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EDITORIAL – BREAST ONCOLOGY

Optimizing Sentinel Node Biopsy After Neoadjuvant Therapy: Striving to Know What We Do Not Know

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Assessment of axillary lymph nodes in breast cancer patients via axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB) has been an integral part of staging and treatment paradigms for many years.[1] Since the advent of SLNB in the 1990s, surgeons have attempted to de-escalate the amount of surgery in the axilla to prevent complications such as lymphedema and neuropathy.[1–3]

Studies suggest that the accurate detection of sentinel lymph nodes in SLNB is as high as 97%, with a false-negative rate (FNR) of 5% to 10% for clinically node-negative patients who have not received neoadjuvant therapy (NAT).[1] A FNR lower than 10% has widely been accepted as sufficient to avoid ALND for patients with negative SLNB, allowing surgeons to prevent axillary complications for a majority of cN0 patients.

Management of the axilla in patients who have undergone NAT, however, remains an area of controversy, with data demonstrating that SLNB often is less accurate for this subset of patients. The two largest prospective studies evaluating SLNB after neoadjuvant chemotherapy are the SENTINA trial and The American College of Surgeons Oncology Group (ACOSOG) Z1071 trial, which demonstrated false-negative rates of 14.2% and 12.6%, respectively, bringing into question the reliability and safety of SLNB for this patient population.[4,5]

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Studies by Boughey et al.[6] and Caudle et al.[7] have yielded strategies for decreasing FNRs, including prioritizing removal of at least three nodes using a dual tracer approach as well as localization and excision of nodes that were biopsied, clipped, and known to be positive before to NAT. Currently, limited data are available on which factors in this patient population are associated with higher FNRs, particularly in cN0 patients, and for which patient populations it is safe in the long term to avoid ALND.

In their paper, "Outcomes of Sentinel Node Biopsy in Women With Breast Cancer Following Neoadjuvant Therapy: Systematic Review and Meta-Analysis of Real-World Data," Lin et al.[8] investigated the accuracy of SLNB after NAT in breast cancer patients. The authors performed a meta-analysis that included 61 prospective and 18 retrospective studies evaluating outcomes of SLNB for 10,680 patients who underwent NAT. This analysis included primary breast cancer patients with clinically positive or negative nodes who underwent SLNB followed by ALND as part of their management, with clear definitions and statistical analyses of sentinel lymph node identification rate and FNR. Furthermore, they stratified their data to identify factors associated with FNR such as stage, receptor status, tumor response, SLNB mapping technique, and number of sentinel nodes removed. The authors found that the pooled estimate of the identification rate was 90.6% and the pooled FNR was 11.8%. They found that estrogen receptor-negative status and retrieval of fewer than three sentinel nodes on SLNB were associated with significantly higher FNRs. Finally, they found that in the cohort of patients who were clinically node-negative before NAT, 26.8% had nodal metastases after NAT.

The study performed by Lin et al.[8] had several notable limitations. Their analysis included studies that were non-randomized controlled trials, introducing the possibility of selection bias. Furthermore, given the pooled analysis of several included studies, there was heterogeneity in the type of NAT used. In addition, NAT in this meta-analysis included chemotherapy, radiation therapy, and endocrine therapy, although the majority of the treatments were chemotherapy. Finally, whereas Lin et al.[8] comment on single versus dual tracer use in their subanalysis of mapping technique and its association with FNRs, they do not address limited axillary dissection. In a subset analysis from the ACOSOG Z1071 trial, the investigators found that the FNR could be as low as 6.8% when patients with clinically positive nodes had their previous positive node clipped and removed with the SLNB specimen.[5] Given this data, the practice of a limited or targeted axillary dissection (TAD) is increasingly used by surgeons to decrease the FNR for patients receiving neoadjuvant chemotherapy and has become an important component of locoregional axillary management, although long-term data on recurrence and survival are needed.

In summary, Lin et al.[8] are to be commended for conducting one of the largest studies to examine which factors may be associated with higher FNRs in SLNB after NAT. A major strength of their study was that it examined both clinically node-positive and node-negative patients, allowing the authors to determine that 26% of the patients found to be clinically node-negative before NAT were pathologically node-positive at the time of surgery, a finding that is higher than might be expected. This finding, as well as outstanding data on the long-term safety of ALND omission after TAD, highlight some of the challenges that remain in the arena of axillary management after neoadjuvant therapy. In collaboration with multidisciplinary partners, including quantitative experts in machine learning, surgeons must focus future research on how clinicians can predict and impute likelihood of response, recurrence, and survival after NAT without subjecting patients to unnecessary surgery and concomitantly morbid sequelae.

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