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ORIGINAL ARTICLE

Implications of omitting sentinel lymph node biopsy on adjuvant decision making for patients with small breast cancers

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Abstract

Background: Selective omission of sentinel lymph node biopsy (SLNB) in patients with early breast cancer limits surgical morbidity. Adoption of this strategy relies on multidisciplinary consensus. Understanding how SLNB omission influences guideline-based adjuvant treatment decisions, and the proportion of patients impacted, can help guide decision-making.

Patients and methods: Data from the National Cancer Database (2018–2020) was used to estimate the proportions of patients with cT1N0 hormone receptor–positive breast cancer for whom adjuvant chemotherapy, CDK4/6 inhibitor therapy, and regional nodal irradiation decisions would be impacted by the absence of lymph node pathology if national treatment guidelines were followed. Because OncotypeDX score is essential to adjuvant decision-making when SLNB is omitted, inverse probability weighting was used to estimate the proportions of interest had all individuals undergone OncotypeDX testing.

Results: There were 119,312 included patients, with an average age of 63 years, 96,454 (80.8%) having invasive ductal histology, and 52,222 (43.8%) having cT1c tumors. The number of patients with SLNB positivity was 13,211 (11.1%). Among postmenopausal women, 7.9% (95% CI, 7.7–8.1) would have had at least one adjuvant decision impacted by the absence of lymph node pathology. For premenopausal women, the affected proportion was 13.7% (95% CI, 13.0–14.7). When ribociclib decision-making was not considered, these estimates were 2.5% for postmenopausal women and 12.6% for premenopausal women.

Conclusions: SLNB omission has a small – but not negligible – influence on adjuvant decision making in postmenopausal women, whereas a larger proportion of premenopausal women would be impacted. The reported estimates may inform multidisciplinary decision-making related to SLNB omission.

KEYWORDS
adjuvant therapy, breast cancer, guideline-concordant care, multidisciplinary decision making, omission of SLNB, sentinel lymph node biopsy (SLNB)

INTRODUCTION

Management of axillary lymph nodes in patients with breast cancer has continued to evolve toward selective omission of surgery to minimize surgical morbidity while maintaining oncologic safety. Until recently, sentinel lymph node biopsy (SLNB) has been the standard for axillary staging in patients with early breast cancer. However, evidence from the SOUND and INSEMA trials demonstrated that SLNB omission is noninferior to SLNB in patients with small, cN0 breast cancer and a negative axillary ultrasound undergoing upfront breast-conserving therapy.[1,2] Although the primary endpoint was 5-year distant disease-free survival in the SOUND trial and 5-year invasive disease-free survival in the INSEMA trial, both trials reported that outcomes were similar regardless of patient assignment to SLNB or its omission, and that the risk of locoregional or distant disease relapse was low.[1,2]

An important caveat to SLNB omission is that nodal involvement discovered following surgical axillary staging plays a role in guiding multidisciplinary team decision making. In particular, the decision to offer adjuvant therapies (e.g., chemotherapy, targeted therapies, regional nodal irradiation) partially depends on axillary staging. As such, the SOUND trial investigators concluded that patients can be spared axillary surgery only when omission does not affect the postoperative treatment plan.[1]

Reassuringly for patients and multidisciplinary teams considering omission of SLNB, the SOUND trial investigators reported that adjuvant systemic therapy and radiotherapy recommendations were similar for patients regardless of whether SLNB was performed.[1] Others have reported similar findings in postmenopausal patients treated at an academic cancer center.[3] Nonetheless, lymph node (LN) pathology remains germane to adjuvant decision making based on existing guidelines.[4] Thus, depending on how these guidelines are followed in the absence of surgical axillary staging, omission of SLNB may affect adjuvant decision making in some settings.

Arguably, decision makers might be better informed by learning the proportion of patients for whom LN pathology would alter their recommendations if current guidelines were followed with cN0 patients treated as pN0 when SLNB is omitted. The aim of this study was to estimate these proportions in the population of patients with cT1N0 hormone receptor (HR)–positive breast cancer.

