Body Mass Index and Mortality among Older Breast Cancer Survivors in the Study of Osteoporotic Fractures

Katherine W. Reeves,1 Kimberly Faulkner,1 Francesmary Modugno,1,2 Teresa A. Hillier,3 Douglas C. Bauer,4 Kristine E. Ensrud,5 and Jane A. Cauley1 for the Study of Osteoporotic Fractures Research Group

1Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh; 2University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania; 3Kaiser Permanente Center for Health Research Northwest/Hawaii, Portland, Oregon; 4Departments of Medicine, Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California; and 5Center for Chronic Disease Outcomes Research, Minneapolis VA Center and Department of Medicine and Epidemiology, University of Minnesota, Minneapolis, Minnesota

Abstract

Background: Breast cancer survival is inversely related to body mass index (BMI), but previous studies have not included large numbers of older women. This study investigated the association between BMI and mortality after breast cancer diagnosis in a cohort of older Caucasian women enrolled in the Study of Osteoporotic Fractures.

Methods: All women were age ≥65 at study entry (N = 533). Cox proportional hazards regression analysis was used to determine the effect of BMI as a continuous variable on risk of all-cause, cardiovascular, any cancer, and breast cancer mortality. Interaction terms were included to evaluate effect modification by age at diagnosis.

Results: Mean age at diagnosis was 78.0 years (SD 5.7) with an average of 8.1 years (SD 4.4) of follow-up after diagnosis. There were 206 deaths during follow-up. The effect of BMI on mortality depended on age (Pinteraction = 0.02). At age 65, the risk of mortality was 1.4 times higher for a BMI of 27.3 kg/m² (95% confidence interval [95% CI], 1.03-2.01) and 2.4 times higher for a BMI of 34.0 kg/m² (95% CI, 1.07-5.45) compared with women with a BMI of 22.6 kg/m². At age 85, risk of death was lower for a BMI of 27.3 kg/m² (hazard ratio, 0.81; 95% CI, 0.65-1.01) or a BMI of 34.0 kg/m² (hazard ratio, 0.61; 95% CI, 0.36-1.02) compared with a BMI of 22.6 kg/m². Similar results were observed for any cancer and breast cancer mortality.

Conclusions: In this population of older women, the effect of increased BMI on risk of mortality after breast cancer varied by age. These results differ from those observed among populations of younger postmenopausal breast cancer survivors. (Cancer Epidemiol Biomarkers Prev 2007;16(7):1468–73)

Introduction

Because of early detection and improved treatment of breast cancer, the percentage of women surviving at least 5 years after diagnosis has increased to 88% (1). The number of breast cancer survivors, therefore, continues to increase; yet, relatively little is known about the survivorship experience of these women. Breast cancer survivors may have more fragile health than that of their same-age peers. The risk of recurrence remains a constant worry, and ~45% of breast cancer patients ages 60 to 69 years at diagnosis and 33% of those ages ≥70 years at diagnosis may experience a recurrence of their cancer (2). Furthermore, the treatments women receive to combat their cancer are not benign. Late effects of treatment potentially include cardiovascular problems (3), decreased bone mineral density (4), and increased risk of endometrial cancer (5-8). Thus, breast cancer survivors may experience significant cardiovascular, fracture-related, and cancer mortality.

Identifying lifestyle factors that can modify the risk of mortality is important for improving the survival experience of women diagnosed with breast cancer. Evidence is accumulating that shows that obesity may be one such factor. Individuals with a body mass index (BMI), defined as weight in kilograms divided by the square of the height in meters, ≥30 kg/m² are considered obese. Among postmenopausal women, obesity confers an increased risk of breast cancer (9). Furthermore, obesity has been linked to increased risk of recurrence (10) and decreased survival (11-13) in postmenopausal women with breast cancer. These associations may result from the peripheral conversion of androstenedione to estrone that occurs in the adipose tissue causing higher levels of estrogen in obese postmenopausal women (14, 15). Alternatively, the poorer prognosis may reflect suboptimal treatment of obese women with breast cancer (16). Studies investigating obesity and survivorship after breast cancer, however, have included few women older than 65 years at diagnosis (11-13) or have specifically excluded this age group (10), and no studies have investigated these relationships in a cohort of older women. This is true despite the fact that the highest rates of breast cancer are observed among women over age 65 (17). The effect of obesity on mortality may be lower among older adults (18-20), and it is possible that results observed among cohorts of younger postmenopausal breast cancer survivors may not apply to older breast cancer survivors.

