Not Performing a Sentinel Node Biopsy for Older Patients With Early-Stage Invasive Breast Cancer

Axillary surgery contributes to morbidity and has not been shown to improve survival in early breast cancer. Women 70 years of age or older with clinically node-negative breast cancer are more likely to have comorbidities and reduced life expectancy, and there is controversy as to whether or not a sentinel node biopsy is warranted in this population. The purpose of our study was to evaluate the safety of not performing a sentinel node biopsy for patients 70 years of age or older with clinically node-negative breast cancer.

Methods | With institutional review board approval from Cedars-Sinai Medical Center, a review of a prospectively maintained database from January 1, 2000, to December 31, 2011, identified 140 women 70 years of age or older with clinical T1-2No breast cancer who underwent breast-conserving surgery without a sentinel node biopsy at our institution. Informed consent was not obtained because the data were de-identified. The clinicopathological characteristics were documented: age at diagnosis, tumor size, histology, grade, estrogen receptor (ER) and progesterone receptor (PR) status, HER2 status, and adjuvant therapy received (radiation, chemotherapy, or hormonal therapy). Locoregional recurrence, breast cancer–specific survival, overall survival, and causes of death were determined. Statistical analysis ($\chi^2$ test and log-rank test) was performed to characterize the study population and determine predictors of overall survival.

Results | Among 140 patients, the median age was 83 years (range, 70-97 years). Tumors were more frequently T1 (74%) than T2 (26%) tumors ($P < .001$), were more frequently grade 2 (62 patients [44%]) than grade 1 (38 patients [27%]) or grade 3 (40 patients [29%]) ($P = .03$), were more frequently positive (86%) than negative for ER (14%) ($P < .001$), were more frequently positive (73%) than negative for PR (27%) ($P < .001$), were more frequently negative (92%) than positive for HER2 (8%) ($P < .001$), and were more frequently of ductal histology (65%) than any other histology (35%) ($P < .001$). More patients did not receive than did receive chemotherapy (98% vs 2%; $P < .001$), radiation (76% vs 24%; $P < .001$), or hormonal therapy (59% vs 41%; $P = .04$). The median follow-up period was 4.5 years. Of 140 patients, 5 (4%) experienced a breast cancer–related event: 1 experienced an axillary recurrence (tumor was negative for ER, PR, and HER2), and 4 patients died of breast cancer (2 patients were negative for ER, PR, and HER2; 1 patient was negative for ER and HER2 and positive for PR; and 1 patient was positive for ER and HER2 and negative for PR). The 5-year overall survival rate was 70%, and the 5-year breast cancer–specific survival rate was 96% (Figure). The most common cause of death was ischemic heart disease. Tumor size was the only factor that correlated with survival.

Discussion | Patients with breast cancer who are 70 years of age or older present challenges in treatment as physicians aim to optimize therapy while accounting for life expectancy, comorbidities, and the effects of treatment on function. Women 70 to 74 years of age with breast cancer have, on average, 3 comorbidities, and for women 75 to 84 years of age, this number increases to 4.1 In addition, 85% of patients with node-negative breast cancer who are 70 years of age or older and 65% of patients with node-positive breast cancer who are 70 years of age or older die of causes unrelated to breast cancer.1 In this age group, survival is not dependent on nodal tumor burden, and a sentinel node biopsy carries morbidity that may be unnecessary.

Our study demonstrated low axillary recurrence and low mortality for patients with clinical T1-2N0 breast cancer who were 70 years of age or older and who underwent breast-conserving surgery without a sentinel node biopsy. Several randomized trials2-5 have demonstrated that the extent of axillary lymph node dissection has been omitted as a standard of care for appropriately selected patients undergoing breast-conserving surgery, a sentinel node biopsy is still relied on to determine prognosis and guide treatment. As adjuvant therapy becomes increasingly guided by genomics, the use of a sentinel node biopsy may be questioned. Early operable breast cancer in older patients tends to be positive for ER, emphasizing the importance of hormonal therapy.6

Figure. Kaplan-Meier Survival Estimates

<table>
<thead>
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<th>No. at Risk</th>
<th>Breast Cancer</th>
<th>Overall</th>
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</thead>
<tbody>
<tr>
<td>Follow-up Year</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>0.00</td>
<td>55</td>
<td>77</td>
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<td>0.50</td>
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Our patient population was largely positive for ER, but only 40% received hormonal therapy. Despite this, only 4% of patients experienced a breast cancer–related event.

Not performing a sentinel node biopsy may avoid potential morbidity and should be reevaluated for patients 70 years of age or older with clinically negative nodes. Patients were unlikely to have treatment recommendations changed based on a sentinel node biopsy, and adjuvant therapy was less likely to be administered, regardless of nodal status. Patients in this subgroup were more likely to die of causes other than breast cancer, and not performing a sentinel node biopsy did not affect survival.

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Letters

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SELECTIVE VS NONSELECTIVE NONSTERoidal ANti-INFLAMMATORY Drugs and ANASTomotic LEakage After Colorectal Surgery

To the Editor We read with interest the article by Hakkarainen et al and wish to commend the authors on their attempt to shed light on the challenging question of nonsteroidal anti-inflammatory drugs (NSAIDs) and the risk for anastomotic leakage after colorectal surgery. A growing body of evidence has implicated NSAIDs, particularly selective NSAIDs, as a risk factor for anastomotic leakage. These types of NSAIDs work by inhibiting the cyclooxygenase (COX) class of enzymes: COX1, which is present throughout the body (including the vascular endothelium, stomach, and kidneys) and COX2, which is predominantly found at the site of injury (triggered by inflammatory mediators).

Hakkarainen et al found a 24% increase in the leak rate in their cohort of patients who underwent bariatric surgery, elective colorectal surgery, or nonelective colorectal surgery. In their subgroup analysis, the association was limited to non-elective colorectal surgery (odds ratio [OR], 1.70 [P = .01]), not elective colorectal surgery (OR, 1.13 [P = .36]). They acknowledged that they could not specify the NSAIDs used in their study, but they believed that nonselective NSAIDs, such as ketorolac tromethamine, were predominantly used.

We feel that there are 2 points requiring emphasis and clarification. First, the classification of selective vs nonselective NSAIDs is often misunderstood. The term selective refers to the newer class of COX2 inhibitors, whereas nonselective NSAIDs are generally thought to indiscriminately inhibit both isoforms. In point of fact, however, this is not the case. Nonselective NSAIDs can inhibit either COX1 or COX2 preferentially. Diclofenac, a nonselective NSAID, behaves like a selective NSAID and, in fact, has an inhibitory profile similar to that of the selective NSAID celecoxib, preferentially inhibiting COX2. Ketorolac, another nonselective NSAID, preferentially inhibits COX1 more so than any other commercially available NSAID.

Second, virtually all NSAIDs have the potential to inhibit both COX enzymes regardless of their selectivity. For example, celecoxib will inhibit 60% of COX1 enzymes at 80% of its maximal inhibitory concentration for COX2. In our article looking at the perioperative use of ketorolac and anastomotic leakage after elective colorectal surgery, we found no association with leakage (OR, 1.21 [P = .66]). We attributed this to ketorolac’s COX1 selectiveness. However, in our subgroup analysis, higher doses were associated with leakage (OR, 1.29 [P = .048]) for every 15-mg increase in ketorolac administered.

Perioperative use of NSAIDs and anastomotic leakage remain important issues in the fast-track era of multimodal pain management. Future studies should address the selectivity of


COMMENT & RESPONSE

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None reported.

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Drs Chung and Gangi had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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