METHODS

Study population and data

We used data from the National Cancer Data Base (NCDB) to study the potential impact of SLNB omission in a national cohort of patients diagnosed with breast cancer. The NCDB is a clinical cancer database initiated and maintained by the Commission on Cancer and the American Cancer Society. The NCDB data are sourced from hospital registries at more than 1500 Commission on Cancer–accredited facilities in the United States, with extensive internal quality monitoring validity reviews.[5] The NCDB collects wide-ranging details on cancer diagnosis, treatment, and follow-up including patient clinical characteristics, diagnostic test results, pathology details, treatments performed, and long-term outcomes. Patient level identifiers are not available to users of the database; therefore, this study was exempt from institutional review board review and approval.

Patients were eligible for inclusion in the cohort if they were diagnosed with cT1N0M0 HR-positive breast cancer, underwent upfront breast-conserving surgery with SLNB, had no cancer history, and had complete treatment and pathologic information available. Patient staging details are reported to the NCDB by individual accredited facilities and clinical staging was performed in accordance with the practice standards at each individual institution, which may not have routinely included axillary ultrasound.

Although the NCDB has collected data on incident cancers since 1989, information on the number of sentinel lymph nodes removed, the total number of regional LNs removed, and the number of positive LNs has only been recorded since 2018. Because this information is pertinent to adjuvant treatment decision making, we restricted the cohort to patients diagnosed between 2018 and 2020.

Variables

The NCDB includes information on patient age, clinical tumor stage, tumor histology, tumor receptor status, tumor grade, pathologic tumor size, the presence of multifocal or multicentric disease, the presence of lymphovascular invasion, and pathologic nodal information. Tumor histology was categorized as invasive ductal, invasive lobular, mixed invasive ductal and lobular, or other cancer (e.g.,

mucinous, papillary, tubular histologies). Because menopausal status is not recorded in the NCDB, we considered patients older than age 50 years to be postmenopausal. This age-based proxy is commonly used and correlates well with more comprehensive definitions of menopause used in epidemiologic studies.[6,7] Patients were considered to have undergone completion axillary LN dissection if 10 or more total axillary LNs were recorded to have been removed.

Treatment guidelines

We categorized patients as meeting or not meeting criteria for adjuvant treatments. For adjuvant chemotherapy and CDK4/6 inhibitor (CDK4/6i) decision making, following national guidelines informed, in part, by the TAILORx and RxPONDER clinical trials,[8–11] we considered patients as falling within categories defined by their menopausal status, number of positive LNs, and OncotypeDx score. For adjuvant radiation and CDK4/6i decision making, we adapted institutional and North American guidelines informed, in part, by the NCIC MA.20, EORTC 22922/10925, monarchE, and NATALEE clinical trials.[11–17] The criteria used for adjuvant therapy recommendations are summarized in Table 1.

Statistical analysis

We described the patient, tumor, and treatment characteristics for the cohort of patients. Stratified by menopausal status, we computed the proportions of patients with SLNB positivity, the proportions undergoing axiallry lymph node dissection (ALND), the proportions with one through three or 4+ positive LNs, and the proportions with measured OncotypeDX score.

Many patients with data in the NCDB did not have OncotypeDX information available. Because OncotypeDX testing may depend on clinical and pathologic information (e.g., we expect that premenopausal patients with multiple positive SLNs are less likely to undergo OncotypeDX testing compared to those with no positive SLNs), the proportions of patients in each OncotypeDX category in a naïve complete case analysis are likely to be biased for the proportions that would be observed had everyone undergone testing. An estimation strategy that considers the dependence of OncotypeDX testing on variables that may be associated with the OncotypeDX score result is expected to be less biased.

Thus, to estimate the proportions of patients meeting criteria for adjuvant therapies had, contrary to fact, all patients undergone OncotypeDX testing, we used inverse probability of measurement weights (IPWs).[18,19] We assumed a logistic model for OncotypeDX measurement conditional on pathologic tumor size, number of positive lymph nodes, microscopic versus macroscopic LN metastases, whether ALND was performed, tumor histology, tumor multifocality, tumor grade, presence of lymphovascular invasion, insurance status, and comorbidity index. The model was used to compute the denominator of the IPWs, and the proportions of patients meeting criteria for adjuvant chemotherapy and regional nodal irradiation (RNI) were computed using the weighted cohort. The mean of the weights among those with measured OncotypeDX was 1.95 (SD, 0.60; minimum, 1.00; maximum, 28.66). As a sensitivity analysis, we considered whether estimates would be affected by restricting the analysis for postmenopausal women to only those aged 50 to 70 years. CIs were constructed by taking percentiles of the sampling distribution, estimated by bootstrapping with 1000 iterations.

