



A multidisciplinary approach to axillary management in early-stage breast cancer: evolution and updates – a narrative review

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Background and Objective: Axillary management in breast cancer has evolved from radical, highly morbid procedures to increasingly individualized and minimally invasive strategies. Historically, axillary lymph node dissection (ALND) served as both a staging and therapeutic procedure, but was associated with complications such as lymphedema, sensory deficits, and reduced shoulder mobility. The introduction of sentinel lymph node biopsy (SLNB) enabled accurate staging with significantly lower morbidity. Landmark clinical trials subsequently demonstrated that completion ALND could often be safely omitted in selected patients with limited sentinel node involvement, paving the way for a more conservative surgical paradigm. This review summarizes historical milestones, current standards, and ongoing trials shaping axillary management emphasizing evidence-based de-escalation, personalized treatment approaches based on multidisciplinary team input, and patient-centered outcomes.

Methods: A comprehensive literature search was conducted in PubMed/MEDLINE, Embase, Cochrane Library, and ClinicalTrials.gov for studies published from January 1985 to September 2025. English-language randomized controlled trials, cohort studies, meta-analyses, and clinical guidelines were included. Studies were screened for relevance, and key landmark trials were included irrespective of date. Due to heterogeneity in designs and outcomes, findings were synthesized narratively.

Key Content and Findings: SLNB is accurate and safe for clinically node-negative (cN0) patients and those converting from node-positive to node-negative after neoadjuvant systemic therapy when technical standards are met, including dual tracers, retrieval of ≥ 3 sentinel lymph nodes (SLNs) and targeted axillary dissection with clipped nodes. Landmark trials demonstrate low recurrence and morbidity with SLNB alone. Omission of SLNB is feasible in older adults and select post-menopausal women with low-risk tumors, particularly when radiotherapy is planned. Radiation therapy and molecular profiling may guide adjuvant therapy decisions, complementing surgical de-escalation and reducing morbidity. Multidisciplinary planning to weave together surgical, radiation and systemic therapy options along with patient-centered decision making are vital to balance oncologic safety and quality of life.

Conclusions: Axillary management is shifting towards personalized and minimally invasive strategies that prioritize reducing morbidity without compromising oncologic outcomes.

Keywords: Axillary management; breast cancer; completion axillary dissection; sentinel lymph node biopsy (SLNB)

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Introduction

Accurate axillary staging is fundamental to the management of early-stage breast cancer, traditionally serving as a key determinant of prognosis and a guide for adjuvant therapy. Historically, the presence of nodal metastases significantly influenced decisions regarding chemotherapy, radiotherapy, and endocrine treatment. As such, complete axillary lymph node dissection (ALND) was long considered essential, due to its diagnostic and therapeutic value even in patients with no clinical evidence of nodal involvement (1). Accumulating evidence from randomized controlled trials eventually prompted a paradigm shift away from routine ALND due to limited survival benefit in low-risk populations and significant morbidity related to lymphedema and its impact on quality of life (QoL) (2-4).

The introduction of sentinel lymph node biopsy (SLNB) offered a less invasive method for axillary staging, minimizing complications like lymphedema and nerve injury while maintaining diagnostic accuracy (5). Simultaneously, advances in systemic therapy and radiotherapy, and the adoption of molecular profiling tools such as Oncotype DX and MammaPrint, have reduced reliance on nodal status for treatment planning. Additionally, hormone receptor-positive (HR⁺), human epidermal growth factor receptor 2 (HER2)-negative tumors—the most common subtype—have shown relatively low axillary recurrence risk, even when axillary intervention is minimized (6,7). Nonetheless, SLNB is not without complications; a proportion of patients still experience adverse effects such as lymphedema and shoulder dysfunction (8).

Modern imaging modalities like high-resolution axillary ultrasound have further improved preoperative staging accuracy, raising questions about the necessity of surgical staging in some patients. Recently, emerging data have suggested that in carefully selected patients omission of SLNB may be both safe and effective, especially among those receiving whole-breast radiotherapy. De-escalation of care needs to be balanced against the possibility of undertreatment which could result in an increased risk of recurrence or disease progression. Furthermore, the impact on adjuvant systemic and radiation therapy necessitates a more nuanced and multidisciplinary approach

to axillary management. Therefore, contemporary axillary management requires collaboration between surgeons, medical oncologists, radiation oncologists, radiologists and pathologists to balance oncologic safety with QoL, minimizing both the risk of overtreatment and undertreatment.

