

Solid Tumors

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Study Bolsters Obesity's Link to Poor Breast Ca Survival

by Ted Bosworth

Chicago—Obesity is associated with substantially increased mortality among women diagnosed with estrogen receptor (ER)-positive early breast cancer before menopause, according to data assembled from 80,000 patients presented at the 2014 annual meeting of the American Society of Clinical Oncology.

The data showed little to no association between obesity and any other type of breast cancer, including ER-positive tumors diagnosed after menopause, in contrast to the results of an earlier meta-analysis published in April in *Annals of Oncology*.

The effect of obesity on pre- rather than postmenopausal breast cancer patients was “the opposite of what we expected” but was highly significant, said investigator Hongchao Pan, PhD, who presented the study at the meeting (abstract 503). Dr. Pan, a senior researcher in the Clinical Trials Service Unit at the University of Oxford, in the United Kingdom, reported that the result was consistent across cancer grade, nodal status and HER2 receptor status.

The data were obtained from 70 clinical trials in early breast cancer that had detailed information about patient characteristics, including body mass index (BMI), menopause status, hormone receptor status and outcomes over extended follow-up. A Cox regression analysis was performed to evaluate the associations.



For the 20,000 premenopausal women with ER-positive breast cancer, the 10-year mortality among those who were obese—defined as a BMI of 30 kg/m² or greater—was 21.5%, which represented an absolute increase of 5% over the 16.6% mortality among those who were not obese. This translated into a relative risk (RR) for death of 1.34 (95% confidence interval [CI], 1.22-1.47; *P*<0.00001; Figure). The RR for death rose steadily in a stepwise fashion for increasing BMIs stratified as less than 20, 20-25, 25-30, 30-35 and more than 35.

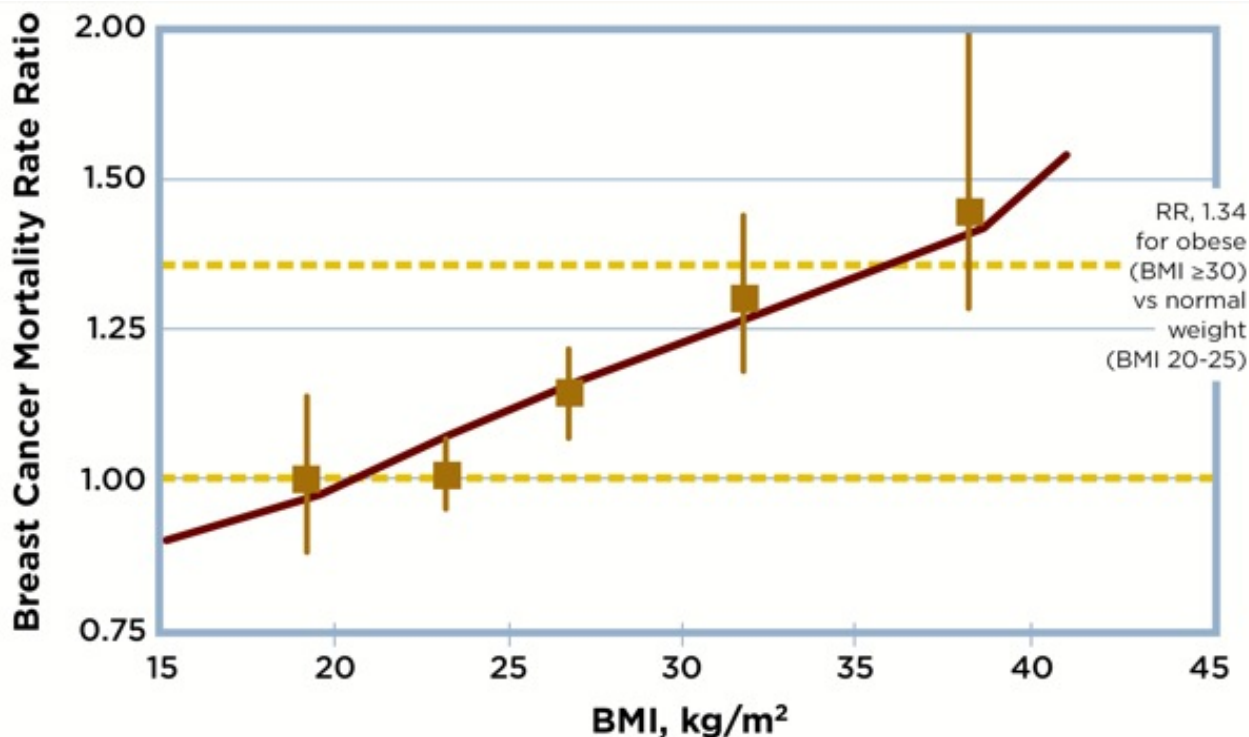


Figure. Premenopausal ER+ breast cancer mortality by BMI.

BMI, body mass index; **ER+**, estrogen receptor–positive; **RR**, relative risk

BMI	n
<20	1,913
20-25	10,189
25-30	5,983
30-35	2,348
35+	1,286

In the postmenopausal women with ER-positive breast cancer, the RR for death of 1.06 was not statistically significant, and there was no change in risk for death for obese compared with non-obese women who had ER-negative breast cancer, regardless of menopausal status.

When the analysis was restricted to ER-positive breast cancer patients aged between 44 and 54 years, the RR for death was 1.34 among premenopausal patients and 1.08 among postmenopausal patients, regardless of age; this finding reinforced menopausal status, not age, as the discriminator for the association between obesity and risk for death.