TABLE 1 Adapted criteria for adjuvant therapies.

Criteria for radiation to regional lymphatics	
One or more axillary lymph nodes (LNs) with macrometastases	**No axillary lymph node (LN) involvement, isolated tumor cells, or micrometastases only**
Age ≤40 years, or ≥3 positive LNs, or Final tumor size >5 cm, or Age <50 years with OncotypeDX > 18, or Age >40 years and meets at least two of the following criteria • Grade 3 • Lymphovascular invasion • OncotypeDX >25	Meets at least three of the following: • Final tumor size >5 cm • pN1(mic) • Multiple LNs with micrometastases • Age ≤45 years • Grade 3 • Lymphovascular invasion • OncotypeDX >25
Criteria for chemotherapy	
Premenopausal	**Postmenopausal**
Any number of positive LNs, or OncotypeDX >25 (consider for OncotypeDX 16–25)	≥4 positive LNs, or OncotypeDX >25
Criteria for CDK 4/6 inhibitor therapy	
Abemaciclib	**Ribociclib**
≥4 positive LNs, or 1–3 positive LNs and either of the following: • Grade 3 • Pathologic tumor size ≥5 cm	≥1 positive LN (excluding microscopic nodal involvement), or Pathologic tumor size > 5 cm, or Pathologic tumor size 2–5 cm and either of the following: • Grade 3 • Grade 2 and OncotypeDX >25

RESULTS

There were 119,312 patients with cT1N0 HR-positive breast cancer diagnosed between 2018 and 2020 who underwent upfront breast-conserving surgery with SLNB, had no cancer history, and had complete treatment and pathologic information available. The majority of patients were older than age 50 years (103,528; 86.8%), had invasive ductal histology (96,454; 80.8%), and had a comorbidity index of 0 (98,352; 82.4%). A plurality of patients had cT1c tumors (52,222; 43.8%). The clinical and pathologic characteristics of the cohort are summarized in Supplementary Table 1.

Axillary lymph node surgery and pathology

The overall proportion of patients with SLNB positivity was 11.1% (13,211 of 119,312). Among postmenopausal patients, 10,816 (10.4%) had a positive SLNB and, of those with a positive SLNB, 3134 (29.0%) had micrometastases only whereas 7682 (71.0%) had at least one LN with macrometastases. Among premenopausal patients, 2395 (15.2%) had a positive SLNB and, of those with a positive SLNB, 682 (28.5%) had micrometastases only whereas 1713 (71.5%) had at least one LN with macrometastases. A flowchart depicting OncotypeDX and axillary lymph node pathology categories for pre- and postmenopausal patients is displayed in Figure 1.

Expected adjuvant treatment recommendations had all patients undergone OncotypeDX testing

The estimated percentage of postmenopausal patients with an OncotypeDX score ≤25 and negative LNs or one through three positive LNs was 88.8%. Based on current national guidelines, chemotherapy would generally not be recommended for these patients regardless of whether their LN pathology was known. The estimated percentage of postmenopausal patients with an OncotypeDX score >25 and negative LNs or any number of positive LNs was 10.8%. Based on current national guidelines, these patients would generally be recommended chemotherapy regardless of whether their LN pathology was known. An estimated 0.4% of patients would have had an OncotypeDX score ≤25 but four or more positive LNs and thus would only be recommended chemotherapy if LN pathology information was available. Estimated proportions of patients by risk category, and corresponding 95% CIs, are presented in Table 2.

For premenopausal patients, the estimated percentage with a low OncotypeDX score ≤15 and negative LNs was 43.7%, the estimated percentage with an intermediate OncotypeDX score of 16 through 25 and negative LNs was 32.4%, and the estimated percentage with a high OncotypeDX score >25 and negative LNs was 8.3%. The estimated percentage with positive LNs and a high OncotypeDX score >25 was 2.0%. Based on current national guidelines, the aforementioned categories of premenopausal patients would be recommended chemotherapy or would not be recommended chemotherapy regardless of whether their LN pathology was known. The estimated percentage of premenopausal patients with a low OncotypeDX score ≤15 and positive LNs was 7.3%. These patients would only be recommended chemotherapy if their LN information were known. Last, the estimated percentage with an intermediate OncotypeDX score of 16 through 25 and positive LNs was 6.2%. These patients are more likely to be offered chemotherapy if their LN pathology were known. Table 2 shows all estimated percentages and corresponding 95% CIs.