In the modern era, the central question is no longer whether we can safely omit or de-escalate axillary surgery, but whether the incremental prognostic information gained justifies the physical and psychological costs borne by patients. This review uniquely integrates patient-reported outcomes, systemic therapy eligibility implications, and radiation decision-making into a unified multidisciplinary framework by highlighting evolving evidence, controversies, and patient experience as a key determinant of axillary management. We present this article in accordance with the Narrative Review reporting checklist (available at <https://abs.amegroups.com/article/view/10.21037/abs-2025-1-68/rc>).

Methods

A comprehensive literature search was performed to identify studies evaluating axillary management strategies in early-stage breast cancer, with a focus on surgical de-escalation, SLNB, ALND, axillary radiotherapy, and omission of axillary surgery.

The following electronic databases were searched (PubMed/MEDLINE, Embase, Cochrane Library and ClinicalTrials.gov). The search included studies published from January 1985 through September 2025, reflecting the modern era of SLNB and axillary de-escalation. Only English-language publications were included.

Studies were eligible if they included patients with early-stage (T1–T2) breast cancer with a clinically node-negative (cN0) axilla or nodal downstaging following neoadjuvant systemic therapy (NAST). Eligible study designs comprised randomized controlled trials, prospective and retrospective cohort studies, meta-analyses, and major clinical practice guidelines evaluating axillary management strategies, including ALND, SLNB, axillary radiotherapy, targeted axillary dissection (TAD), or omission of axillary surgery. Case reports, small case series, studies restricted to metastatic, inflammatory, or recurrent breast cancer,

Table 1 The search strategy summary

Items	Specification
Date of search	September 30, 2025
Databases and other sources searched	Electronic databases searched included PubMed/MEDLINE, Embase, Cochrane Library and ClinicalTrials.gov. Additional sources included reference lists of relevant articles, key clinical trials, and international guideline documents
Search terms used	A combination of MeSH terms and free-text keywords related to breast cancer and axillary management were used, including: “Breast Neoplasms”, “early-stage breast cancer”, “axillary management”, “sentinel lymph node biopsy”, “axillary lymph node dissection”, “axillary radiotherapy”, “regional nodal irradiation”, “de-escalation”, “omission”, “neoadjuvant therapy”, “targeted axillary dissection”, “overall survival”, “disease-free survival”, “locoregional recurrence”, “quality of life”, and “lymphedema”. Filters were applied for human studies and English language
Timeframe	January 1985–September 2025
Inclusion and exclusion criteria	Inclusion criteria: randomized controlled trials, prospective and retrospective cohort studies, systematic reviews, and meta-analyses evaluating axillary management strategies in early-stage breast cancer; studies reporting oncologic outcomes and/or QoL outcomes; English-language publications Exclusion criteria: case reports, small case series (<10 patients), non-human studies, studies focusing exclusively on metastatic breast cancer, and articles without extractable outcome data relevant to axillary management
Selection process	Titles and abstracts were screened by primary author. Full-text articles were retrieved for potentially eligible studies and assessed independently. Discrepancies were resolved through discussion, and when necessary, consultation with senior author
Any additional considerations	Landmark clinical trials (e.g., ACOSOG Z0011, AMAROS, IBCSG 23-01, SOUND, SENOMAC, SINODAR-ONE) were included irrespective of publication date due to their clinical relevance

CENTRAL, Cochrane Central Register of Controlled Trials; QoL, quality of life.

non-human studies, and abstract-only publications without full-text availability were excluded. Titles and abstracts were screened for relevance, followed by full-text review when indicated, and reference lists of included studies and relevant guidelines were manually reviewed to identify additional eligible articles. Due to heterogeneity in study designs and reported outcomes, results were synthesized narratively rather than quantitatively. *Table 1* summarizes the search strategy.

Upfront surgery

The evolution of surgical axillary management

When Halsted’s radical mastectomy was first introduced in 1894, the axillary lymph nodes were considered the transit point between the breast and distant metastasis. This notion led to the practice of removal of all axillary lymph nodes regardless of clinical or radiologic nodal findings. Over time, ALND was being routinely performed for not only therapeutic purposes but also staging and prognostication (1,9). The presence of positive lymph nodes became an indication for adjuvant systemic therapy and consideration

of radiotherapy to the chest wall and/or regional lymph nodes even before the subtypes of breast cancer by receptor status were discovered. Unfortunately, ALND was associated with high morbidity, including lymphedema, sensory nerve injury, and impaired shoulder mobility (2).