The present analysis sought to describe the distribution of causes of mortality among older breast cancer survivors and how BMI affected their risk of death. The Study of Osteoporotic Fractures (SOF) provides a unique opportunity to investigate mortality in breast cancer survivors in a prospective cohort of Caucasian women ages 65 years and older at enrollment and with up to 20 years of follow-up data available.

Materials and Methods

Study Population. All women included in this analysis were participants in the SOF. The SOF cohort and methods...
have been described previously (21-23). Briefly, SOF recruited participants using voter registration lists from four U.S. clinical sites (Baltimore, Minneapolis, Monongahela Valley near Pittsburgh, and Portland) between 1986 and 1988. The primary goal of SOF was to identify risk factors for osteoporotic fractures in a prospective cohort of older women. Eligible participants were female, ages 65 years or older, ambulatory, and had not received a bilateral hip replacement. The initial SOF cohort consisted of 9,704 Caucasian women. All women provided written informed consent, and this study was approved by institutional review boards at each participating institution. A total of 540 women from the initial SOF cohort were diagnosed with breast cancer after their enrollment into SOF and had complete follow-up through February 2006; three women who were overweight (BMI <18.5 kg/m²) and four women with a missing value for baseline BMI were excluded from the present analysis. Thus, the final sample included 533 women.

Data Ascertainment. Data on SOF participants have been collected at clinical examinations at baseline and about every 2 years thereafter and through periodic telephone contacts and mailings. At entry into SOF and at subsequent clinical visits, height was measured using a wall-mounted stadiometer (Holtain), and weight was measured using a balance beam scale in light indoor clothing. Height and weight were used to calculate BMI. Data on other covariates in this analysis were obtained at baseline or year 2. Incident cases of breast cancer have been documented through self-report and validated using medical records, hospital discharge summaries, pathology reports, and death certificates as described previously (24). Upon adjudication, ~98% of self-reported cases of breast cancer were confirmed and counted as breast cancer outcomes. Self-report of breast cancer was obtained at each follow-up visit, and hospital discharge summaries and death certificates were searched for information regarding breast cancer upon report of a participant’s death. Stage at diagnosis, estrogen receptor (ER) status, and progesterone receptor (PR) status were also recorded (if available) and adjudicated by a single SOF physician investigator who assigned International Classification of Disease, Ninth Revision (ICD-9) codes. Follow-up on the cohort was 99% complete (25).

Four causes of death were considered in this analysis: all-cause (all deaths regardless of ICD-9 code), cardiovascular (ICD-9 codes 401 to <405, 410 to <415, 425, 427.5, 428, 429.2, 430 to <439, 440 to <445, 450 to <459, 470 to <476, or 798.), any cancer (ICD-9 codes 140 to <240), and breast cancer mortality (ICD-9 codes 174 to <175).

Statistical Analysis. Descriptive analyses were conducted to describe mortality and the distribution of possible confounders in this population; ANOVA and χ² tests were used to evaluate differences in continuous and categorical variables, respectively, by BMI category. BMI was categorized into normal (18.5-24.9 kg/m²), overweight (25.0-29.9 kg/m²), and obese (≥30 kg/m²; ref. 26). Baseline BMI was chosen as the primary independent variable because it preceded breast cancer diagnosis for all women and was believed to be representative of women’s usual adult weight before breast cancer. Kaplan-Meier curves were constructed to describe the survival experience of the study population stratified by BMI category. Unweighted log-rank tests were used to assess differences in survival among the BMI groups. Age-adjusted mortality rates were calculated within each BMI category using Poisson regression, and differences between overweight or obese women and normal women were assessed using Wald tests of the coefficients for overweight and obese in the Poisson model.

Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for the effect of BMI on risk of mortality while controlling for potential confounders. BMI was included as a continuous variable to increase power for the regression analyses. Potential confounders were chosen based on prior knowledge of a relationship with mortality from breast cancer and/or cardiovascular disease; these included age at diagnosis (continuous), history of stroke at baseline (no, yes), history of heart disease at year 2 (no, yes, missing), height was measured using a wall-mounted stadiometer (Holtain), and weight was measured using a balance beam scale in light indoor clothing. Height and weight were used to calculate BMI. Data on other covariates in this analysis were obtained at baseline or year 2.

Incident cases of breast cancer have been documented through self-report and validated using medical records, hospital discharge summaries, pathology reports, and death certificates as described previously (24). Upon adjudication, ~98% of self-reported cases of breast cancer were confirmed and counted as breast cancer outcomes. Self-report of breast cancer was obtained at each follow-up visit, and hospital discharge summaries and death certificates were searched for information regarding breast cancer upon report of a participant’s death. Stage at diagnosis, estrogen receptor (ER) status, and progesterone receptor (PR) status were also recorded (if available) and adjudicated by a single SOF physician investigator who assigned International Classification of Disease, Ninth Revision (ICD-9) codes. Follow-up on the cohort was 99% complete (25). Four causes of death were considered in this analysis: all-cause (all deaths regardless of ICD-9 code), cardiovascular (ICD-9 codes 401 to <405, 410 to <415, 425, 427.5, 428, 429.2, 430 to <439, 440 to <445, 450 to <459, 470 to <476, or 798.), any cancer (ICD-9 codes 140 to <240), and breast cancer mortality (ICD-9 codes 174 to <175).

Results

table 1 presents the distribution of demographic and breast cancer characteristics among 533 Caucasian women diagnosed with breast cancer during SOF follow-up. The average age of these women at diagnosis was 78.0, and the average BMI at SOF enrollment was 27.1 kg/m². About one quarter (24.2%) of the women were obese. The majority of women never smoked (64.0%) and had no history of diabetes (93.8%), stroke (98.3%), heart attack (93.6%), or congestive heart failure (99.1%). Obese women were more likely to report a history of diabetes (P < 0.001) or hypertension (P = 0.02) than normal or overweight women. Smoking status was significantly associated with BMI: 13.6% of normal BMI women were current smokers versus 7.4% overweight and 2.3% obese (P < 0.001).

On average, women were diagnosed with breast cancer 7.5 years (SD 4.3) after enrolling into SOF. The time between enrollment and diagnosis of breast cancer did not differ across BMI categories (P = 0.60). Women most frequently presented with stage I or II disease (75.7%) that was ER (68.9%) and PR (54.0%) positive. A significant proportion of women had either borderline or unknown ER and PR status. ANOVA showed that these women tended to have an earlier time to breast cancer diagnosis than those with known ER status (P = 0.03); yet, this did not reach statistical significance for PR status (P = 0.11). The majority of these women were diagnosed with in situ (53.6%) or stage I/II (39.1%) disease. Breast cancer characteristics were not significantly different among categories of BMI. Average follow-up after breast cancer diagnosis was 8.1 years (SD 4.4) and did not vary by BMI category (P = 0.87). At the end of follow-up, 206 women were deceased: 56 from
A significant interaction was observed between BMI category and the outcome of death from any cause (Pinteraction = 0.02). To illustrate the effect modification, estimated HRs were calculated at five age levels (65, 70, 75, 80, and 85 years old at diagnosis) and for the mean BMI of the normal (22.6 kg/m²), overweight (27.3 kg/m²), and obese (34.0 kg/m²) women. For a woman ages 65 years at diagnosis, the risk of all-cause mortality was higher as BMI increased (BMI 22.6 kg/m²: HR, 1.00, reference; BMI 27.3 kg/m²: HR, 1.08; 95% CI, 0.92-1.27; BMI 34.0 kg/m²: HR, 2.41; 95% CI, 1.07-5.45). As age increased, however, those with higher BMI had either a similar risk of all-cause mortality (at age 75: BMI 22.6 kg/m²: HR, 1.00, reference; BMI 27.3 kg/m²: HR, 1.08; 95% CI, 0.92-1.27; BMI 34.0 kg/m²: HR, 1.21; 95% CI, 0.82-1.77) or a lower risk of all-cause mortality (at age 85: BMI 22.6 kg/m²: HR, 1.00, reference; BMI 27.3 kg/m²: HR, 0.81; 95% CI, 0.65-1.01; BMI 34.0 kg/m²: HR, 0.59; 95% CI, 0.36-1.02) as those with lower BMI.