The estimated percentage of patients without features meeting criteria (Table 1) for CDK4/6i was 97.9% for abemaciclib and 89.6% for ribociclib; 2.9% would meet criteria for ribociclib regardless of LN pathology. The estimated percentage who would only meet criteria had LN pathology been known was 2.1% for abemaciclib and 7.5% for ribociclib. Table 3 shows all estimated percentages and corresponding 95% CIs.

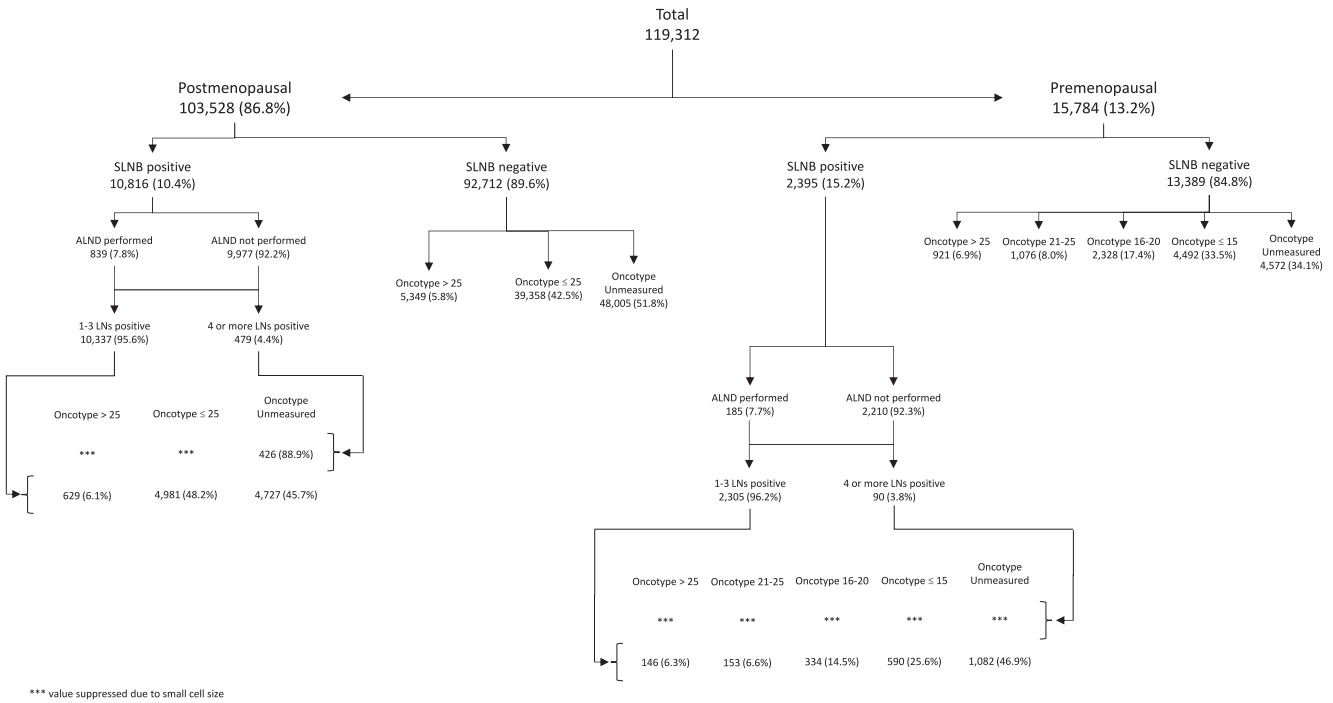

FIGURE 1 Flowchart depicting the numbers and proportions of patients in each risk group based on genomic recurrence risk score and axillary staging.

TABLE 2 Estimated proportion of patients meeting criteria for chemotherapy by risk category.

	LN pathology	OncotypeDX score	Chemotherapy recommended?	Estimated percentage[a]	95% CI
Postmenopausal	Negative	≤25	No	79.7	(79.4–80.0)
	Negative	>25	Yes	9.5	(9.3–9.7)
	1-3 LNs+	≤25	No	9.1	(8.9–9.3)
	1-3 LNs+	>25	Yes	1.2	(1.1–1.3)
	4+ LNs+	≤25	Yes	0.4	(0.3–0.5)
	4+ LNs+	>25	Yes	0.1	(0.1–0.2)
Premenopausal	Negative	≤15	No	43.7	(42.6–44.7)
	Negative	16–20	Consider	22.3	(21.3–23.2)
	Negative	21–25	Consider	10.1	(9.5–10.7)
	Negative	>25	Yes	8.3	(7.8–8.9)
	Positive	≤15	Yes	7.3	(6.7–7.8)
	Positive	16–20	Yes	4.2	(3.7–4.9)
	Positive	21–25	Yes	2.0	(1.7–2.6)
	Positive	>25	Yes	2.0	(1.6–2.3)

Abbreviation: LN, lymph node.

