Body Mass Index, Weight Change, and Death in Older Adults

The Systolic Hypertension in the Elderly Program

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The relation between relative weight and health differs between young and old. In older populations, weight change may cloud the association between a single relative weight and health outcomes. To determine whether weight or weight change is a more important determinant of mortality in a population of older adults, the authors analyzed data from the Systolic Hypertension in the Elderly Program (1984–1990), a randomized clinical trial testing the efficacy of antihypertensive drug treatment to reduce the risk of stroke in older adults (aged 60 years or more) with isolated systolic hypertension. After adjustment for covariates, an average annualized weight loss of at least 1.6 kg/year (odds ratio = 4.9), a weight loss between 1.6 and 0.7 kg/year (odds ratio = 1.7), a weight gain of more than 0.5 kg/year (odds ratio = 2.4), and a baseline body mass index of less than 23.6 (odds ratio = 1.4) all had a significant (p < 0.05) association with all-cause mortality compared with a referent group that was weight stable and of intermediate body mass index (23.6 to <28.0 kg/m²) and weight change (–0.7 to <0.5 kg/year). The authors conclude that, in older adults, dynamic measures (e.g., annualized weight change) of weight change predict mortality better than do static weight measures (e.g., baseline body mass index). Even in those with high or low baseline body mass index, weight stability is associated with a lower mortality risk. Am J Epidemiol 2002;156:132–8.

Abbreviations: CI, confidence interval; SHEP, Systolic Hypertension in the Elderly Program.

The relation between relative weight and mortality varies with age. In younger persons, a high body mass index is associated with an increased risk of diabetes, heart disease, and a number of other health conditions. Conversely, in older adults, a low body mass index is more strongly associated with mortality risk (1–9). Some of the discrepancy between the findings at younger versus older ages may be due to a failure to account for the dynamic nature of body mass and its interplay with chronic disease. For example, in relatively weight-stable older adults, the association between low body mass index and mortality is less evident, while weight loss from middle age is associated with increased mortality (2, 3, 5, 10).

The nature of the dynamic interplay between weight and mortality is not well described in older populations. Data from younger populations suggest that both weight loss (particularly unintentional loss) and weight variability predispose to elevated mortality risk (11–23). In older adults, weight loss is also associated with increased mortality risk (6, 24–27). However, most of these studies determine weight change based on recalled weight from decades earlier (1, 3, 5, 10). Thus, the prognostic significance of weight change over short periods has not been well addressed in older populations. To examine the simultaneous effect of static and dynamic measures of weight on mortality in older populations, we examined a cohort of participants in the Systolic Hypertension in the Elderly Program (SHEP). SHEP was a multicenter, randomized clinical trial to test the efficacy of antihypertensive drug treatment to reduce the risk of nonfatal

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and fatal stroke in older adults (aged 60 or more years) with isolated systolic hypertension.

MATERIALS AND METHODS

Design and participants

SHEP was a randomized, double-blind, placebo-controlled clinical trial funded jointly by the National Heart, Lung, and Blood Institute and the National Institute on Aging. The methods of SHEP have been described in detail elsewhere (28). Each participant was weighed at baseline and at subsequent quarterly follow-up visits, and vital status was known at the end of the study for all but three participants. Of 4,736 SHEP participants, 455 (9.6 percent) died during the study. The average length of follow-up was 4.5 years.

For this analysis, subjects were included if they had at least three weight measures obtained at least 1 year prior to death, loss to follow-up, or the end of SHEP. We excluded 251 subjects (including the three whose vital status was unknown). Of the other 248 subjects, 186 did not complete 1 year in the study, and the other 62 did not have at least three weight measurements at least 1 year prior to death, loss to follow-up, or the end of SHEP. Thus, our study included 4,485 of the original 4,736 SHEP participants and 351 of the 455 deaths.

Analyses

Our primary outcome was all-cause mortality. We evaluated cause-specific mortality (cardiovascular disease and cancer) as a secondary endpoint. The body mass index (weight (kg)/height (m)²) determined at the baseline SHEP visit was our static measure of weight. Our dynamic measure was individual annualized weight change. It was estimated as change in kilograms per year based on the regression of all available weights on time from baseline until 1 year from the end of follow-up.

Baseline body mass index and weight change were divided into quintiles for analytical purposes with the two contiguous quintiles with the lowest mortality rates serving as the referent group. The median baseline body mass index was 22, 24.8, 26.9, 29.3, and 34.1 kg/m² in quintiles 1–5, respectively. The median weight change was –2.5, –1.1, –0.4, 0.2, and 1.2 kg/year in weight change quintiles 1–5, respectively. The second and third quintiles of baseline body mass index (23.6 to <28 kg/m²) were used as the referent category and, for weight change, the third and fourth quintiles (–0.7 to 0.5 kg/year) were used as the referent category.

