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The Evolution of Axillary Surgery in Breast Cancer-Towards De-escalation

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The primary goals of axillary surgery in breast cancer are multifactorial and include ensuring accurate staging, guiding adjuvant therapy decisions, predicting recurrence, achieving local control, and, most importantly, improving overall survival. As axillary lymph node status remains a crucial prognostic indicator, there is a constant attempt to balance oncologic safety with reducing morbidity-particularly lymphedema-to enhance patients' quality of life.

Over the past century, axillary surgery for breast cancer has experienced a significant change. This journey commenced with the radical approach pioneered by Halsted (operation vs. no operation-40% survival advantage in operated arm), where axillary lymph node dissection (ALND) was the norm. But in the 1970s, the NSABP B-04 trial marked a pivotal turning point. The 25-year follow-up statistics, published in 2002, demonstrated no significant survival difference between ALND and axillary radiotherapy (RT) in node-positive patients.[1] This led the medical community to pursue less invasive methods and to encourage the surgical de-escalation of axillary surgery.

A major milestone in this transition was the landmark Z0011 trial, building on earlier work, including the 1994 study by Giuliano et al. that established sentinel lymph node biopsy (SLNB) as the standard method for axillary staging in clinically node-negative (cN0) patients.[1] Subsequent trials like IBCSG 23-01 and Z0011 validated that SLNB alone is adequate in patients with low axillary burden, making ALND unnecessary.[1] From 2013 onward, this approach became the standard clinical practice.

In 2017, the National Comprehensive Cancer Network (NCCN) guidelines further revised these criteria, recommending against ALND even in the presence of micrometastases, independent of their number.[2] The AMAROS and Z0011 trials collectively concluded that patients with 1-2 positive SLNs might safely avoid additional dissection.[1] According to the AMAROS, Z001, and OTOASOR trial results, even in patients with < 3 positive SLN, the omission of axillary dissection did not result in significant differences in terms of local recurrence, disease-free survival, or overall survival.[1] More recently, the INSEMA study revealed that for women over 50 with hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative, grade 1-2 clinical N0, clinical T1 tumors, axillary surgery might be omitted.[3]

Large cohort studies and meta-analyses have solidified the evidence for limited axillary intervention, particularly in older patients. A comprehensive meta-analysis by Liang et al.[4] provided substantial evidence that omitting axillary intervention in cN0 patients aged > 70 years did not adversely affect survival. The 2023 NCCN guidelines recommend that ALND should be considered only if the axillary status would directly impact systemic therapy or RT decisions.[5]

Even more conservative insights were provided by the SOUND trial, suggesting that SLNB might be omitted altogether in patients with a median age of 60 years with the hormone-positive HER2-negative subtype when chemotherapy is not planned. Omitting axillary evaluation, however, in younger populations, may still represent a clinical challenge.[6]

Looking ahead, the 2025 ASCO guideline update recommends: "Clinicians should not recommend routine SLNB in select patients who are postmenopausal and ≥ 50 years of age and with negative findings on preoperative axillary ultrasoundfor grade 1-2, small (≤ 2 cm), hormone receptor-positive, HER2-negative breast cancer and who undergo breast-conserving therapy."[7]

The role of SLNB post-therapy in the neoadjuvant setting has been clarified. Kahler-Ribeiro-Fontana et al.[8] demonstrated that in patients with cN1 staging before neoadjuvant therapy, performing SLNB post-treatment did not affect the 10-year survival rate. Montagna et al.[9] confirmed that even if the clipped node cannot be detected, dual tracer techniques and removal of ≥ 3 SLNs are usually adequate, as the clipped node is frequently one among the SLNs. Based on the ACOSOG Z1071 study results, SLNB has been demonstrated to be a safe technique in patients with initially node-positive disease who convert to node-negative status following neoadjuvant therapy when dual tracers are used and at least three SLN are retrieved.[10]

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For individuals with isolated ductal carcinoma in situ (DCIS), the 2024 NCCN guidelines recommend SLNB only if mastectomy is planned or if excision is anticipated to compromise the viability of a subsequent SLNB. For patients undergoing breast-conserving surgery, even for those with high-grade DCIS, comedonecrosis, or lesions > 5 cm, SLNB is typically not indicated.[11] Ongoing trials such as BOOG 2013-08, SOAPET, and NAUTILUS aim to ascertain whether axillary surgery can be totally avoided in patients with stage cN0 disease.[12] INSEMA results show that omitting SLNB in ultrasound-negative patients does not influence rates of local recurrence, distant metastasis, or mortality.[3]

The SENOMAC trial, which included patients with stage T3 tumors, revealed no significant difference between the SLNB and ALND arms.[13] SLNB and targeted axillary dissection after neoadjuvant therapy did not significantly differ in locoregional recurrence, 5-year disease-free survival, or disease-specific survival variables in the NEOSENTITURK trial.[14] The OPBC-05/ICARO study results validated the omission of ALND in patients with micrometastases detected on SLNB following neoadjuvant therapy.[15] Upcoming results from the TAXIS trial-which focuses on patients with up to three macrometastases and who have undergone neoadjuvant therapy-may further support the decision to completely avoid axillary surgery.[13]

In conclusion, the journey from extensive axillary dissection to SLN sampling and, more recently, to selective omission of axillary surgery reflects a larger trend toward individualized, less invasive cancer treatment. The key to this transition is determining whether axillary staging information will alter the course of treatment. We are currently investigating if ALND can be safely omitted, even in patients with positive SLNs following neoadjuvant therapy. The practice of axillary surgery may soon be rendered obsolete.

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