[a]Estimated percentage of the population, had everyone undergone OncotypeDX testing, computed by inverse probability weighting and assuming a logistic model for OncotypeDX measurement conditional on clinicopathologic variables.

TABLE 3 Estimated proportion of patients meeting criteria for adjuvant CDK4/6 inhibitor therapy by risk category.

	Risk category	Estimated percentage[a]	95% CI
Abemaciclib	Meets criteria only if LN pathology known	2.1	(2.0–2.3)
	Does not meet criteria	97.9	(97.7–98.0)
Ribociclib	Macrometastases, meets criteria for ribociclib only if LN pathology known	7.5	(7.3–7.7)
	Macrometastases, meets criteria for ribociclib regardless of LN pathology	0.6	(0.6–0.8)
	Micrometastases/node-negative, meets criteria for ribociclib regardless of LN pathology	2.3	(2.2–2.4)
	Does not meet criteria	89.6	(89.3–89.8)

Abbreviation: LN, lymph node.

[a]Estimated percentage of the population, had everyone undergone OncotypeDX testing, computed by inverse probability weighting and assuming a logistic model for OncotypeDX measurement conditional on clinicopathologic variables.

The estimated percentage of patients without features meeting criteria (Table 1) for RNI was 96.4%, while the percentage of patients with high-risk features that would meet criteria for RNI regardless of whether their LN pathology was known was 1.5%. The remaining 2.1% of patients would meet criteria for RNI only if their LN pathology was known. Table 4 shows all estimated percentages and corresponding 95% CIs.

As shown in Table 5, 7.9% of postmenopausal women would have one or more adjuvant decisions impacted by LN pathology information. For premenopausal women, this estimated percentage was 13.7%. When ribociclib decision making was not considered, these estimates were 2.5% for postmenopausal women and 12.6% for premenopausal women. Estimates for postmenopausal women were not qualitatively different when considering only the age 50 to 70 year category.

DISCUSSION

We sought to understand the degree to which SLNB omission impacts adjuvant therapy decision making in patients with small cN0 HR positive breast cancers undergoing breast-conserving therapy. We estimated that, if following existing guidelines, the percentage of postmenopausal patients whose adjuvant treatment recommendations would be affected by SLNB information is low, at 7.9%; that the percentage of premenopausal patients whose

TABLE 4 Estimated proportion of patients meeting criteria for adjuvant regional nodal irradiation by risk category.

LN pathology	Risk category	Estimated percentage[a]	95% CI
Micrometastases/node-negative	Meets criteria without LN pathology	1.1	(1.0–1.2)
Micrometastases/node-negative	Meets criteria only if LN pathology known	0.4	(0.3–0.5)
Micrometastases/node-negative	Does not meet criteria	90.4	(90.2–90.6)
Macrometastases	Meets criteria without LN pathology	0.4	(0.3–0.5)
Macrometastases	Meets criteria only if LN pathology known	1.7	(1.6–1.9)
Macrometastases	Does not meet criteria	6.0	(5.8–6.1)

Abbreviation: LN, lymph node.

[a]Estimated percentage of the population, had everyone undergone OncotypeDX testing, computed by inverse probability weighting and assuming a logistic model for OncotypeDX measurement conditional on clinicopathologic variables.

TABLE 5 Estimated proportion of patients meeting criteria for one or more adjuvant therapies by risk category.

Risk category	Estimated percentage[a]	95% CI
Postmenopausal and ≥1 adjuvant decision would be affected by LN pathology	7.9	(7.7–8.1)
Premenopausal and ≥1 adjuvant decision would be affected by LN pathology	13.7	(13.0–14.7)
Premenopausal and 1 or more adjuvant decision would be, or might be,[b] affected by LN pathology	15.1	(14.4–16.1)

Abbreviation: LN, lymph node.

