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Non-sentinel Lymph Node Metastatic Burden in Patients Undergoing Mastectomy With One or Two Positive Sentinel Lymph Nodes: Implications of Omitting Axillary Lymph Node Dissection

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Abstract

Background

Omission of axillary lymph node dissection (ALND) is increasingly accepted for patients with a limited number of metastatic sentinel lymph nodes (SLNs), and this approach is now being extended to patients treated with mastectomy. After mastectomy, however, the total number of metastatic axillary nodes still informs adjuvant chemotherapy, cyclin-dependent kinase 4/6 (CDK4/6) inhibitor eligibility, and radiotherapy field design, and this information is lost when ALND is omitted. This exploratory, descriptive study quantified the non-SLN metastatic burden that would have remained undetected had ALND been omitted in mastectomy patients at our institution.

Methodology

We retrospectively reviewed patients with clinically node-negative breast cancer who underwent SLN biopsy followed by completion ALND for a positive SLN at Kanazawa University Hospital between January 2022 and April 2026. Patients treated with neoadjuvant chemotherapy or breast-conserving surgery were excluded. Patients with one or two positive SLNs were defined as the ALND-omission candidate group. The primary endpoint was the proportion of candidates with four or more metastatic axillary nodes in total (SLNs plus non-SLNs; pathological nodal stage 2 (pN2) or higher). Secondary endpoints were the proportion of candidates with any non-SLN metastasis and the proportion with four or more non-SLN metastases; these were compared between patients with one and two positive SLNs. 95% confidence intervals (CIs) were calculated by the Clopper-Pearson method, and proportions were compared with Fisher's exact test. No multivariable or predictive modeling was performed.

Results

Twenty-seven patients were analyzed (median age 53 years, range 41-79; total mastectomy 25, skin-sparing mastectomy 1, nipple-sparing converted to skin-sparing mastectomy 1). Twenty-six tumors (96.3%) were luminal type. The omission candidate group comprised 21 patients (77.8%): 17 with one positive SLN and four with two positive SLNs. Four or more total positive nodes (pN2 or higher) were found in seven of 21 candidates (33.3%; 95% CI 14.6-57.0%), any non-SLN metastasis in 11 (52.4%; 95% CI 29.8-74.3%), and four or more non-SLN metastases in five (23.8%; 95% CI 8.2-47.2%). pN2 or higher disease was found in four of 17 patients (23.5%) with one positive SLN and in three of four (75.0%) with two positive SLNs (P = 0.088); four or more non-SLN metastases were found in 11.8% versus 75.0% (P = 0.028). Four of the seven pN2-or-higher patients had invasive lobular carcinoma, and three had primary tumors larger than 80 mm.

Conclusions

In this small single-center mastectomy cohort, omitting ALND for one or two positive SLNs would have left non-SLN metastases undetected in about half of patients and would have understaged roughly one-third as pN1 rather than pN2 or higher. A high nodal burden was observed more often with two positive SLNs than with one, although the two-SLN subgroup was very small and this observation is hypothesis-generating. Because pN stage still informs adjuvant decisions after mastectomy, these data suggest that ALND omission in this setting should be accompanied by careful patient selection and a predefined adjuvant strategy; prospective studies with outcome data are needed to define that strategy.

Categories: Radiology, Pathology, Oncology
Keywords: axillary lymph node dissection, breast cancer, nodal staging, non-sentinel lymph node metastasis, sentinel lymph node biopsy

Introduction

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Axillary lymph node dissection (ALND) was long the standard treatment for breast cancer with sentinel lymph node (SLN) metastasis, but it carries substantial morbidity, including lymphedema, sensory disturbance, and impaired shoulder function [1]. Over the past 15 years, several randomized trials have shown that ALND can be safely omitted in selected patients with a positive SLN. The ACOSOG Z0011 trial demonstrated non-inferior 10-year overall survival without ALND in patients with *cT1-2 cN0* disease and one or two positive SLNs treated with breast-conserving surgery and whole-breast irradiation [2]. The EORTC AMAROS trial showed that axillary radiotherapy provides regional control equivalent to ALND with significantly less lymphedema [3,4], and the IBCSG 23-01 trial established that ALND is unnecessary for SLN micrometastases [5]. Because these trials enrolled predominantly breast-conserving patients, their applicability to patients undergoing mastectomy remained uncertain, in part because whole-breast tangential fields incidentally irradiate the lower axilla [6], whereas postmastectomy radiotherapy is not uniformly given.

