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Have the American College of Surgeons Oncology Group Z0011 trial results influenced the number of lymph nodes removed during sentinel lymph node dissection?

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Abstract

BACKGROUND: The American College of Surgeons Oncology Group Z0011 trial results have the potential to bias the number of sentinel lymph nodes (SLNs) surgeons remove and axillary lymph node dissections (ALNDs) performed.

METHODS: A single-institution prospectively collected database was queried for T1 to T2 clinically node-negative breast cancer patients.

RESULTS: A total of 923 patients underwent breast conserving therapy with SLN biopsy. The mean number of SLNs retrieved before the trial's presentation (June 2010) was 2.7 compared with 2.6 after ($P = .19$). The mean number of SLNs retrieved before the trial's publication (February 2011) was 2.7 compared with 2.5 after ($P = .10$). Overall, the rate of completion ALND in patients with SLN macrometastases decreased from after presentation (84% to 63%; $P < .01$) and publication (83% to 62%; $P < .01$).

CONCLUSIONS: There was no difference in the number of SLNs harvested after either the Z0011 trial presentation or publication; however, surgeons should be aware of the potential for bias. The trial appears to influence practice management with fewer completion ALNDs performed after its release.

The management of the axilla in clinically node-negative breast cancer has evolved dramatically over the past several decades. As recent as the early 1990s, the treatment of potentially curable breast cancer included removal of level I and II axillary nodes.[1] Routine axillary lymph node dissection (ALND) was challenged when Giuliano et al[2,3] demonstrated sentinel lymph node biopsy (SLNB) could accurately stage the axilla and further reports demonstrated decreased surgical morbidity with SLNB alone. In cases of positive sentinel lymph nodes (SLNs), completion ALND remained standard practice[4]; however, a trend to forgo completion ALND in certain subsets of patients emerged with the new millennium.[5,6] Most recently, the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial showed

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noninferiority for overall and disease-free survival in patients with particular tumor characteristics undergoing breast conserving therapy (BCT) and SLNB alone as compared with patients undergoing SLNB with completion ALND followed by whole breast radiation and systemic therapy.[7] After the trial was published, the American Society of Breast Surgeons released a position statement on axillary management of breast cancer patients stating that routine ALND may not be required for patients undergoing BCT that meet the following criteria: T1 to T2 tumors, 2 or less positive SLNs on SLNB without extracapsular extension, and patient acceptance to complete whole breast radiation and adjuvant systemic therapy.[8]

In breast cancer, there are commonly 1 to 4 SLNs in the axilla, and determining, which nodes are considered SLNs involves some degree of subjective interpretation by the operating surgeon. Factors influencing the number of SLNs removed have been reviewed, and prior reports suggest that indeed surgeons may retrieve more SLNs when the risk of metastasis is perceived to be greater.[9] Palpable tumors and surgeons with less experience are associated with removing more SLNs,[10] and clinical variables such as younger patient age ($\leq$50 years) and larger tumor size (T2 vs T1) are also associated with a greater number of SLNs retrieved.[9] In addition to patient age and tumor size, at our institution we found that more SLNs were retrieved in patients with higher grade tumors (grade 2 or 3 vs 1) and in those who had received neoadjuvant chemotherapy. The results of the ACOSOG Z0011 trial have the potential to likewise bias surgeons' attitudes toward SLN mapping in new ways. A recent study reviewed the impact of the trial on performance rates of SLNB vs SLNB with ALND[11]; however, no studies to date have evaluated if the results of the trial have influenced the number of SLNs retrieved. We hypothesized the belief may exist that there is less importance to the axillary lymph nodes (ALNs) in general, which could result in fewer SLNs being removed or that removal of all potential SLNs is of greater importance if no completion ALND will be performed, thus resulting in more SLNs being removed. We reviewed our institutional breast cancer database to determine if the Z0011 trial has impacted the number of SLNs harvested in patients undergoing BCT or the rate of completion ALND.

Materials and Methods

Approval was obtained from the institutional review board. A prospectively collected database of breast cancer patients was queried for all clinically node-negative breast cancer patients with T1 to T2 tumors who underwent BCT with SLNB by 3 surgeons at a single institution over a 10-year period (July 2003 to June 2013). The institutional SLNB technique was to perform dual tracer mapping with Tc-99-labeled sulfur colloid and isosulfan blue. The radioactive colloid was injected in a periareolar intradermal position and isosulfan blue was injected subdermally overlying the tumor or in a subareolar position. Nodes that were blue had a blue lymph channel leading to them, were the most radioactive, had gamma counts greater than or equal to 10% of the most radioactive lymph node, had gamma counts greater than or equal to 4 times the background lymph nodes, or were palpably suspicious were considered SLNs.

SLN counts were compared by time periods before and after the ACOSOG Z0011 trial abstract was presented at the American Society of Clinical Oncology Annual Meeting in June 2010 (July 2003 to May 2010 vs June 2010 to June 2013) and before and after the trial was subsequently published in the Journal of the American Medical Association in February 2011 (July 2003 to January 2011 vs February 2011 to June 2013). Z0011 criteria were not available from the database across the study period; however, the rate of completion ALND across all patients with SLN macrometastases was analyzed. Student t tests were performed to determine if more or fewer SLNs were removed and if fewer completion ALNDs were performed in patients with positive SLNs after the presentation and publication of the Z0011 trial results. For each comparison, a P value $< .05$ was considered statistically significant.

Results

In total, 923 patients underwent BCT with SLNB for T1 to T2 breast cancer from July 2003 to June 2013. The mean age of the entire cohort was 66 years (range, 31 to 94 years), and 100% were women. The majority of tumors were T1 (85%) and the mean tumor size was 1.36 $\pm$ .77 cm. The same 3 surgical oncologists performed all procedures during the 10 years; surgeon 1 = 452 procedures (49%), surgeon 2 = 277 procedures (30%), surgeon 3 = 194 procedures (21%). The mean and median numbers of SLNs harvested per patient for the entire cohort were 2.7 and 2, respectively.

Before and after the Z0011 trial presentation in June 2010, 674 and 249 SLNBs were performed, respectively. The average patient age in each group before and after presentation was 66 years ($P = .99$) and the average tumor size for both groups was 1.35 cm (1.35 cm $\pm$ .79 prepresentation vs 1.35 cm $\pm$ .71 postpresentation; $P = .96$). The mean number of SLNs retrieved before the presentation was 2.7 (95%

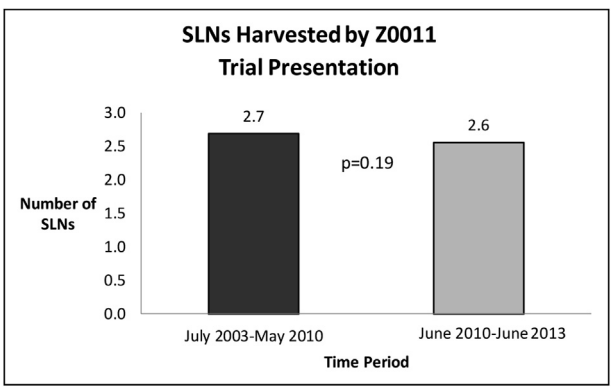

Figure 1 Mean number of SLNs harvested before and after the Z0011 trial presentation.