[a]Estimated percentage of the population, had everyone undergone OncotypeDX testing, computed by inverse probability weighting and assuming a logistic model for OncotypeDX measurement conditional on clinicopathologic variables.

[b]Chemotherapy decisions "might be" affected by lymph node pathology for premenopausal women when the OncotypeDX score is 16–25 and they do not otherwise meet criteria for chemotherapy.

adjuvant therapy recommendations would be impacted is higher, at 13.6%; and, that ribociclib decision making would be the primary factor impacting postmenopausal women but not premenopausal women.

Recent studies have reported that SLNB omission does not, on average, significantly alter adjuvant treatment decisions,[1,3,20] even though patients with LN metastases are more likely to receive adjuvant therapies.[21–24] Potential explanations for these ostensibly paradoxical findings include that multidisciplinary teams may err toward prescribing adjuvant therapies more often than recommended when SLNB is omitted, or some patients foregoing recommended adjuvant therapies despite LN metastases when SLNB is performed. For clinicians and patients considering SLNB omission, a relevant question is: how many patients would be impacted by SLNB omission *if* adjuvant treatment recommendations were consistently followed? Our findings extend and complement recent studies by answering this question. Assuming that patients who omit SLNB are considered LN negative for adjuvant decision making purposes and that guideline-based adjuvant treatment recommendations are consistently followed, our estimates suggest a limited – but not negligible – impact for postmenopausal women and a greater impact for premenopausal women.

Although our study suggests that the potential impact of SLNB on adjuvant decision making would be limited, especially in postmenopausal women, it reinforces that some patients who would have been recommended adjuvant chemotherapy or RNI, based on LN pathology, would not receive the same recommendation if SLNB were omitted and assumed to be negative. It is less clear the extent to which recurrence and survival would be affected in this subset of patients due to adjuvant therapy omission. Adjuvant therapy utilization is influenced by guideline recommendations that are unlikely to change in the absence of high-quality evidence from randomized clinical trials with long follow-up (>5 years) given the potential for late recurrences in HR-positive breast cancer. However, these guidelines may need to be adapted sooner to provide more explicit recommendations to multidisciplinary teams treating patients who forgo SLNB.

Although the influence of SLNB on chemotherapy decisions has diminished in the era of genomic profiling, its impact on radiotherapy planning remains more central. Recommendations on adjuvant radiation therapy, including RNI, which was assessed in this study, and partial breast irradiation (PBI) or radiation omission, which were not considered in this study, have historically relied on surgical nodal staging. Nodal status continues to inform patient eligibility for PBI, which has similar effectiveness compared with whole breast radiation in preventing invasive breast tumor recurrence for eligible patients, and is typically reserved for pN0 disease.[25,26] Finally, pathologically negative nodal status is a requirement for participation in clinical trials investigating radiotherapy omission, such as the DEBRA trial.[27] With SLNB omission, risk stratification for treatment decision making may increasingly depend on alternative markers of risk (e.g., genomic-based risk scores). The adapted guidelines for RNI considered in this study (Table 1) incorporate a genomic-based risk score, consistent with our institutional guidelines.[17] To minimize the impact of SLNB omission on adjuvant therapy decision making, future guidelines, and the trials that inform them, will need criteria that are independent of axillary lymph node pathology.

The benefit of SLNB omission is avoidance of several nontrivial axillary surgical morbidities, including hematoma, seroma, wound infection, upper extremity lymphedema, axillary paresthesia, axillary web syndrome, decreased upper extremity range of motion, and pain.[28–31] Indeed, patient reported outcomes from the INSEMA trial are consistent with reduced pain, reduced arm swelling, and improved arm mobility when SLNB is omitted.[32] As such, consequences of SLNB omission in adjuvant therapy decision making must be weighed against improvement in quality of life for patients both in the short and long term.

The recently published results of the SOUND and INSEMA trials have galvanized discussion around SLNB omission, but results of other randomized trials comparing SLNB and no axillary surgery are also anticipated in the near future.[1,2,32–34] The NAUTILUS and BOOG 2013-08 randomized trials included women with cT1/T2 breast cancer planned to undergo breast-conserving surgery, assigning patients to SLNB versus its omission in South Korea (NAUTILUS) and the Netherlands (BOOG 2013-08).[35,36] Together, these studies are expected to provide robust evidence regarding the average long-term outcomes of SLNB omission in women with early breast cancer.

