HHS Public Access

Author manuscript

JAMA Oncol. Author manuscript; available in PMC 2019 February 01.

Published in final edited form as:

JAMA Oncol. 2018 February 01; 4(2): 250–251. doi:10.1001/jamaoncol.2017.3625.

Management of the Node-Positive Axilla in Breast Cancer in 2017: Selecting the Right Option

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The variety of options now available for managing the breast cancer patient with axillary nodal metastases is confusing. For more than 100 years, axillary dissection (ALND) was the standard approach, but now, sentinel node biopsy (SLNB) alone, SLNB plus nodal radiotherapy, and neoadjuvant chemotherapy are all alternatives supported by evidence. This viewpoint will review the data informing patient selection for each of these approaches with the goal of minimizing the use of ALND and its associated morbidity.

A negative physical examination of the axilla is sufficient to identify patients who are candidates for axillary staging with SLNB. Patients with palpable, clinically suspicious lymph nodes should undergo needle biopsy to confirm the presence of cancer. In the presence of palpable nodal metastases, the only option for avoiding ALND is the use of neoadjuvant therapy. This has been reviewed elsewhere, and this discussion pertains to the patient with a normal clinical examination. Controversy exists regarding the need for routine preoperative axillary ultrasound ± needle biopsy to triage patients to ALND. Trials examining alternatives to ALND discussed below defined eligibility based on physical examination alone, and studies suggest that performance of ALND based solely on abnormal-appearing nodes on ultrasound or a needle biopsy containing tumor result in an unnecessary ALND in 32% to 71% of cases.[1,2]

The approach to patients with metastases in 1 or 2 sentinel nodes varies with the breast procedure being performed. In those having breast-conserving surgery with whole breast irradiation (BCT), randomized trials provide evidence for safe, less morbid alternatives to ALND. The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial and the Radiotherapy or Surgery of the Axilla After a Positive Sentinel Node (AMAROS) trial randomized patients with T1 or T2, clinically node-negative breast cancers undergoing BCT and found to have metastases in 1-2 sentinel nodes to ALND or no further axillary treatment (ACOSOG Z0011) or axillary radiotherapy (AMAROS).[3,4] At 5 years, no differences in nodal recurrence, disease-free survival, or overall survival were seen in either study. Ten-year results of ACOSOG Z0011 confirm the stability of these findings. Although the AMAROS trial tells us that axillary radiotherapy results in local control and survival outcomes equivalent to those seen with ALND, but with a lower risk of lymphedema,[3] it

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

does not tell us that all patients need axillary radiotherapy since similar excellent outcomes were reported in ACOSOG Z0011 without specific treatment of the axillary node field.[4]

High-level evidence to decide which patients require axillary radiotherapy is lacking. In a prospective study of 793 consecutive node-positive patients meeting ACOSOG Z0011 eligibility criteria and treated with SLNB alone, no isolated nodal recurrences were seen and the 5-year risk of any nodal recurrence was 1.4%, with only 21% of the group selected for nodal irradiation.[5] The controversy regarding the need for nodal radiotherapy in the presence of positive nodes has been fueled by the MA.20[6] and European Organisation for Research and Treatment of Cancer (EORTC) 22922-10925[7] studies which compared radiotherapy to the breast alone to treatment of the breast and node fields in patients with nodal metastases undergoing BCT with ALND. Both studies showed a significant decrease in locoregional recurrence and metastatic breast cancer, and a 1-2% overall survival difference at 10 years with radiotherapy, leading some to advocate nodal irradiation for all node-positive patients. The modest benefit of radiotherapy in these large studies, coupled with its modest toxicity, argue against this approach. At present, features predictive of heavier nodal tumor burden such as extent of nodal involvement, microscopic extracapsular tumor extension in the sentinel nodes, larger primary tumor size, and lymphovascular invasion are used to select higher-risk patients for nodal irradiation after SLNB. In contrast to the options available for patients undergoing breast conservation with 1 or 2 sentinel node metastases, patients with metastases to ≥ 3 sentinel nodes who were not included in ACOSOG Z0011 or AMAROS require ALND.

For patients undergoing mastectomy, ALND is indicated if any sentinel node metastases are present. This group was excluded from ACOSOG Z0011, and only 248 patients in AMAROS had mastectomy,[3] so the importance to regional control of the radiotherapy that is part of BCT is uncertain. Evidence supports 2 exceptions to the need for ALND in node-positive mastectomy patients. Two studies randomizing patients with sentinel node micrometastases to ALND versus no treatment included patients having mastectomy.[8,9] Both showed no difference in disease-free survival between groups, suggesting that ALND is not necessary in patients with micrometastases, even in the absence of radiotherapy. The AMAROS trial[3] demonstrated that breast and limited nodal irradiation are equivalent to ALND, so when the finding of sentinel node metastases coupled with other tumor features is sufficient indication for postmastectomy radiotherapy without knowledge of the total number of nodes involved, ALND is not necessary. A limitation of this approach is that limited pathologic information is available at the time of mastectomy, so a decision on the need for ALND may need to be deferred until complete pathology is available, necessitating a second surgery.

Another alternative proven to reduce the incidence of axillary metastases prior to surgery is the use of neoadjuvant chemotherapy. In clinically node-negative patients undergoing BCT, regardless of hormone receptor or HER2 status, neoadjuvant therapy did not decrease the need for ALND when ACOSOG Z0011 was applied. In contrast, in those with HER2 positive or triple negative breast cancers treated with mastectomy, neoadjuvant therapy significantly reduced the need for ALND (odds ratio [OR] 0.19 HER2+, OR 0.25 triple negative) in multivariable analysis in a retrospective study of 1980 patients.[10] The

overarching goal when selecting an axillary management strategy is to reduce the use of ALND. The optimal approach to achieve this goal will depend upon the type of breast surgery being performed, and the hormone receptor and HER2 status of the tumor; however, ALND should no longer be considered routine management of the node-positive breast cancer patient.

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