The SENOMAC trial addressed this gap. It randomized 2,766 patients with cT1-3 cN0 breast cancer and one or two SLN macrometastases, approximately 36% of whom underwent mastectomy, to completion ALND or no further axillary surgery; recurrence-free survival at five years was non-inferior without ALND [7], and updated results presented in 2026 confirmed non-inferior five-year overall survival [8]. Almost all SENOMAC participants received adjuvant radiotherapy, including regional nodal irradiation, after mastectomy. On the basis of this evidence, the 2026 edition of the Japanese Breast Cancer Society (JBCS) Breast Cancer Treatment Guidelines added a weak recommendation (clinical question CQ2b) that ALND may be omitted after mastectomy in patients with no more than two SLN macrometastases, provided that appropriate radiotherapy is delivered [9].

Although ALND no longer appears to confer a survival benefit in this population, the staging information it provides has not become irrelevant. Pathological nodal (pN) stage remains an independent prognostic factor across breast cancer subtypes [10], and the total number of positive axillary nodes continues to enter several adjuvant treatment decisions: the indication for adjuvant abemaciclib in hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative disease depends in part on whether four or more nodes are involved [11]; the 21-gene recurrence score is validated only for patients with up to three positive nodes [12]; and the number of involved nodes guides the use and extent of postmastectomy radiotherapy and regional nodal irradiation [13-15]. When ALND is omitted after mastectomy, these decisions must be made without knowing whether residual non-SLN disease is present, and a patient whose true nodal stage is pN2-3 is recorded as pN1. A post hoc analysis of SENOMAC showed that completion ALND upstaged 12.5% of patients to pN2-3 but argued against performing ALND solely to identify candidates for CDK4/6 inhibitor therapy because of its arm morbidity [16]. How often such nodal understaging would occur in a Japanese mastectomy population, in which mastectomy is often selected because of extensive disease, has not been described.

At our institution, patients undergoing mastectomy with a positive SLN on intraoperative frozen section have uniformly undergone completion level I-II ALND, whereas in breast-conserving patients ALND is already omitted for one or two positive SLNs. This cohort therefore allows the non-SLN status of every mastectomy patient who would have been eligible for ALND omission to be examined directly. In anticipation of extending ALND omission to mastectomy patients in line with the revised guideline, we conducted an exploratory, descriptive analysis of this cohort. The primary objective was to quantify the proportion of ALND-omission candidates (one or two positive SLNs) whose total number of positive axillary nodes, counting SLNs and non-SLNs together, was four or more (pN2 or higher) and who would therefore have been understaged had ALND been omitted. The secondary objectives were to describe the frequency and extent of non-SLN metastasis itself, and to compare these proportions between patients with one and two positive SLNs. Given the size of the cohort, no multivariable or predictive analysis was planned; the characteristics of patients with a high nodal burden are reported descriptively.