Similar interactions were observed for death from any cancer (Pinteraction = 0.08) and death from breast cancer (Pinteraction = 0.05). Among women age 65 at diagnosis, the risk of death from any cancer was four times higher for an overweight BMI and five times higher for an obese BMI compared to a normal BMI. However, there was no significant difference in survival rates among BMI categories for breast cancer-specific mortality, with the exception of women age 85 (BMI < 22.6 kg/m²: HR, 0.81; 95% CI, 0.50-1.30; BMI ≥ 22.6 kg/m²: HR, 3.36; 95% CI, 1.28-8.78).

Table 1. Baseline demographics and breast cancer characteristics of study sample, stratified by baseline category of BMI

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All (N = 533)</th>
<th>Normal (BMI &lt; 22.6 kg/m²)</th>
<th>Overweight (BMI 22.6-27.3 kg/m²)</th>
<th>Obese (BMI ≥ 27.3 kg/m²)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at breast cancer diagnosis, mean (SD)</td>
<td>78.0 (5.7)</td>
<td>77.8 (5.7)</td>
<td>78.2 (5.8)</td>
<td>77.9 (4.0)</td>
<td>0.77</td>
</tr>
<tr>
<td>Age at breast cancer diagnosis, n (%)</td>
<td>65-69</td>
<td>43 (8.1)</td>
<td>20 (10.0)</td>
<td>14 (6.9)</td>
<td>9 (7.0)</td>
</tr>
<tr>
<td>70-74</td>
<td>127 (23.8)</td>
<td>43 (21.5)</td>
<td>48 (23.5)</td>
<td>36 (27.9)</td>
<td></td>
</tr>
<tr>
<td>75-79</td>
<td>165 (31.0)</td>
<td>63 (31.5)</td>
<td>68 (33.3)</td>
<td>34 (26.4)</td>
<td></td>
</tr>
<tr>
<td>≥ 85</td>
<td>144 (27.0)</td>
<td>56 (28.0)</td>
<td>52 (25.5)</td>
<td>36 (27.9)</td>
<td></td>
</tr>
<tr>
<td>BMI at visit 1, mean (SD)</td>
<td>27.1 (4.8)</td>
<td>22.6 (1.7)</td>
<td>27.3 (1.4)</td>
<td>34.0 (3.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Age-adjusted mortality rates of breast cancer survivors in SOF stratified by BMI category (mean follow-up after diagnosis 8.1 ± 4.4 y)