Published in 1977, the National Surgical Breast and Bowel Project (NSABP) B-04 trial investigated whether less extensive surgery with or without regional nodal irradiation (RNI) would compromise outcomes, challenging the long-held “centrifugal spread” theory of cancer (10). It demonstrated that radical mastectomy offered no survival advantage over total mastectomy or limited axillary treatment among 1,700 patients, establishing the principle that more extensive surgery does not necessarily translate into better outcomes in breast cancer. While RNI improved locoregional recurrence rates, there was no survival benefit compared to observation alone of the axilla. As a result, this trial became the cornerstone of the idea that systemic therapy would be key to improving survival rather than more radical surgeries. A 25-year follow-up demonstrated no overall survival (OS) benefit to radical mastectomy compared to less extensive surgery, laying the foundation

for subsequent trials that validated modified radical mastectomy and breast conservation surgeries as well as de-escalation of axillary surgery (11).

The concept of SLNB emerged from the idea that tumor cells spread through lymphatic channels to the first draining lymph node, also called the sentinel lymph node. If the sentinel lymph node is free of cancer, downstream nodes are very unlikely to harbor metastases. The ALMANAC trial, published in 2006, was one of the earliest large prospective randomized studies to compare SLNB with ALND in patients with cN0 breast cancer. Evaluating more than 1,000 patients, the study demonstrated that SLNB resulted in significantly lower postoperative morbidity, including markedly reduced rates of lymphedema, sensory loss, shoulder dysfunction, and overall arm disability. Patients undergoing SLNB also experienced faster recovery, less postoperative pain, and better QoL scores. Although the study was not designed to evaluate survival outcomes, its strong morbidity data supported the shift toward SLNB as a less invasive and safer alternative for staging the axilla (3).

The NSABP B-32 trial further solidified SLNB as the standard of care. In this pivotal randomized study of more than 5,000 cN0 patients, OS, disease-free survival (DFS), and regional control were statistically equivalent between patients with negative sentinel lymph nodes who underwent SLNB alone and those who underwent completion ALND. Importantly, the SLNB group experienced significantly lower rates of lymphedema, pain, and shoulder dysfunction, confirming that accurate staging could be achieved with dramatically reduced morbidity (12,13). Together, the ALMANAC and NSABP B-32 trials established SLNB as the preferred approach for early-stage breast cancers with clinically negative axillae, while ALND remained reserved for patients with biopsy-proven axillary metastasis or sentinel node–positive disease prior to the era of de-escalation (4,5).

The idea of ‘less is more’ led to the proposal of further de-escalation strategies in axillary management. The ACOSOG Z0011 phase III non-inferiority trial demonstrated that ALND could be safely omitted in patients with T1–T2 tumors and 1–2 positive SLNs undergoing breast-conserving surgery (BCS) and radiotherapy, with no significant difference in survival or recurrence but with lower lymphedema and morbidity (13,14). It is important to note that 96% of patients enrolled received some form of adjuvant medical therapy although it was not a requirement to enroll. Similarly, the IBCSG 23-01 study demonstrated similar 10-year DFS between

SLNB versus SLNB with completion ALND (76.8% *vs.* 74.9%) among patients with micro-metastatic sentinel lymph nodes defined as ≤ 2 mm focus after breast conserving surgery or mastectomy (15).

The AMAROS phase III non-inferiority trial offered an alternative surgery-free approach to axillary management, demonstrating that axillary radiotherapy was non-inferior to ALND in patients with positive SLNs, with similar 10-year axillary recurrence (0.93% with ALND *vs.* 1.82% with radiotherapy) but fewer side effects (2). In this study, 17% of patients underwent mastectomy as their primary breast surgical procedure. Subsequently, another single center trial OTOASOR trial confirmed the AMAROS findings. Among 2,073 patients with early breast cancer and low SLNB burden, axillary nodal irradiation was noninferior to completion ALND in terms of survival and regional recurrence (16). Furthermore, real-world studies have also demonstrated low rates of recurrence collectively redefining axillary management with the focus shifting from extensive surgical clearance to multidisciplinary, risk-adapted treatment (16).