Materials And Methods

Study design and patients

This single-institution retrospective study reviewed consecutive patients with breast cancer who underwent sentinel lymph node biopsy (SLNB) followed by completion ALND for SLN metastasis at Kanazawa University Hospital between January 2022 and April 2026. Patients were identified from the prospectively maintained surgical database of the Department of Breast Surgery, which records all breast cancer operations, and were cross-checked against the operative records for ALND. Of the 29 patients identified, those who received neoadjuvant chemotherapy (n = 1) and those who underwent breast-conserving surgery (n = 1) were excluded. Consequently, 27 patients who underwent mastectomy without neoadjuvant chemotherapy were included in the analysis (total mastectomy, n = 25; skin-sparing mastectomy (SSM), n = 1; nipple-sparing mastectomy (NSM) converted intraoperatively to SSM, n = 1) (Figure *1*). The study was approved by the Medical Ethics Committee of Kanazawa University (approval No. 2025-312 (115089)), and the requirement for individual informed consent was waived in favor of an opt-out procedure.

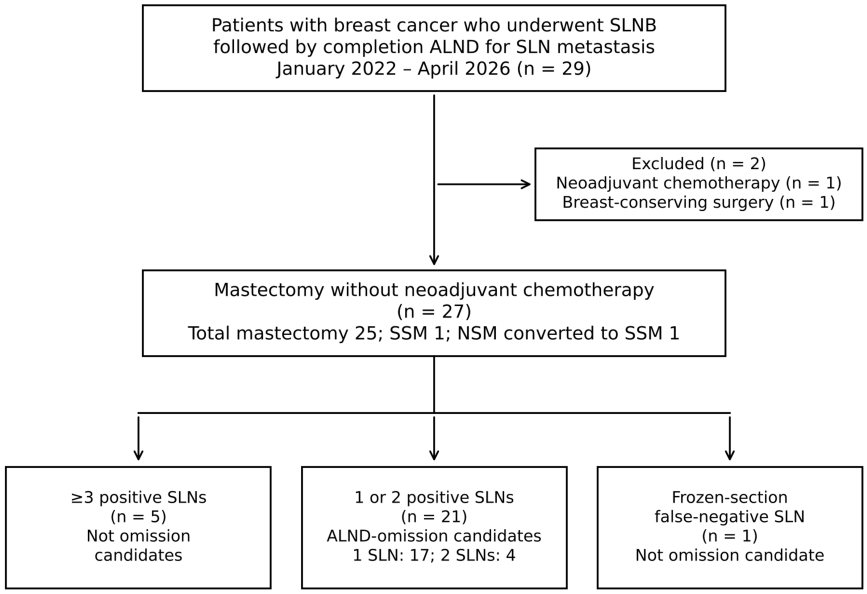


FIGURE 1: Patient selection flow

ALND: axillary lymph node dissection; NSM: nipple-sparing mastectomy; SLN: sentinel lymph node; SLNB: sentinel lymph node biopsy; SSM: skin-sparing mastectomy.

Preoperative axillary assessment and definition of cN0

All patients were clinically node-negative (cN0) before surgery. Clinical nodal status was assessed by physical examination and by axillary ultrasonography performed as part of the routine preoperative work-up, which also included mammography and contrast-enhanced breast magnetic resonance imaging. On ultrasonography, a lymph node was regarded as suspicious when it showed focal or diffuse cortical thickening of 3 mm or more, effacement or displacement of the fatty hilum, a rounded shape, or non-hilar blood flow; nodes without these features were classified as cN0. When a node was considered indeterminate, ultrasound-guided fine-needle aspiration cytology was performed; this was done in five of the 27 patients and was negative for malignancy in four and indeterminate (suspicious but not diagnostic of malignancy) in one. All 27 patients were therefore managed as cN0 and proceeded to SLNB.

Institutional axillary management policy

During the study period, the axillary management of cN0 breast cancer at our institution depended on the type of breast surgery. For breast-conserving surgery, intraoperative SLN assessment was not performed; patients with one or two positive SLNs on permanent pathology received axillary irradiation without ALND, and those with three or more positive SLNs underwent ALND as a second operation. For mastectomy (total mastectomy, SSM, or NSM), intraoperative frozen-section analysis was performed, and any SLN metastasis prompted immediate completion ALND. Postmastectomy radiotherapy to the chest wall and supraclavicular region, with or without the internal mammary chain, was recommended for node-positive patients according to the final pathological nodal status.

