



# Omitting axillary surgery in breast cancer treated with neoadjuvant chemotherapy

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*Comment on:* Zaborowski AM, Doogan K, Clifford S, *et al.* Nodal positivity in patients with clinically and radiologically node-negative breast cancer treated with neoadjuvant chemotherapy: multicentre collaborative study. *Br J Surg* 2024;111:znad401.

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Axillary surgery has traditionally been used to control axillary metastasis and provide staging for further treatment planning. However, landmark trials like the ACOSOG Z0011 have demonstrated that axillary treatment does not offer a survival benefit, leading to a significant shift towards less aggressive management in early breast cancer (1). As a result, surgical approach has shifted from extensive axillary lymph node dissection (ALND) to the standardization of the less invasive sentinel lymph node biopsy (SLNB). Building on these trends, prospective trials are now exploring the possibility of omitting axillary surgery altogether in patients with clinically and radiologically node-negative early breast cancer.

The SOUND trial by Gentilini *et al.* was among the first to demonstrate that omitting axillary surgery is noninferior to SLNB in patients with small breast cancers (up to 2 cm) and negative axillary lymph node on ultrasonography (USG) (2). The success of such trials depends on accurate assessment of nodal burden to avoid clinical recurrences due to undetected disease. In the SOUND trial, the false-negative rate (FNR) for USG-determined nodal status was 13.7%. Currently, trials are ongoing for patients with larger tumors (up to 5 cm), including the NAUTILUS, INSEMA, BOOG 2013-08, and SOAPET trials (3).

Attention has now turned to de-escalating or omitting axillary surgery in patients who have received neoadjuvant chemotherapy (NCT). The ICARO study retrospectively examined the omission of ALND in patients with isolated tumor cells after NCT and found no significant difference in any invasive recurrence rates between those who underwent ALND and those who did not (4). Prospective trials, such as Alliance A001102, TAXIS, and ADARNAT were designed earlier to investigate if axillary radiotherapy could replace ALND in patients who have positive sentinel lymph nodes following NCT (5-7). Additionally, a retrospective analysis study using the National Cancer Database of 30,821 NCT patients with cT1-2, cN0-1 breast cancer found that nodal positivity was less than 2% in human epidermal growth factor receptor 2-positive (HER2<sup>+</sup>) or triple-negative breast cancer (TNBC) when there was no residual tumor in the breast following a good response to NCT (8). Consequently, three prospective trials (ASLAN, ASICS, EUBREAST-01) are investigating the safety of omitting axillary surgery in patients with a pathologic complete response in the breast.

Despite these trends, concerns remain about omitting axillary surgery, primarily due to the potential for missing

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metastatic lymph nodes and losing crucial nodal information needed for treatment planning. False negatives could result in patients not receiving necessary adjuvant systemic therapy or radiotherapy.

A recent study by Zaborowski *et al.* provides real-world insights into lymph node positivity rates after NCT (9). This multicenter, retrospective study assessed post-NCT nodal status in 371 patients with clinically and radiologically node-negative breast cancer, all with negative post-NCT axillary lymph node on USG. The overall nodal positivity was 12.7%, with the highest rates in hormone receptor (HR)<sup>+</sup>/HER2<sup>-</sup> breast cancer (29.0%), followed by HR<sup>+</sup>/HER2<sup>+</sup> (13.8%), TNBC (6.5%), and HR<sup>-</sup>/HER2<sup>+</sup> (5.6%). These results are similar to those reported by Barron *et al.* in cT1–2, cN0 patients (8).

When planning future trials on omitting axillary surgery post-NCT, it is crucial to consider acceptable FNRs. The SOUND trial had an USG FNR of 13.7%, while the FNR for SLNB itself was 9.8% in the NSABP B-32 trial (10). For patients converting from clinical node-positive (cN+) to clinical node-negative (ycN0) status, SLNB FNRs were reported to exceed 10% in most of studies: 14.2% in SENTINA, 12.6% in ACOSOG Z1071, and 13.3% in SN FNAC (11-13). Future trials for omitting axillary surgery in post-NCT patients might include TNBC and HER2<sup>+</sup> patients meeting the criteria from Zaborowski *et al.*, and consider HR<sup>+</sup>/HER2<sup>-</sup> patients with a good breast response to NCT.

The inclusion criteria for cN0 in Zaborowski *et al.*'s study were very strict, utilizing both USG and positron emission tomography (PET)/computed tomography (CT) for axillary staging. While routine PET/CT could improve the accuracy of predicting negative axillary lymph node status, it may reduce the study's generalizability. Magnetic resonance imaging is currently recommended for use in patients who have received NCT, and its role in lymph node evaluation should be considered in future studies.

Overall, the findings from Zaborowski *et al.* offer valuable evidence on nodal status in cT1–3, cN0 breast cancer post-NCT, supporting the design and refinement of further trials on de-escalating axillary surgery in selected patients.

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