Contemporary axillary management

In this de-escalation continuum, subsequent studies paved the way for omission of SLNB among older adults ≥ 70 years of age. The IBCSG 10-93 trial was among the first to question the necessity of axillary surgery in older women. In this randomized study of more than 450 patients ≥ 60 years old with cN0, HR-positive breast cancer treated with adjuvant endocrine therapy, omission of axillary clearance demonstrated equivalent survival outcomes and better early QoL measures compared with axillary surgery (17). The subsequent CALGB 9343 study evaluated women ≥ 70 years undergoing lumpectomy and adjuvant endocrine therapy, randomizing them to receive or omit whole-breast radiation. All participants were clinically node-negative, and the trial showed no difference in OS regardless of whether radiation was administered—indirectly supporting reduced emphasis on aggressive axillary staging in this population (18). Further support came from Martelli *et al.*, who reported a 15-year follow-up of women ≥ 70 years treated without ALND. They found no breast cancer-specific mortality benefit from ALND and observed very low axillary recurrence rates, suggesting that even SLNB could be safely omitted in select older adults (19). Together, these studies helped shift practice toward minimizing or eliminating axillary surgery in low-risk older patients.

However, uncertainty remains for individuals with higher-risk features such as lymphovascular invasion, high-grade tumors, and HER2-positive disease.

More recently, the SOUND and INSEMA trials evaluated the safety of omission of SLNB altogether in those with early-stage breast cancer who are cN0 in the axilla confirmed by a negative axillary ultrasound. The SOUND phase III trial demonstrated that omission of axillary surgery is noninferior to SLNB for distant DFS in patients with cN0 T1–T2 breast cancer that is HR⁺ HER2-negative and negative axillary ultrasound. At 5 years, distant DFS was 98.0% in the no axillary surgery group versus 97.7% in the SLNB group, with no significant difference in axillary recurrence (0.4% *vs.* 0.3%) or OS (20). Similarly, the INSEMA phase III non-inferiority trial demonstrated that omission of SLNB in patients with cN0 T1–T2 HR⁺ HER2-negative breast cancer undergoing BCS was noninferior to SLNB for 5-year invasive DFS [91.9% *vs.* 91.7%, hazard ratio (HR) 0.91, 95% confidence interval (CI): 0.73–1.14], with low rates of axillary recurrence (1.0% *vs.* 0.3%) and improved patient-reported outcomes including less lymphedema, better arm mobility and less pain with movement (21). Notably, this study included postmenopausal women over the age of 50 years with grade 1 or 2 tumors. These trials suggest that in carefully selected populations, axillary surgery may be unnecessary, ushering in a new era of highly individualized axillary management. Given the relatively short follow-up of SOUND and INSEMA trials and the prolonged natural history of HR⁺ breast cancer, multidisciplinary discussions remain essential when considering omission of SLNB to ensure appropriate patient selection and alignment with surgical, radiation and systemic treatment decisions.

Long-term outcomes including regional recurrence rates and DFS are currently lacking. Even in cN0 patients, a small proportion of patients harbor micrometastases or isolated tumor cells (ITCs) (12). There is data to suggest individuals with micrometastases or ITCs tend to have a worse prognosis compared to those who do not (22). Without SLNB, occult metastases may go undetected, potentially impacting staging accuracy and prognosis. In addition, the criteria for omission of SLNB is quite specific and restricted to those deemed to have low-risk tumors. Hence, this is not suitable for those with higher-risk disease or when nodal status could influence adjuvant systemic therapy decisions. While randomized trials strongly support axillary de-escalation, real-world implementation is complicated by patient heterogeneity, tumor biology, and

institutional practice variation. The uptake of this approach has been slow especially in younger post-menopausal women in the absence of long-term follow-up for SOUND and INSEMA trials given the potential for late recurrences in those with HR⁺ HER2-negative breast cancers.

In summary, for clinically node-negative early-stage breast cancer, SLNB is the standard axillary staging procedure. If SLNs are negative, no further axillary surgery is needed. However, omission of SLNB for patients ≥ 70 years with HR⁺/HER2-negative, cN0, T1 tumors, and for some postmenopausal women ≥ 50 years with small, low-grade HR⁺/HER2-negative tumors undergoing upfront surgery may be considered (23). This approach minimizes morbidity compared to ALND (24). Omission of ALND is recommended for most patients with 1–2 positive SLNs who undergo BCS followed by radiotherapy based on ACOSOG Z0011 and AMAROS trial data. For individuals undergoing mastectomy with 1–2 positive SLNs, axillary radiation may replace ALND if adjuvant radiotherapy is planned (23). ALND is reserved for patients with ≥ 3 positive SLNs, gross extranodal extension, or residual nodal disease after neoadjuvant therapy. For micro-metastatic disease (>0.2 mm but ≤ 2.0 mm), ALND may be omitted based on multidisciplinary discussions (12,13). Notably, certain subgroups—such as those undergoing mastectomy with >2 positive SLNs—were excluded from pivotal trials, creating uncertainty in their management (25).