<table>
<thead>
<tr>
<th>Vital status</th>
<th>Total, n (%)</th>
<th>Normal; 18.5 to &lt; 25 kg/m² (n = 200)</th>
<th>Overweight; 25 to &lt; 30 kg/m² (n = 204)</th>
<th>Obese ≥ 30 kg/m² (n = 129)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>327 (61.4)</td>
<td>122 (61.0)</td>
<td>126 (61.8)</td>
<td>79 (61.2)</td>
<td>—</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>206 (38.7)</td>
<td>78 (39.0)</td>
<td>78 (38.2)</td>
<td>50 (38.8)</td>
<td>13.93 (8.47-22.89)</td>
</tr>
<tr>
<td>Death from cardiovascular disease</td>
<td>56 (10.5)</td>
<td>23 (11.5)</td>
<td>19 (9.3)</td>
<td>14 (10.9)</td>
<td>3.36 (1.28-8.78)</td>
</tr>
<tr>
<td>Death from any cancer</td>
<td>68 (12.8)</td>
<td>22 (11.0)</td>
<td>32 (15.7)</td>
<td>14 (10.9)</td>
<td>8.77 (3.81-20.19)</td>
</tr>
<tr>
<td>Death from breast cancer</td>
<td>45 (8.4)</td>
<td>17 (8.5)</td>
<td>17 (8.3)</td>
<td>11 (8.5)</td>
<td>5.90 (2.16-16.12)</td>
</tr>
</tbody>
</table>
obese woman (HR, 4.20; 95% CI, 1.23-14.31) and nearly twice higher for an overweight woman (HR, 1.81; 95% CI, 1.09-3.00) compared with a woman of normal BMI. At age 80 and above, women with higher BMI were observed to have a lower risk of death from any cancer (at age 85: BMI 22.6 kg/m²: HR, 1.00, reference; BMI 27.3 kg/m²: HR, 0.72; 95% CI, 0.47-1.09; BMI 34.0 kg/m²: HR, 0.45; 95% CI, 0.16-1.22), although this effect did not reach statistical significance. Similar results were observed for death from breast cancer. An obese woman age 65 had a five times higher risk of death from breast cancer compared with a same-age woman of normal BMI (HR, 4.93; 95% CI, 1.12-21.70). Conversely, an obese woman age 85 had a lower risk of death from breast cancer compared with a same-age woman of normal BMI (HR, 0.30; 95% CI, 0.08-1.09), although this did not reach statistical significance.

The effect of BMI on risk of death from cardiovascular disease was not observed to depend on age (Pinteraction = 0.49). Furthermore, increased BMI was not independently associated with risk of death from cardiovascular disease after breast cancer diagnosis. The risk of cardiovascular mortality was similar among women with BMIs of 34.0 kg/m² (HR, 0.99; 95% CI, 0.51-1.91), 27.3 kg/m² (HR, 1.00; 95% CI, 0.76-1.31), and 22.6 kg/m² (reference).

We evaluated whether differences in change in BMI between baseline and diagnosis existed by age or baseline BMI category using ANOVA. These analyses revealed a borderline significant interaction between age and BMI category (Pinteraction = 0.10), such that the oldest (≥75) obese women decreased in BMI an average of 1 to 2 units, whereas those of normal weight or overweight averaged less than a 1-unit increase in BMI between baseline and diagnosis (data not shown). There were no differences in BMI change by baseline BMI category among women ages 65 to 74 years.

A number of women were unable to attend a clinical visit at year 2 and provided only questionnaire data at that time. We evaluated whether their lack of attendance may have indicated poor health early in the study and therefore biased our results. In sensitivity analyses restricted to the 480 women with a clinical visit at year 2, we observed similar results as in our entire cohort, although point estimates and P values were slightly attenuated. The interaction between age at diagnosis and BMI for all-cause mortality remained statistically significant (Pinteraction = 0.046).

Discussion

The effect of elevated BMI on risk of all-cause, any cancer, and breast cancer mortality varied by age in this cohort of older breast cancer survivors. At younger ages (e.g., age 65 and 70 years), women with higher BMI also had a higher risk of all-cause, any cancer, and breast cancer mortality. Increasing BMI seemed to have no effect on these outcomes among women age 75 at diagnosis. Among the oldest women (e.g., age 80 and

Figure 1. Kaplan-Meier survival curves for all-cause and cause-specific mortality stratified by BMI category. Unweighted log-rank tests for equality of survival curves by BMI category: A, all cause (P = 0.98); B, cardiovascular (P = 0.86); C, cancer (P = 0.29); D, breast cancer (P = 0.99).
85 years), those with higher BMI were observed to have a lower risk of death from any cause, any cancer, or breast cancer. Although in some cases, the point estimates of these hazards ratios did not reach statistical significance, a trend toward BMI having a positive effect among the younger women in the cohort (e.g., age 65 years), no effect among the women in the middle of the age range of the cohort (e.g., age 75 years), and an inverse effect among the oldest women in the cohort (e.g., 85 years) is apparent. BMI had no effect on risk of cardiovascular mortality after a breast cancer diagnosis in this prospective cohort of SOF participants ages ≥65 years at diagnosis.

