, and the interaction between them. Hazard ratios were adjusted for age, education, smoking, alcohol consumption, total physical activity, postmenopausal hormone therapy (women only), living alone (women only), and marital status (men only) and family history of myocardial infarction.
Table 1. Baseline characteristics* according to heart failure (HF) hospitalization or mortality

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 36,873)</th>
<th></th>
<th>Men (n = 43,487)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No HF (n = 36,491)</td>
<td>HF (n = 382)</td>
<td>No HF (n = 42,769)</td>
<td>HF (n = 718)</td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td>61.6 (9.1)</td>
<td>73.2 (7.1)</td>
<td>&lt;0.001</td>
<td>59.7 (9.5)</td>
</tr>
<tr>
<td>Physical activity (MET hr/d)</td>
<td>42.5 (4.8)</td>
<td>41.3 (5.0)</td>
<td>&lt;0.001</td>
<td>41.6 (4.9)</td>
</tr>
<tr>
<td>Alcohol consumption (g/day)</td>
<td>4.2 (5.3)</td>
<td>2.0 (3.5)</td>
<td>&lt;0.001</td>
<td>10.4 (10.4)</td>
</tr>
<tr>
<td>Cigarette smoking (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>53.9</td>
<td>61.9</td>
<td>36.7</td>
<td>29.5</td>
</tr>
<tr>
<td>Past</td>
<td>23.2</td>
<td>16.0</td>
<td>38.8</td>
<td>43.6</td>
</tr>
<tr>
<td>Current</td>
<td>22.9</td>
<td>22.2</td>
<td>24.5</td>
<td>26.9</td>
</tr>
<tr>
<td>Married or living with a partner (%)</td>
<td>76.1</td>
<td>56.1</td>
<td>&lt;0.001</td>
<td>83.0</td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>73.9</td>
<td>89.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>7.8</td>
<td>3.2</td>
<td>14.2</td>
<td>7.7</td>
</tr>
<tr>
<td>University</td>
<td>18.3</td>
<td>7.1</td>
<td>16.9</td>
<td>7.4</td>
</tr>
<tr>
<td>Family history of MI (%)</td>
<td>17.3</td>
<td>26.6</td>
<td>&lt;0.001</td>
<td>16.4</td>
</tr>
<tr>
<td>History of MI (%)</td>
<td>1.4</td>
<td>5.8</td>
<td>&lt;0.001</td>
<td>4.1</td>
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<tr>
<td>History of diabetes (%)</td>
<td>3.4</td>
<td>11.3</td>
<td>&lt;0.001</td>
<td>7.6</td>
</tr>
<tr>
<td>History of hypertension (%)</td>
<td>20.8</td>
<td>42.7</td>
<td>&lt;0.001</td>
<td>23.5</td>
</tr>
<tr>
<td>History of high cholesterol (%)</td>
<td>8.4</td>
<td>11.8</td>
<td>0.02</td>
<td>16.1</td>
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<td>Postmenopausal hormone therapy (%)</td>
<td>51.5</td>
<td>44.4</td>
<td>0.008</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Measures of adiposity</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.2 (3.9)</td>
<td>26.0 (4.3)</td>
<td>&lt;0.001</td>
<td>25.8 (3.3)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>83.9 (11.0)</td>
<td>88.2 (12.6)</td>
<td>&lt;0.001</td>
<td>96.0 (10.0)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.82 (0.10)</td>
<td>0.84 (0.10)</td>
<td>&lt;0.001</td>
<td>0.94 (0.07)</td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>0.51 (0.07)</td>
<td>0.54 (0.08)</td>
<td>&lt;0.001</td>
<td>0.54 (0.06)</td>
</tr>
</tbody>
</table>

* Mean (standard deviation) or percent.

† P-values from t-tests or Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical variables.
Table 2. Association* between an interquartile range increase in anthropometric measures and heart failure hospitalization or mortality by age

<table>
<thead>
<tr>
<th>Interquartile range</th>
<th>Age 60</th>
<th>Age 65</th>
<th>Age 70</th>
<th>Age 75</th>
<th>P for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>22.5-27.2 kg/m²</td>
<td>1.39 (1.15-1.68)</td>
<td>1.30 (1.13-1.49)</td>
<td>1.21 (1.09-1.35)</td>
<td>1.13 (1.02-1.27)</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>77-90 cm</td>
<td>1.50 (1.25-1.79)</td>
<td>1.39 (1.21-1.60)</td>
<td>1.29 (1.15-1.46)</td>
<td>1.20 (1.06-1.36)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.77-0.86</td>
<td>1.12 (1.01-1.25)</td>
<td>1.09 (0.99-1.19)</td>
<td>1.05 (0.97-1.15)</td>
<td>1.02 (0.93-1.13)</td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>0.47-0.55</td>
<td>1.42 (1.16-1.74)</td>
<td>1.33 (1.14-1.55)</td>
<td>1.24 (1.10-1.41)</td>
<td>1.16 (1.02-1.32)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.6-27.7 kg/m²</td>
<td>1.54 (1.37-1.73)</td>
<td>1.44 (1.32-1.56)</td>
<td>1.34 (1.26-1.43)</td>
<td>1.25 (1.16-1.35)</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>90-102 cm</td>
<td>1.46 (1.32-1.62)</td>
<td>1.41 (1.30-1.52)</td>
<td>1.35 (1.25-1.46)</td>
<td>1.30 (1.18-1.43)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.90-0.98</td>
<td>1.14 (1.05-1.23)</td>
<td>1.12 (1.04-1.19)</td>
<td>1.10 (1.02-1.18)</td>
<td>1.08 (0.98-1.19)</td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>0.51-0.58</td>
<td>1.44 (1.30-1.59)</td>
<td>1.39 (1.28-1.51)</td>
<td>1.34 (1.24-1.45)</td>
<td>1.30 (1.18-1.43)</td>
</tr>
</tbody>
</table>

* Hazard ratios and 95% confidence intervals estimated from Cox proportional hazards models which allowed the baseline hazard to vary by age and adjusted for age, education, smoking, alcohol consumption, total physical activity, postmenopausal hormone therapy (women only), living alone (women only), and marital status (men only) and family history of myocardial infarction.
Adiposity and Incidence of Heart Failure Hospitalization and Mortality: A Population-based Prospective Study
Emily B. Levitan, Amy Z. Yang, Alicja Wolk and Murray A. Mittleman

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