Sentinel lymph node mapping and surgical procedure

Sentinel lymph nodes were identified by radioisotope (99mTc-phytate, injected the day before or on the morning of surgery) and indocyanine green fluorescence. All radioactive or fluorescent nodes, together with any palpably firm node encountered in the SLN basin, were removed and submitted as SLNs; a threshold based on the radioactivity count was not applied. Patients with SLN metastasis on frozen section underwent level I-II ALND during the same operation. No patient in the cohort underwent level III dissection.

Pathological evaluation

All specimens were examined at the Department of Diagnostic Pathology, Kanazawa University Hospital, in accordance with the General Rules for Clinical and Pathological Recording of Breast Cancer of the JBCS (18th edition) and the JBCS Breast Cancer Treatment Guidelines [9]. Each SLN was sliced at 2-mm intervals

perpendicular to its long axis, and all slices were submitted. For intraoperative diagnosis, the slices were frozen and examined on hematoxylin and eosin (HE)-stained frozen sections, one section per slice. The residual tissue was then fixed in 10% buffered formalin, embedded in paraffin, and examined on HE-stained permanent sections of every slice; the final SLN status was based on the permanent sections. Immunohistochemistry for cytokeratin was not performed routinely, and nodal metastases were assessed on HE staining alone, which is the standard method specified in the JBCS General Rules. Non-SLNs retrieved from the ALND specimen were identified by manual dissection of the fat, bisected along the long axis (nodes small enough to be submitted whole were not sectioned), and examined on one HE-stained section of the maximal cut surface per block.

Sentinel lymph node metastases were classified as macrometastases (>2 mm), micrometastases (>0.2-2 mm), or isolated tumor cells (≤0.2 mm) according to the eighth edition of the Union for International Cancer Control (UICC) TNM classification [17]. Nodes containing macrometastasis or micrometastasis were counted as positive; isolated tumor cells were not. Pathological tumor size (pT) and pathological nodal stage (pN) were determined according to the same classification, with pN based on the total number of positive lymph nodes, SLNs, and non-SLNs combined. Estrogen receptor, progesterone receptor, HER2, and Ki-67 status were determined by immunohistochemistry (with in situ hybridization for HER2 2+ cases), and subtypes were defined as luminal (hormone receptor-positive, HER2-negative), HER2-positive, or triple-negative.

Data collection and handling of missing data

Clinicopathological data were extracted from the electronic medical records and the pathology reports. The variables required for the study endpoints (type of surgery, number of SLNs removed, number of positive SLNs, number of positive non-SLNs, and final pN stage) were complete for all 27 patients, and no patient was excluded for missing data. Histological grade was not reported in nine patients, seven of whom had invasive lobular carcinoma, and lymphovascular invasion was recorded in only seven patients because it was not consistently reported during the earlier part of the study period; extracapsular extension and the total number of lymph nodes retrieved by ALND were not recorded in the database. These variables were therefore not analyzed, and no imputation was performed.

Definitions and endpoints

Patients with one or two positive SLNs were defined as candidates for ALND omission, in accordance with the eligibility criteria of the SENOMAC trial and the 2026 JBCS guideline. The patient with a false-negative frozen section and the patients with three or more positive SLNs were not omission candidates and are presented for completeness only.

Two distinct quantities were examined and are reported separately throughout. The first is the total number of positive axillary nodes, that is, positive SLNs plus positive non-SLNs, which determines the pN stage. The second is the number of positive non-SLNs alone, which represents the disease that would have remained in the axilla had ALND been omitted. The primary endpoint was the proportion of omission candidates with four or more positive axillary nodes in total, corresponding to pN2 or higher, which was defined as a high nodal burden; these patients would have been recorded as pN1 had ALND been omitted. Secondary endpoints were the proportion of candidates with any non-SLN metastasis and the proportion with four or more non-SLN metastases. All three proportions were compared between patients with one and those with two positive SLNs.