We used logistic regression (SAS version 8.1, PROC LOGIST; SAS Institute, Inc., Cary, North Carolina) to model mortality as a function of both baseline body mass index and weight change. Covariates included in the final model are gender, age group in quartiles (≤66, 67–71, 72–76, and >76 years), current smoking status at baseline, and the presence or absence of cardiovascular comorbidity status at baseline (defined as a previous myocardial infarction, stroke, or a history of diabetes). Covariates considered but not included in our final models were race, a history of smoking, and SHEP treatment group (active vs. placebo). All variables are categorical, and dummy coding was used. Interactions of covariables and the main effects of baseline body mass index and weight change were evaluated and found not to be significant.

Institutional review boards at the respective clinical field centers approved the SHEP study.

RESULTS

Of 4,485 SHEP participants included in our study, 351 died (mortality rate = 7.83 percent). Of these deaths, 148 (42.2 percent) were related to cardiovascular disease, 135 (38.4 percent) were related to cancer, and 68 (19.4 percent) were due to other causes. The all-cause mortality rates by demographic and other characteristics are shown in table 1. Males, smokers, participants aged 67 or more years, or subjects with cardiovascular comorbidity were associated with an increased risk of all-cause mortality. Race, a history of smoking, and the SHEP treatment group assignment were not associated with all-cause mortality in this subset of SHEP participants.

Figure 1 shows the relation between baseline body mass index and mortality and the relation between annualized weight change and mortality. Persons in the lowest baseline body mass index quintile (<23.6 kg/m²) had the highest mortality rate (9.4 percent). Somewhat surprisingly, subjects in the highest quintile of baseline body mass index (≥31.0 kg/m²) had the lowest mortality rate (6 percent). For weight change, there is a U-shaped relation showing that extremes of weight change are associated with the highest mortality. The lowest mortality rates of 3.6 percent and 4 percent were for the third and fourth quintiles (weight loss of 0.7 kg/year to weight gain of 0.5 kg/year) where weight was relatively stable over time.

The simultaneous relation among baseline body mass index, weight change, and mortality is shown in figure 2. Death rates are based on 120–257 participants in each of the 25 cells. The highest mortality rate of 22.6 percent was observed in those with both the lowest body mass index at baseline (<23.6 kg/m²) and the greatest subsequent average weight loss (>1.6 kg/year). The lowest mortality rate (1.2 percent) was observed in those in both the fourth quintile of baseline body mass index (28–<31 kg/m²) and the third quintile of average weight change (loss of 0.7–<0.1 kg/year). Within each category of body mass index, the relation of weight change with mortality is approximately U shaped.

The results of the logistic regression model including both static weight (three categories of baseline body mass index coded as dummy variables representing quintiles 1, 4, and 5) and weight change measures (three categories of annualized weight change coded as dummy variables representing quintiles 1, 2, and 5) and covariates are shown in table 2. Participants in the weight categories were compared with a referent group composed of those in both quintiles 2 and 3 of baseline body mass index (23.6 to <28.0 kg/m²) and quintiles 3 and 4 of weight change (–0.7 to <0.5 kg/year).

Both weight loss and weight gain were associated with mortality. When adjustment was made for the baseline body mass index and other covariates, the morality odds ratios
were 4.9 (95 percent confidence interval (CI): 3.5, 6.8) and 1.7 (95 percent CI: 1.2, 2.4) for persons in the first (<1.6-kg/year loss) quintile and second (1.6- to <0.7-kg/year loss) quintile of weight change, respectively. Persons in the fifth quintile of weight change (≥0.5-kg/year gain) were also more likely to die than were persons in the referent group (odds ratio = 2.4, 95 percent CI: 1.7, 3.5).

With regard to baseline body mass index, those in the lowest quintile (<23.6 kg/m²) had a 35 percent increased odds of mortality (odds ratio = 1.35, 95 percent CI: 1.0, 1.7) relative to the referent group. We observed two interactions in those in the highest two quintiles of baseline body mass index with weight change. Participants with a baseline body mass index from 28 to less than 31 kg/m² and a weight gain of greater than or equal to 0.5 kg/year had a higher than anticipated odds of death (odds ratio = 4.8, 95 percent CI: 3.0, 7.7). Moreover, participants with a baseline body mass index of greater than or equal to 31 kg/m² and a weight loss of less than 1.6 kg/year had lower mortality than anticipated from the association of weight loss considered on its own (odds ratio = 2.9, 95 percent CI: 1.8, 4.8).