Neoadjuvant therapy

Surgical axillary management after NAST

Historically, NAST was reserved for patients with inoperable cancers. Over time, its indications have steadily expanded to include tumor downstaging to facilitate less extensive breast surgery, axillary downstaging, and postoperative tailoring of adjuvant therapy based on response to NAST. Despite these broadening indications, the major clinical trials that have shaped axillary management have primarily enrolled patients undergoing upfront surgery, leaving the optimal approach for those receiving NAST less clearly defined. Recognition that NAST can convert axillary nodes from positive to negative in a substantial proportion of patients, particularly in those with triple-negative or HER2-positive breast cancer, highlighted an opportunity to reconsider the extent of axillary surgery. This shift began with NSABP B-27, which demonstrated the potential for improved nodal response

following NAST (26).

Axillary management of clinically node-positive (cN1) to clinically node-negative (ycN0) following NAST

In ACOSOG Z1071, patients with biopsy-proven node-positive (cN1) disease who converted to ycN0 after NAST underwent SLNB. The trial showed that the false-negative rate (FNR) of SLNB was 12.6% (with >10% deemed to be unacceptably high FNR per pre-specified acceptable threshold). However, this FNR decreased from 12.6% to <10% when key technical refinements were incorporated, including the use of dual tracers, retrieval of three or more sentinel lymph nodes, pre-NAST placement and post-NAST removal of a clip in the biopsied positive node (i.e., TAD), and optimal patient selection guided by axillary ultrasound (27). The higher FNR observed in this trial was largely attributed to factors like altered lymphatic drainage after NAST, residual nodal disease not captured by limited SLN sampling and the failure to excise the originally positive lymph node when not marked, emphasizing the importance of technical refinements to improve the accuracy of SLNB.

Similarly, the SENTINA trial further reinforced that SLNB is feasible post NAST, reporting a false negative rate of 14.2% which was further lowered to less than 5% with removal of multiple lymph nodes and dual mapping (28). A meta-analysis highlighted the importance of the number of sentinel lymph nodes retrieved with decreasing false negative rates from 20% to 12% to 4% with retrieval of one, two and three sentinel lymph nodes respectively (29). These trials demonstrated that SLNB is a safe and reliable staging approach for patients with clinically node-negative down-staged axilla provided technical standards are met. They also paved the way for the modern TAD method. The AXSANA trial (NCT04373655) is a non-randomized observational trial comparing invasive DFS and axillary recurrence with various axillary staging techniques post NAST including TAD, SLNB and ALND.

For those with cN2–N3 disease, it is common practice to consider ALND with RNI irrespective of response to NAST due to low representation of this population in the trials evaluating SLNB following NAST comprising 19–30% of the study population (30,31). However, for those having a radiologic complete response or ypN0, SLNB is not discouraged by National Comprehensive Cancer Network (NCCN) guidelines.

Axillary management of persistent node-positive disease following NAST (ycN+) and following NAST and surgery (ypN+)

For those with ycN+ macrometastatic disease following NAST, ALND has been the recommended approach due to concern for higher risk of local recurrence (32). For those with ypN+ macrometastatic disease, once again ALND is the recommended axillary surgery. However, the management of axilla in patients with minimal lymph node burden following NAST including micrometastases and ITCs is an evolving field. While the safety of omitting ALND in the upfront setting for low lymph node burden has been well demonstrated, it is unclear if this can be extrapolated to the population receiving NAST with residual disease. In a single center observational study by Moo *et al.* evaluating more than 700 patients undergoing SLNB following NAST, 64% of those with micrometastasis and 17% of those with ITCs had additional lymph node involvement at the time of ALND, respectively (33). However, a retrospective cohort study (OPBC-07/microNAC) from multiple, global cancer centers showed low axillary recurrence at 3 years regardless of ALND *vs.* no ALND (1.7% *vs.* 2.3%, $P=0.92$) with nearly 80% receiving RNI. Notably, the triple negative breast cancer population had a higher risk of recurrence without ALND (8.7% *vs.* 2.4%, $P=0.02$). Similarly, ICARO randomized clinical trial enrolling more than 500 patients demonstrated no statistically significant difference in 5-year rate of invasive recurrence between those undergoing SLNB or ALND in those with residual ITCs (34). Finally, a meta-analysis evaluating oncological outcomes among patients with ypN+ disease treated with SLNB reported no difference in OS [odds ratio (OR) 0.90, 95% CI: 0.64–1.26, $P=0.54$] or 5-year rate of axillary recurrence (OR 1.08, 95% CI: 0.64–1.83, $P=0.77$) (35). Interestingly, a retrospective study from Spain demonstrated a ratio of positive SLNs (defined as number of positive SLNs to number of SLNs removed) ≥ 0.5 to be an independent risk factor of positive residual axillary disease with author suggesting use of this parameter as a guiding factor to determine optimal surgical management (36). The 2019 St. Gallen consensus panel recommended that patients with clinically positive axilla or with macro metastases on SLNB following NAST, undergo a completion ALND. There was lack of consensus on optimal management of residual micro-metastatic lymph nodes, but favoring consideration of ALND, unless regional nodal radiotherapy is being considered (37). SLNB with