It was noted that tumors were somewhat smaller in normal-weight women at the time of diagnosis than in obese women, but the effect of obesity persisted after adjusting for this variable. There was no heterogeneity when looking at the overall effect of obesity on mortality when patients were grouped by different variables, such as breast conservation or type of chemotherapy.

This is not the first study to associate obesity with increased mortality among breast cancer patients, but it is one of the largest and provides compelling evidence that the risk is greatest for premenopausal women with ER-positive disease, implicating ovarian activity in this association.

Despite this, not all the evidence suggests that the risk is confined to premenopausal women. In the meta-analysis, recently published in *Annals of Oncology* (Chan et al. 2014 April 27. [Epub ahead of print]), the RR for breast cancer death in the presence of obesity before diagnosis was 1.50 (95% CI, 1.13-2.00) in premenopausal women and 1.34 (95% CI, 1.21-1.48) in postmenopausal women.

These data do not necessarily contradict the data from Pan et al, according to Doris Chan, the study's first author, who is completing a PhD in the Department of Epidemiology and Biostatistics at the Imperial College's School of Public Health, in London. Unlike the pooled analysis conducted by Pan et al, which used data from women participating in clinical trials, the meta-analysis led by Ms. Chan also included observational studies.

Patients participating in trials "could be younger, better educated and healthier," speculated Ms. Chan, who noted that the association between obesity and higher mortality in the study by Pan et al also was positive in postmenopausal women, even if it was not statistically significant. She suggested that more data are needed from population-based studies that "are more applicable to a wider range of breast cancer survivors."

Indeed, Ms. Chan indicated that these two studies may have more similarities than differences. "Both studies highlighted evidence that excess body fatness leads to poorer survival in women with breast cancer," she said. "This is supported by plausible biological mechanisms, including tumor proliferation, increased cell survival and angiogenesis."

Drs. Pan and Ms. Chan reported no relevant financial relationships.

Weight Gain Common After Breast Cancer Diagnosis

Chicago—Within a year of a diagnosis of breast cancer, nearly half of patients gain significant body weight, according to data from a prospective cohort study. By the end of two years, the proportion grows to more than 60%. This finding confirms anecdotal reports and raises concern in the context of evidence that increased weight may adversely affect prognosis.

The factors involved in weight gain after a diagnosis of breast cancer may be complex, according to data presented by a team of investigators from the hematology/oncology program at Northwestern University's Robert H. Lurie Comprehensive Cancer Center, in Chicago. At the 2014 annual meeting of the American Society of Clinical Oncology (ASCO; abstract 1543), they reported that certain types of breast cancer and certain genetic polymorphisms were associated with an increased likelihood of weight gain.

In this study, 120 women were recruited at Northwestern and evaluated at the time of diagnosis and then every six months for body mass index (BMI), nutritional status and exercise levels. In addition, patients were genotyped for single nucleotide polymorphisms (SNPs) in the *FTO* gene, which had been previously shown by two of the authors

of this study, Virginia G. Kaklamani, MD, and Maureen Sadim, to be related to both breast cancer and obesity (Kaklamani et al. *BMC Med Genet* 2011;12:52, PMID: 21489227).

At the end of 12 months, 45.3% of patients had a significant increase in BMI, and this rose to 60.9% at the end of 24 months, according to Dr. Kaklamani, an associate professor in the Division of Hematology/Oncology. Although neither chemotherapy nor endocrine therapy was associated with weight gain after controlling for age, race, baseline BMI, nutritional status and exercise levels, patients with progesterone receptor–positive breast cancer were significantly more likely than other breast cancer subtypes to experience significant weight gain. Moreover, two SNPs—rs9939609 and rs1477196—were associated with increased likelihood of weight gain.



Several studies have associated obesity with adverse outcomes in breast cancer, including a new study at the 2014 ASCO annual meeting in premenopausal women (see related story), but it is unclear whether weight gain after diagnosis also adversely affects outcome and if prevention of weight gain can provide a protective effect. Data from this study suggest that the pathologies of obesity and breast cancer may share a common mechanism, piquing interest in understanding whether weight control is a meaningful goal in the management of patients with breast cancer.

—*T.B.*

Dr. Kaklamani and Ms. Sadim reported no relevant financial relationships.

ASCO Targets Link Between Obesity and Ca in New Initiative

In its first policy statement on the connection between obesity and cancer, the American Society of Clinical Oncology (ASCO) called for increased education, research and advocacy to reduce the epidemic, both as a leading cause of cancer and as a hurdle in the care of patients with cancer.

The society outlined four priorities, including increased education and awareness about links between obesity and cancer, development of new physician tools and resources, intensified and coordinated research, and policy changes to increase access to obesity screening, diagnosis and treatment.

In addition to the recommendations, the release emphasizes that obesity is projected to soon overtake tobacco as the leading preventable cause of cancer in the United States.

“With nearly three in four Americans obese or overweight, obesity has become a tremendous public health challenge that also impacts cancer care and prevention today,” ASCO immediate past president Clifford A. Hudis, MD, FACP, said in a statement. “We can’t allow obesity to undo decades of progress in prevention, early diagnosis and treatment of cancer.”

Supporting ASCO’s stance, studies related to breast cancer and colorectal cancer have strengthened the association between obesity and cancer and increased mortality. The related story

on this page describes a recent study that underscores the connection of obesity to lower survival among premenopausal women. Additionally, data presented at the annual American Association for Cancer Research International Conference on Frontiers in Cancer Prevention Research showed that young Swedish men who were obese or had blood markers indicating high levels of inflammation were 2.37 times more likely to develop colorectal cancer later in life than those who were normal weight as adolescents (see <http://bit.ly/1CEmljv>).

—*Paul Bufano*