The adjusted odds ratios for covariates in the final model are 1.60 (95 percent CI: 1.27, 2.02) for male sex, 2.28 (95 percent CI: 1.69, 3.07) for being a smoker at baseline, and 1.94 (95 percent CI: 1.48, 2.55) for being in the high cardiovascular disease risk group at baseline. For age, with the lowest quartile as the referent group, the adjusted odds ratios are 1.89 (95 percent CI: 1.29, 2.76) for subjects aged 67–71 years, 2.58 (95 percent CI: 1.75, 3.79) for subjects aged 72–76 years, and 4.63 (95 percent CI: 3.20, 6.71) for subjects aged 77 years or more. To check for possible interactions with these mortality determinants, we stratified the results by
FIGURE 1. Mortality risk by baseline body mass index (A) and by average annualized weight change (B), Systolic Hypertension in the Elderly Program, 1984–1990. The error bars represent 95% confidence intervals.

FIGURE 2. Mortality risk by baseline body mass index (BMI) and average annualized weight change (quintile medians displayed), Systolic Hypertension in the Elderly Program, 1984–1990. The error bars represent 95% confidence intervals.
each of the covariates. Our findings were similar in each stratum of age group, gender, smoking status, or the presence of cardiovascular comorbidity (data not shown).

We were interested to see if the patterns of association were influenced by the weights measured between 1 and 2 years prior to death. When we eliminated at least the last 2 years of data before the final evaluation (death or loss to follow-up), figures 1 and 2 looked very similar to the ones displayed. After the last 2 years of data were censored, there were only 281 deaths among 4,392 subjects with at least three weight values. As shown in table 2, the regression model showed similar patterns of association compared with the primary analysis, although the associations between weight loss and mortality diminished slightly. We used Pearson’s chi-squared test to determine that our model fit using the 1-year lag also showed a good fit of the data for the 2-year lag. If the model had not fit, then we might suspect that our results were heavily influenced by weight changes that occurred in the 2 years before death.

Our findings were not markedly different for the two most common causes of death. Table 2 presents the modeled relation between baseline body mass index-annualized weight change and cardiovascular disease-cancer mortality. For cardiovascular disease mortality, the odds ratios are essentially the same as those for all-cause mortality. For cancer mortality, the same is true except that baseline body mass index was not associated with the risk of cancer death. The results of the 68 other deaths also showed a similar pattern (data not shown). In addition, the overall model gave a good fit for the different subsets evaluated.

**DISCUSSION**

We found that, among participants in SHEP, a multipoint measure of weight change predicted mortality better than a single relative weight measure did. Across all levels of body mass index measured at the baseline visit, the relation between weight change during SHEP and all-cause mortality is U shaped. Even at a very high or low baseline body mass index, weight stability is associated with the lowest mortality risk. For the baseline body mass index, only the low body mass index (<23.6 kg/m²) was independently associated with mortality, reinforcing the findings from a previous investigation from SHEP (29). The picture was complicated slightly by statistical interactions suggesting that those at high body mass index who gain weight are at especially high risk and that those at the highest body mass index who are losing weight have relatively lower mortality. These interactions do not, however, qualify our main findings. Our findings were consistent by age, gender, smoking status, and the presence of cardiovascular comorbidities.

**TABLE 2. Simultaneous influence of weight change and baseline body mass index on adjusted* mortality odds ratios, Systolic Hypertension in the Elderly Program, 1984–1990**

<table>
<thead>
<tr>
<th>Weight change or body mass index category</th>
<th>All deaths ( (n = 351) )</th>
<th>Cardiovascular disease deaths ( (n = 148) )</th>
<th>Cancer deaths ( (n = 135) )</th>
<th>2-year lag† ( (n = 281) )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Referent group‡</strong></td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Weight change categories</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. (&lt;1.6-kg/year loss)</td>
<td>4.92</td>
<td>5.05</td>
<td>3.82</td>
<td>3.74</td>
</tr>
<tr>
<td>2. (1.6- to &lt;0.7-kg/year loss)</td>
<td>1.71</td>
<td>1.90</td>
<td>1.58</td>
<td>1.46</td>
</tr>
<tr>
<td>3. (≥0.5-kg/year gain)</td>
<td>2.41</td>
<td>2.25</td>
<td>2.60</td>
<td>2.30</td>
</tr>
<tr>
<td><strong>Baseline body mass index categories</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. (&lt;23.6 kg/m²)</td>
<td>1.35</td>
<td>1.39</td>
<td>1.03</td>
<td>1.44</td>
</tr>
<tr>
<td>5. (28.0–&lt;31.0 kg/m²)</td>
<td>1.02</td>
<td>1.30</td>
<td>1.08</td>
<td>1.30</td>
</tr>
<tr>
<td>6. (≥31.0 kg/m²)</td>
<td>1.15</td>
<td>1.22</td>
<td>1.23</td>
<td>1.27</td>
</tr>
<tr>
<td><strong>Weight change-baseline body mass index interactions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. (interaction: 3 with 5)</td>
<td>1.94</td>
<td>1.71</td>
<td>1.25</td>
<td>1.37</td>
</tr>
<tr>
<td>8. (interaction: 1 with 6)</td>
<td>0.52</td>
<td>0.49</td>
<td>0.57</td>
<td>0.74</td>
</tr>
</tbody>
</table>