Table 2 Current indications for ALND in the era of axillary de-escalation

Clinical scenario	Rationale for ALND
Residual nodal disease after NAST (ypN+)	Persistent disease indicates high residual tumor burden; SLNB/TAD inadequate for local control
Failure of SLNB or TAD (e.g., <2 SLNs retrieved, single tracer, clipped node not removed)	High FNR without optimal mapping; ALND needed for accurate staging
≥3 positive sentinel nodes on upfront surgery	Exceeds Z0011 criteria; suggests higher axillary tumor burden
Gross extracapsular extension of nodal metastasis	Associated with extensive axillary disease; generally, not eligible for de-escalated approaches
Mastectomy patients with positive SLNs who will not receive postmastectomy radiation	AMAROS allows ALND omission only if axillary RT is provided; without RT, ALND is indicated
Clinically bulky or matted nodes (cN2–cN3) at presentation managed with upfront surgery	Extensive nodal disease unsuitable for SLNB; ALND required for disease control
Axillary recurrence after prior SLNB	Salvage treatment requires definitive axillary clearance

ALND, axillary lymph node dissection; FNR, false-negative rate; NAST, neoadjuvant systemic therapy; RT, radiation therapy; SLN, sentinel lymph node; SLNB, sentinel lymph node biopsy; TAD, targeted axillary dissection.

RNI may be reasonable among those with micrometastases or ITCs in non-high-risk subtypes if determined so by multidisciplinary input due to limited prospective evidence. The results of the ALLIANCE A011202 (NCT01901094) phase III trial will be critical in defining whether ALND can be omitted in favor of radiation in residual node-positive patients in future guidelines.

Radiation therapy (RT) considerations following NAST

With de-escalation of surgical axillary therapies, RT de-escalation may also be feasible in certain scenarios. RNI has been recommended historically for everyone with cN+ disease at presentation irrespective of response to NAST although more recent data suggests we are possibly overtreating a subset of patients who achieve pathological complete response (pCR). NRG Oncology/NSABP-B-51/ RTOG 1304 trial looking at omission of RNI in those who achieved nodal pCR demonstrated no difference in 5-year invasive breast cancer recurrence-free interval between RNI and no RNI (92.7% *vs.* 91.8%, $P=0.51$) or isolated locoregional recurrence-free interval (99.3% *vs.* 98.4%, $P=0.09$) (38). In an exploratory analysis, the effect of RNI was noted to be variable by breast cancer subtype with HR⁺ breast cancer having a significant impact on invasive breast cancer recurrence and death (HR 0.41, 95% CI: 0.17–0.99) while triple negative breast cancer had none (HR 2.30, 95% CI: 1.00–5.25). This suggests the ability to forego RNI without compromising oncologic outcomes in select situations where

pCR is attained in the axilla. For those with ypN+ tumors following NAST, RNI with whole breast radiotherapy or post-mastectomy radiation is recommended depending on breast conservation surgery or mastectomy (39).

Who still needs an ALND? *Table 2* summarizes scenarios requiring the need for ALND.

Considerations while omitting SLNB

Axillary management for early-stage breast cancer must strike a balance between maintaining oncologic safety while also minimizing morbidity. Ongoing considerations include identifying the most appropriate candidates for complete omission of SLNB, optimizing imaging and surgical techniques, as well as implications of adjuvant systemic therapy and radiation.

Limitations of imaging in lieu of SLNB for staging

Omitting SLNB often depends on imaging modalities to rule out nodal involvement. Axillary ultrasound is an important tool for refining nodal staging, but its sensitivity and specificity are inconstant (40). Variability in practice and interpretation can potentially affect outcomes. The negative predictive value for axillary ultrasound is approximately 80% translating into a 10–30% possibility of missing metastases despite negative ultrasound (41,42).

