Breast Cancer Care in Old Age: Where Do We Go From Here?

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Breast cancer is a disease primarily of older women. The cumulative risk for this disease reaches its maximum well into the ninth decade of life (1). It is also a serious disease in older women. The approximate 10-year risk of disease recurrence for women 70 years of age or older who are lymph node negative with 1- to 5-cm tumors is 20%-30%; the risk for women with one to three positive lymph nodes and tumors of any size is 50%; the risk for women with four or more positive lymph nodes and tumors of any size is 80% (2). These risks are especially clinically relevant because recent gains in life expectancy have occurred at the end of life: The average life expectancy of an 85-year-old woman is nearly 6.5 years (3).

During the past decade, several studies (4-9) have documented age-related variations in care among patients with early stage breast cancer. These studies were conducted in a variety of health care settings and geographic regions. They have demonstrated age-related differences in diagnostic and prognostic evaluation as well as in initial treatment patterns. As a result of these studies, there has been heightened interest in understanding, in particular, variations in the use of mastectomy versus breast-conserving surgery with or without radiation therapy among older women and the impact of these variations on patient outcomes.

In this issue of the Journal, Ballard-Barbash et al. (10) have added to our understanding of age-related variations in breast cancer care through the use of a unique dataset that links Medicare claims records with data from nine tumor registries participating in the Surveillance, Epidemiology, and End Results (SEER) Program. Studying older women with newly diagnosed early stage disease, these investigators have documented the independent effects of age and comorbidity on the use of breast-conserving surgery versus mastectomy and on the use of radiation therapy following breast-conserving surgery. Specifically, they found that women aged 80 years or more, those with two or more comorbid conditions, and those with stage I disease were more likely to receive breast-conserving surgery. In contrast, among those receiving breast-conserving surgery, the oldest old (≥80 years of age) were much less likely to receive postoperative radiation therapy. In multivariate modeling, both age and comorbidity were independently associated with the receipt of postoperative radiation therapy. The oldest old and those with two or more comorbid conditions were less likely to receive radiation therapy.

Particular strengths of this study include the enrollment of a large cohort of patients (n = 18,704) cared for in nine different geographic settings, the careful attention to statistical control for potentially confounding factors, and the use of a validated measure of comorbidity. Nonetheless, the limitations of the data raise questions about the validity and the interpretation of the findings.

First, differential ascertainment of comorbidity may have importantly biased the data. A comorbidity score could not be calculated for 15% of the sample. Moreover, the authors note that only 36% of women who underwent breast-conserving surgery without axillary lymph node dissection had a reference hospitalization identified for the purpose of calculating the comorbidity index. Since it is the oldest old who are least likely to undergo axillary lymph node dissection (8), underascertainment of comorbidity in this group may have magnified the independent effect of age on the receipt of treatment. This possibility is supported by the fact that, for example, although there were 1352 women 80 years old or older who underwent breast-conserving surgery, only 220 of the entire sample undergoing breast-conserving surgery had two or more clinically important comorbid conditions. Not only do 80% of persons 65 years old or older have at least one chronic condition, but also the prevalence of chronic diseases increases dramatically with age, and multiple chronic conditions are especially common among older women (11).

Second, as Ballard-Barbash et al. (10) noted, the SEER database does not contain any information about functional status, social support, or patient preferences. In old age, functional status is a better predictor of mortality and other adverse events such as nursing home placement than is comorbidity (12). Furthermore, impaired function and diminished social support are particularly common among the oldest old. In particular, because of gender disparities in life expectancy, older women are frequently single and lack family or other supports (13). Because functional status and social support issues may limit an older woman's ability both to access and to tolerate radiation therapy, forgoing postoperative radiation therapy may not be an unreasonable decision, particularly in view of data not only suggesting low disease recurrence rates among older women receiving breast-conserving surgery but no postoperative radiation therapy (14-16), but also suggesting no significant survival advantage for those receiving breast-conserving surgery plus postoperative radiation therapy in comparison with those receiving breast-conserving surgery alone (17).

Third, the SEER database also does not contain any information about tamoxifen therapy. For example, we do not know how many women who underwent breast-conserving surgery

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were treated with tamoxifen in place of postoperative radiation therapy. Anecdotally, this pattern of care is relatively common among the oldest old, although this practice has not been studied systematically.

Fourth, and perhaps most importantly, the dataset does not include detailed outcome information. Indeed, few data are available that address outcomes among older women. What data there are suggest that, with respect to mortality, age-related variations in treatment patterns may be less important than stage (1,18). Furthermore, the oldest old are more likely to die with their disease rather than of it (19,20). Unfortunately, physicians are very inaccurate in their assessments of a given patient’s future life expectancy, and we do not know how variations in treatment have an impact on the often more relevant outcomes of functional status and quality of life.

Given these limitations, where do we go from here? It is important to remember that age-related variations in care are not unique to breast cancer patients. Such variations have been noted not only in patients with other cancers (21-23), but also in patients with other diseases (24,25). The U.S. population is aging rapidly; yet we lack the scientific knowledge base to guide our clinical decision-making. Because of the increasing heterogeneity that is the hallmark of aging, generalizing from studies of younger patients is not always appropriate.

If we are to design studies to address questions of efficacy and effectiveness in old age, what are the essential elements that must be incorporated? First, we need studies of the oldest old. The findings reported by Ballard-Barbash et al. (10) highlight the fact that it is the group 80 years old or older about whom we know very little; this lack of knowledge is manifested by large variations in how they are treated. Although efforts should be made to design clinical trials for this age group, the known barriers to enrolling these patients into such trials (26,27) mean that considerable education of physicians, patients, and their families will be required before such trials will be feasible, purely from the standpoint of sample size. Even if adequate sample sizes can be achieved, there will always be concerns about generalizability, which will be magnified only in studies of the oldest old.

Second, we need to conduct studies that include the broadest range of older patients. Most likely, these studies will be observational. Although methodologically challenging, they offer the best prospect for answering many of the questions about which we care most. For example, we might learn about variations in outcomes among patients who have received breast-conserving surgery, with or without postoperative radiation therapy, by performing careful follow-up studies of patients treated in geographic regions with high and low rates of postoperative radiation therapy following breast-conserving surgery. These studies will require careful attention to such potential confounding variables as functional status and health-related quality of life. Moreover, they must recognize that patients themselves are the best sources of this information. Investigators conducting research on aging have developed psychometrically sound methods for measuring these variables in older persons (28). These measures, however, have been incorporated infrequently into studies of cancer patients. Thoughtful incorporation of these measures into future studies will require the close collaboration of geriatricians, oncology specialists, epidemiologists, and health services researchers, at the very least.

Age is the most important risk factor for the development of breast cancer and many other diseases. Our challenge is to develop a sound body of scientific knowledge upon which we can draw to make the best decisions for and with our older patients. They deserve no less.

References

GETTING THE FACTS ON 5 A DAY
How Americans are doing when it comes to fruits and vegetables

Why eat five?
As the link between diet and overall health continues to gain attention, public awareness of the benefits of fruits and vegetables has expanded. In a recent survey, 1,003 people were asked how likely they thought it is that eating fruits and vegetables can help reduce the risk of several health conditions. Perceived health benefits most frequently mentioned were:

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<thead>
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<th>Prevent Heart Disease</th>
<th>Lose or Maintain Weight</th>
<th>Prevent Cancer</th>
<th>Lower Fat in Your Diet</th>
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<tr>
<td>59%</td>
<td>64%</td>
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Source: National Cancer Institute
A National Cancer Institute Graphic