* Adjusted for gender, age group in quartiles, current smoking status, and the presence of myocardial infarction, diabetes, or stroke at baseline.
† Only weight change occurring more than 2 years prior to death or the end of the study is considered.
‡ Baseline body mass index: 23.6 to <28.0 kg/m²; and weight change: –0.7 to <0.5 kg/year.
It should be kept in mind that our results pertain to a trend in weight based on a line fitted through multiple weight measures for each participant. They do not apply to differences between two consecutive weight measurements. For example, the median average weight gain associated with higher mortality was 1.2 kg/year. This amount of gain is likely within the range of normal weight fluctuation for an individual, so a 1.2-kg increase between two measures a year apart for an individual may not be of great clinical concern. Rather, our data indicate that a trend of increasing weight is a source of concern. For weight loss, data from clinical populations suggest that a 5 percent weight loss over a 6-month to a year interval is a marker for occult disease (24, 25). A study looking at the prognostic significance of unintentional weight loss in older male Department of Veterans Affairs patients found that a 4 percent weight loss between two measures taken a year apart best discriminated between those who died during the follow-up period and those who did not (30).

The purpose of determining weight change based on measures collected at least a year prior to death was to reduce the influence of terminal illness on the results. It is uncertain if this was sufficient. When we determined weight change based on measures collected at least 2 years prior to death, the relation between weight loss and mortality diminished slightly. This suggests that the relations we observed were not explained solely by terminal decline. In addition, our results were similar across the major causes of death in SHEP, cardiovascular disease or cancer, implying that weight change is involved in the final common pathways leading to death.

Our findings are in contrast to those of Mikkelsen et al. (18), who found a U-shaped relation in both static and dynamic weight measures and all-cause mortality. Some researchers (6, 11, 16), focusing on weight change, found that both weight loss and weight gain were associated with all-cause mortality, while Wannamethee and Shaper (21) found that weight gain is associated with cardiovascular disease mortality and weight loss with cancer and non-cardiovascular disease mortality.

Many investigators (3, 5, 13, 14, 19, 26, 27, 31) have found weight loss to be associated with all-cause mortality. This finding tends to be for long-term weight loss. Yaari and Goldbourt (23) separated voluntary and involuntary weight loss and found both to be associated with a small increase in mortality. Other investigators (12, 23) have examined weight variability and found it to be associated with all-cause mortality. In contrast to these investigators, Iribarren et al. (15) found that both weight loss and weight fluctuation were unrelated to death among healthy, nonsmoking Japanese-American men.

There are several strengths and limitations to our study. The data set we analyzed was unique in a number of ways. We evaluated an older population that was followed over a short period of time with multiple weight values during that time. These data were not dependent upon recalled weight values from some distant past (such as lifetime maximum or minimum). However, because the sample was derived from a clinical trial of antihypertensive drug treatment for isolated systolic hypertension, the results of this study may be of limited generalizability. However, isolated systolic hypertension is a common finding in older adults. The prevalence in older adults ranges from 7 percent in persons aged 60–69 years to more than 20 percent in persons aged 80 years or more (28). Finally, we do not have measures of voluntary versus involuntary weight change throughout the study.

Although there is concern about overweight as a risk factor of morbidity and mortality (9), our findings indicate, at least in SHEP participants, that dynamic measures of weight (weight loss or gain) supersede a single weight measure (especially overweight) in predicting all-cause mortality. Because we cannot separate voluntary from involuntary weight loss in our sample, these data cannot be used to guide weight loss recommendations in the elderly. However, our results do suggest that older adults, at all levels of body mass index, experiencing either a continuing weight gain or weight loss may be at higher risk for all-cause mortality and should be monitored closely.

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