Patient preferences

Minimizing surgical morbidity remains a key priority, yet

both patients and clinicians may be hesitant to omit axillary staging due to concerns about risk of recurrence and loss of prognostic information (24,43). Incorporating shared decision-making and clear communication regarding risk, benefits and evidence-based options is essential to align treatment with patient values and expectations. In addition, the shared wisdom of a multidisciplinary provider team is key to nuanced management of these individuals.

Global implications and generalizability

It is prudent to note that the resources to be able to safely omit SLNB require access to good axillary imaging, availability of genomic tests and long-term surveillance which is not uniformly available globally. Therefore, SLNB may be the best staging tool in resource-limited settings.

Implications on adjuvant endocrine therapy

For HR⁺ HER2-negative cancers, systemic endocrine therapy like tamoxifen and aromatase inhibitor is recommended based on tumor biology and size, not nodal status alone. Therefore, omission of SLNB has minimal therapeutic impact from an endocrine therapy perspective. However, duration of endocrine therapy may be impacted as extended endocrine therapy may be recommended to individuals with lymph node-positive cancers due to higher risk of recurrence. Notably, axillary de-escalation trials implicitly assume adherence to long-term endocrine therapy. In real world practice, up to 30% of patients may discontinue endocrine therapy due to adverse effects impacting QoL (44). This could subsequently increase the risk of recurrence in individuals with unknown axillary burden.

Implications on adjuvant chemotherapy and targeted therapy

Adjuvant chemotherapy decisions are typically guided by tumor genomic profiling through an Oncotype Dx or MammaPrint (45). This may be modestly affected in younger or higher risk cohorts where nodal involvement would traditionally influence treatment or genomic assay eligibility; however, in older adults or low-risk patients, chemotherapy is rarely indicated.

The absence of nodal status information could have potential implications on choice and duration of adjuvant CDK4/6 inhibitors. The monarchE and NATALEE trials have shown improvements in invasive DFS for individuals with HR⁺ HER2-negative breast cancer with addition of abemaciclib and ribociclib respectively (46-50). Adjuvant

abemaciclib also demonstrated a marginal OS benefit for individuals with high-risk of recurrence defined as 4 or more lymph nodes or those individuals with 1–3 lymph nodes with other high-risk features like tumor size of ≥ 5 cm or grade 3 disease (48). Notably, NATALEE had a broader inclusion criterion for eligibility with all individuals with lymph node-positive disease being eligible for adjuvant ribociclib use. A post-hoc analysis of SENOMAC trial found that performing an ALND to identify pN2–3 nodal status (at least 4 lymph node metastases) in patients with breast cancer and subsequent qualification for adjuvant abemaciclib was associated with a substantial risk of severe or very severe impairment of physical arm function (51). Using data from the monarchE cohort, it was calculated that ALND would need to be performed in 104 patients to avoid one invasive DFS event at 5 years with adjuvant abemaciclib, with 9 patients having severe or very severe impairment of physical arm function 1 year after surgery. Among post-menopausal women, 7.9% would have at least one adjuvant therapy decision impact by omitting SLNB, whereas it was 13.4% among pre-menopausal women. However, if adjuvant ribociclib decision was not considered, this came down to 2.5% among postmenopausal women and 12.6% among premenopausal women. Therefore, currently recommended cohort for omission of SLNB (postmenopausal, more than 50 years of age with T1–T2 HR⁺ HER2-negative breast cancer, grade 1–2 with no suspicious lymph nodes on imaging) has a low likelihood of requiring adjuvant ribociclib or abemaciclib. Future adjuvant systemic studies should not factor in number of pathological lymph nodes as they are less likely to be available with rapidly evolving axillary de-escalation strategies.

Implications for radiotherapy

Radiotherapy was a vital part of breast conservation surgery in both SOUND and INSEMA with 97.6% and 100% of patients receiving radiation in these trials (20,21). Although 8.7% and 11.6% of patients in these trials had macro metastases in the surgically removed axillary lymph nodes, only 0.4% and 1% risk of axillary recurrence over five years was observed in the no-SLNB arms suggesting incidental radiation coverage to the axillary area may have played a role in eradicating occult nodal involvement. This was similar to the ACOSOG Z0011 results where no difference was noted between ALND and observation following positive SLNB for patients receiving whole breast irradiation (WBI) despite ~27% patients having macro

metastases in non-sentinel lymph nodes (13).