These results, which find an age-dependent association between BMI and survival from postmenopausal breast cancer, differ from those reported in a number of previous studies, in which obese postmenopausal breast cancer survivors had poorer survival (11-13, 27-30). One study, however, reported that whereas there was a significant association between BMI and increased all-cause mortality in their entire cohort, this association did not exist among the postmenopausal women (HR, 0.84; 95% CI, 0.28-2.56; ref. 10). Other studies have reported no association between elevated BMI and survival from postmenopausal breast cancer (31, 32), and one reported that lower weight before diagnosis is predictive of a poorer prognosis (33), although no stratification by menopausal status was conducted in this study. Interestingly, some previous studies of premenopausal and postmenopausal women have reported that obese women have tumor characteristics associated with poorer prognosis, such as advanced stage and grade, larger tumor size, and more frequent involvement of nodes (34-36); yet, BMI was not associated with breast cancer characteristics in SOF.

Previous studies, however, have not been conducted using a cohort comprised entirely of women ages 65 years and older at diagnosis. Most prior studies have included women ages 65 years and older at diagnosis; yet, this age group accounted for less than 50% of the study population in those studies where it was possible to determine the age distribution (11, 12, 29, 35, 37-39). Two studies did not include any women over age 65 years at diagnosis (10, 40). The results reported here are likely due to the unique age characteristics of the SOF cohort. Among older adults, the risk of death associated with obesity may be lower (20), or even inverse (19), with a BMI around 30 kg/m² associated with minimal risk of death (18). Reviews of the literature have also concluded that elevated BMI does not increase the risk of mortality in older adults except in cases of extreme obesity (41, 42). Indeed, our results show that increased BMI may have little effect, or even a positive effect, on survival after breast cancer at older ages. It is possible that older individuals who are overweight have greater physiologic reserves and so are better equipped to deal with weight loss that may occur as a result of breast cancer. It has also been hypothesized that the lack of increased mortality among overweight and obese older adults is due to a survival bias, in that only obese individuals who are less susceptible to the effects of obesity survive to become older adults (42). Thus, the BMI categories typically used in adult populations may not be applicable to older adults. Breast cancer incidence rates increase with age, and the highest rates are observed among women ages 75 to 79 years (447.3 per 100,000; ref. 17). Thus, breast cancer among older adults is a significant public health problem, and further studies of older breast cancer survivors are necessary to confirm the findings reported here.

This analysis has many strengths in addition to including a large cohort of women diagnosed with breast cancer after age 65. The SOF cohort is well characterized, and long-term follow-up data are available. The vast data available on other risk factors for mortality allowed for control of possible confounders in this analysis. Breast cancer cases and mortality outcomes were adjudicated using a variety of sources. Finally, data on height and weight were measured in the clinic rather than obtained by self-report. It is known that women underreport their true weight (43) and older women also tend to overestimate their height (44, 45), thus leading to significant underestimation of calculated BMI (43, 45). The use of measured height and weight data eliminates the potential bias of self-reported BMI.

There are a number of factors that limit this study, however. First, although nearly 40% of the breast cancer survivors had died during follow-up, cause-specific analyses were underpowered due to small numbers of events. The interactions between BMI and age on risk of death from any cancer and from breast cancer were of borderline statistical significance (Pinteraction = 0.08 and Pinteraction = 0.05, respectively) and may have reached statistical significance had a larger number of

Table 3. Estimated HR for the effect of BMI at SOF enrollment on mortality after breast cancer diagnosis