Importantly, the trials comparing SLNB with its omission required that all patients undergo axillary ultrasound during staging. One limitation of our study is that axillary ultrasound was not routinely used for all patients newly diagnosed with breast cancer in the United States, and the proportion of patients in the study who underwent this staging investigation is unknown. Nevertheless, the probability of SLNB positivity observed in this study (11.1%) was similar to that observed in the SLNB arm of the SOUND trial (13.7%).[1] Given the high negative predictive value of axillary ultrasound,[37] we would expect that, had all patients in our cohort undergone staging with axillary ultrasound, the proportion of cN0 patients with a positive SLNB would have been even lower. Thus, our estimates of the impact of LN pathology information on adjuvant recommendations may overstate the affected proportions of patients in settings where axillary ultrasound is routinely performed.

Other limitations of our study include that the conclusions depend on clinicians practicing according to the specified guidelines. In settings where breast cancer multidisciplinary teams practice differently, the proportions of patients affected by LN pathology may be different from those we estimated. This limitation may become particularly relevant if adjuvant therapy guidelines and practice patterns continue to change, relying more on tumor biology (quantified via, e.g., biomarkers) and less on LN pathology. Because OncotypeDX results were not available for all patients in the NCDB, our study conclusions also depend on IPW estimates that may be biased to the extent that our model for OncotypeDX measurement is misspecified. Last, although we focused on adjuvant chemotherapy, CDK4/6 inhibitors, and RNI, other adjuvant therapy options may be impacted by the decision to omit SLNB. As examples, eligibilities for PBI,[38] omission of irradiation altogether,[39,40] and adjuvant poly (adenosine diphosphate–ribose) polymerase inhibitors[41] depend, in part, on LN pathology.

Our findings demonstrate that adjuvant decisions for postmenopausal patients with small cN0 HR-positive breast cancers undergoing breast-conserving therapy are unlikely to be affected by LN pathology. Adjuvant therapy decisions for premenopausal women were more likely to depend on LN pathology, and SLNB omission in this population may have a greater impact on clinical decision making and oncologic outcomes. These findings are useful to patients and multidisciplinary teams considering a tailored, risk-based approach to axillary management in early breast cancer.

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AUTHOR CONTRIBUTIONS

Kerollos Nashat Wanis: Conceptualization; methodology; data curation; writing—original draft; writing—review & editing; and formal analysis. **Melissa P. Mitchell**: Writing—review & editing. **Sharon H. Giordano**: Writing—review & editing. **Jennifer Keating Litton**: Writing—review & editing. **Simona F. Shaitelman**: Writing—review & editing. **Nina Tamirisa**: Writing—review & editing. **Isabelle Bedrosian**: Writing—review & editing. **Wenli Dong**: Data curation and writing—review & editing. **Yu Shen**: Data curation; methodology; and writing—review & editing. **Kelly K. Hunt**: Writing—review & editing. **Puneet Singh**: Writing—review & editing. **Susie X. Sun**: Writing—review & editing. **Abigail S. Caudle**: Writing—review & editing. **Henry M. Kuerer**: Writing—review & editing. **Funda Meric-Bernstam**: Writing—review & editing. **Rosa F. Hwang**: Writing—review & editing. **Taiwo Adesoye**: Writing—original draft; writing—review & editing; and conceptualization. All authors contributed to the interpretation of the data analysis and to revisions of the manuscript.

CONFLICT OF INTEREST STATEMENT

Henry M Kuerer reported receiving personal fees from NEJM Group, UpToDate, McGraw Hill Professional, and Endomagnetics Ltd. outside the submitted work. Kelly K Hunt reported receiving personal fees from ArmadaHealth and AstraZeneca; grants to the institution from Cairn Surgical, Eli Lilly & Co., Lumicell outside the submitted work. Rosa F Hwang reported receiving travel compensation and grants to the institution from Intuitive Surgical Inc. outside of the submitted work. Simona F Shaitelman reported consulting for Lumicell, and receiving research support from Artidis and ExactSciences outside the submitted work. Taiwo Adesoye reported a one time consulting fee from Boehringerlabs, and speaker fees from ASCO Advantage, Sociedade Catarinense de Mastologia and Cardinal Health.

DATA AVAILABILITY STATEMENT

NCDB data analyzed in this study were used under license and are not publicly available. These data are available upon reasonable

request, with permission of the NCDB. The underlying code for this study is available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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