Yet the challenge remains in determining the appropriate criteria for RNI in the absence of the sentinel node. RNI was demonstrated on the NCIC-CTG MA.20 trial of more than 1800 patients, roughly 90% of whom had early-stage node-positive disease, to improve 10-year DFS (82% *vs.* 77%, HR 0.76, 95% CI: 0.61–0.94) (52). The EORTC 22922/10925 trial enrolled roughly 4,000 patients with either involved nodes or medially/centrally located tumors without lymph node involvement (53). At the 10-year follow-up, this study revealed improved breast cancer mortality (12.5% *vs.* 14.4%, HR 0.82, 95% CI: 0.7–0.97) and DFS (82.0% *vs.* 77.0%, HR 0.76, 95% CI: 0.61–0.94) with a trend towards an OS benefit. Based on these studies patients who may benefit from RNI risk undertreatment in the absence of surgical assessment of the axilla.

Contrarily, data already exists for the omission of radiotherapy in certain low-risk breast cancers without surgical staging of the axilla. The CALGB 9343 trial looked at WBI *vs.* observation in women aged 70 years and over with small, low-grade estrogen receptor-positive breast primaries with clinically negative axillary nodes and who were taking adjuvant endocrine therapy (18). The 10-year local recurrence-free rate was 98% (95% CI: 96–99%) with radiotherapy *vs.* 90% (95% CI: 85–93%) without and no differences in time to mastectomy, distant metastases, breast cancer-specific survival, or OS. The IDEA trial looked at a younger population of age 50–69 years, pT1N0 HR⁺ and HER2-negative tumors with an Oncotype recurrence score ≤ 18 who agreed to at least 5 years of endocrine therapy and randomized them to WBI or observation. Although this study included only 200 patients, no difference was seen at 5 years for overall and cancer-specific survival (100%) with similar crude rates of overall recurrence at 5.0% or less (54). There are several ongoing trials such as the PRECISION study looking at whether other genetic assays can identify younger patients that may safely omit radiotherapy. Such lines of investigation may also eventually be tailored to identify those without surgical axillary staging who can safely omit RNI.

Future directions in axillary management

Future directions in axillary management for early-stage, cN0 T1–T2 breast cancer are centered on further de-escalation of surgeries, individualized treatment based on tumor biology and reduction of treatment-related morbidity.

Studies like NAUTILIUS are evaluating de-escalation in a broader patient population including younger patients and those with other subtypes of breast cancer. They are expected to further refine patient selection for surgical omission strategies (55). Alliance A011202/MAC19 are investigating feasibility of omission of ALND in individuals with residual nodal disease following NAST, with all participants receiving nodal radiotherapy. These studies seek to determine the oncologic safety of SLNB alone or TAD in the post neoadjuvant setting with pathologically positive lymph nodes (24,27).

Treatment algorithms are increasingly informed by tumor biology rather than purely anatomic staging. Molecular assays and genomic classifiers now play a major role in determining the need for systemic therapy, reflecting a shift from nodal burden to biologic risk assessment in treatment decision-making (24).

Patient perspective

From the patient's standpoint, axillary management decisions in early-stage breast cancer extend far beyond oncologic outcomes. Concerns about lymphedema, pain, arm mobility, and psychological distress significantly influence treatment preferences. Studies have shown that patients often prioritize QoL and functional outcomes when offered a choice between more and less invasive surgical approaches (56,57). The omission of SLNB may reduce anxiety related to postoperative complications, hospital recovery, and body image, especially among older adults or those with comorbidities. However, some patients also express fear that less surgery could equate to less thorough treatment, highlighting the importance of clear, empathetic communication (58,59). Shared decision-making, supported by risk prediction tools and individualized counseling, is essential to align treatment strategies with patients' values and expectations. The evolving trend toward de-escalation underscores the need to view auxiliary care not just through an oncologic lens, but also through the lived experiences of patients.

Conclusions

The management of the axilla in cN0 T1–T2 breast cancer has transformed from radical dissection to more conservative approaches grounded in strong clinical evidence. While SLNB remains the current standard, recent studies suggest that SLNB may also be safely

omitted in selected low-risk patients, marking a shift toward individualized, QoL-oriented care. Taken together, these developments support a growing rationale for de-escalating axillary surgery, especially in older patients with biologically favorable disease and planned adjuvant radiotherapy. This shift reflects an overarching goal in oncology: to personalize treatment in a way that maximizes efficacy while minimizing harm. However, implications on adjuvant systemic therapy and adjuvant radiation should be considered in treatment planning. This underscores further the need for a multidisciplinary team in optimally managing these patients.

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Footnote

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