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>BMI HR (95% CI)</th>
<th>Pinteraction*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>22.6 kg/m²</td>
<td>27.3 kg/m²</td>
</tr>
<tr>
<td>Death from any cause</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>1.00</td>
<td>1.44 (1.03-2.01)</td>
</tr>
<tr>
<td>70</td>
<td>1.00</td>
<td>1.25 (0.99-1.58)</td>
</tr>
<tr>
<td>75</td>
<td>1.00</td>
<td>1.08 (0.92-1.27)</td>
</tr>
<tr>
<td>80</td>
<td>1.00</td>
<td>0.94 (0.81-1.09)</td>
</tr>
<tr>
<td>85</td>
<td>1.00</td>
<td>0.81 (0.65-1.01)</td>
</tr>
<tr>
<td>Death from cardiovascular disease †</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>1.00</td>
<td>1.00 (0.76-1.31)</td>
</tr>
<tr>
<td>70</td>
<td>1.00</td>
<td>1.81 (1.09-3.00)</td>
</tr>
<tr>
<td>75</td>
<td>1.00</td>
<td>1.44 (1.02-2.02)</td>
</tr>
<tr>
<td>80</td>
<td>1.00</td>
<td>1.14 (0.90-1.44)</td>
</tr>
<tr>
<td>85</td>
<td>1.00</td>
<td>0.91 (0.69-1.19)</td>
</tr>
<tr>
<td>Death from breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>1.00</td>
<td>1.93 (1.05-3.56)</td>
</tr>
<tr>
<td>70</td>
<td>1.00</td>
<td>1.45 (0.96-2.18)</td>
</tr>
<tr>
<td>75</td>
<td>1.00</td>
<td>1.08 (0.80-1.46)</td>
</tr>
<tr>
<td>80</td>
<td>1.00</td>
<td>0.81 (0.57-1.16)</td>
</tr>
<tr>
<td>85</td>
<td>1.00</td>
<td>0.61 (0.35-1.04)</td>
</tr>
</tbody>
</table>

Note: Each model is adjusted for a separate set of covariates based on stepwise backward model building. Any cause: age, diabetes, smoking status, hypertension, stage, ER status; cardiovascular: age, diabetes, history of stroke, hypertension; any cancer: age, stage, ER status, history of heart attack; breast cancer: smoking status, stage, ER status.

*From a likelihood ratio test of the model containing an interaction between age and BMI compared with the main effects model.

†No significant interaction between age and BMI was observed for the outcome of death from cardiovascular disease (for all ages).
outcomes have been observed. Additionally, this analysis included only Caucasians, and women were in generally good health at SOF baseline; thus, these women may not be representative of the general population of breast cancer survivors. No information on treatments received for breast cancer was available, thus confounding by type of treatment received might exist. However, we had information on stage at diagnosis and ER/PR status and were able to control for these prognostic factors in our analyses. Furthermore, the BMI of the women at SOF baseline was used as the independent variable of interest, and because the average time between SOF enrollment and diagnosis of breast cancer was ~7.5 years, many women may have gained or lost weight before their diagnosis. We evaluated this potential for bias by calculating the change in BMI between baseline and diagnosis. No differences by BMI category existed among women ages 65 to 74 years, but among women ages ≥75 years, mean BMI decreased among the obese but was stable among the normal and overweight. Thus, the present results should be unbiased for women ages 65 to 74 years but may be biased among those over age 75 as some women classified as obese at baseline may have been classified as overweight or normal at the time of their breast cancer diagnosis. It is a strong possibility, however, that such weight loss among the oldest obese women may have resulted from undetected disease before the clinical diagnosis of breast cancer. As the baseline weight measurements were likely to be representative of women’s usual adult weight and less influenced by latent disease, we believe that the baseline measure of BMI is the most appropriate for use in these analyses. We also found that the effect of increased BMI on mortality depended on age in this cohort of older breast cancer survivors. Although elevated BMI might be detrimental to the post-diagnosis survival of women at younger ages, as women approach their mid-70s increased BMI may be less of a concern. As the U.S. population increases in both age and BMI, further studies of the effect of BMI on survival among older women diagnosed with breast cancer are necessary.

References
Body Mass Index and Mortality among Older Breast Cancer Survivors in the Study of Osteoporotic Fractures

Katherine W. Reeves, Kimberly Faulkner, Francesmary Modugno, et al.


Updated version
Access the most recent version of this article at:
http://cebp.aacrjournals.org/content/16/7/1468

Cited articles
This article cites 42 articles, 11 of which you can access for free at:
http://cebp.aacrjournals.org/content/16/7/1468.full.html#ref-list-1

Citing articles
This article has been cited by 3 HighWire-hosted articles. Access the articles at:
/content/16/7/1468.full.html#related-urls

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.