Statistical analysis

Categorical variables are presented as numbers and percentages, and continuous variables as medians with ranges. The 95% confidence intervals (CIs) for proportions were calculated using the Clopper-Pearson exact method. Comparisons of proportions between groups were performed using Fisher's exact test. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Because of the small sample size, all between-group comparisons were prespecified as exploratory; no adjustment for multiple comparisons was made, and no multivariable or predictive model was constructed. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [18].

Results

Patient characteristics

The characteristics of the 27 patients are summarized in Table *1*. The median age was 53 years (range 41-79). Twenty-five patients underwent total mastectomy, one underwent SSM, and one underwent NSM that was converted intraoperatively to SSM. The predominant histological type was invasive ductal carcinoma (17 patients), followed by invasive lobular carcinoma (seven patients); two patients had mixed ductal and lobular carcinoma, and one had invasive ductal carcinoma with a micropapillary component. Twenty-six tumors (96.3%) were luminal type, and one (3.7%) was triple-negative; no HER2-positive tumors were included. The median pathological tumor size was 23 mm (range 1.5-120 mm), and five tumors (18.5%) exceeded 50 mm. A median of three SLNs were removed per patient (mean 3.1, range 1-6). Final pathological

stage was IIA in five, IIB in eight, IIIA in 10, and IIIC in four patients; thus 14 patients (51.9%) had stage III disease. Final nodal stage was pN1 in 12, pN2 in six, and pN3 in nine patients.

Characteristic	Value
Age, years, median (range)	53 (41-79)
Type of mastectomy, n	
Total mastectomy	25
SSM	1
NSM converted to SSM	1
Histological type, n	
IDC	17
ILC	7
Mixed IDC/ILC	2
IDC with micropapillary component	1
Intrinsic subtype, n (%)	
Luminal	26 (96.3)
Triple-negative	1 (3.7)
HER2-positive	0 (0)
Pathological tumor size, mm, median (range)	23 (1.5-120)
Tumor >50 mm, n (%)	5 (18.5)
Number of SLNs removed, median (mean, range)	3 (3.1, 1-6)
Number of positive SLNs, n (%)	
0 (frozen-section false negative)	1 (3.7)
1	17 (63.0)
2	4 (14.8)
≥3	5 (18.5)
Pathological stage, n	
IIA	5
IIB	8
IIIA	10
IIIC	4
Pathological N stage, n	
pN1	12
pN2	6
pN3	9

TABLE 1: Characteristics of the 27 patients who underwent mastectomy with completion ALND.

ALND: axillary lymph node dissection; HER2: human epidermal growth factor receptor 2; IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; NSM: nipple-sparing mastectomy; SLN: sentinel lymph node; SSM: skin-sparing mastectomy.

Distribution of positive sentinel lymph nodes

Seventeen patients (63.0%) had one positive SLN, four (14.8%) had two, and five (18.5%) had three or more. In one patient (3.7%), the SLN was negative on intraoperative frozen section, but ALND was performed because multiple firm nodes were palpated in the axilla during surgery; permanent pathology confirmed six positive non-SLNs. This patient was not included in the omission candidate group. The ALND-omission candidate group (one or two positive SLNs) therefore comprised 21 of 27 patients (77.8%).

Nodal burden in the omission candidate group

Among the 21 omission candidates, the primary endpoint of four or more positive nodes in total (pN2 or higher) was met in seven patients (33.3%; 95% CI 14.6-57.0%). Had ALND been omitted, all seven would have been recorded as pN1 (one or two positive nodes). With respect to the secondary endpoints, non-SLN metastases were identified in 11 patients (52.4%; 95% CI 29.8-74.3%), and five patients (23.8%; 95% CI 8.2-47.2%) had four or more non-SLN metastases (Table *2*, Figure *2*). Among the 11 patients with non-SLN involvement, the number of positive non-SLNs was one in two patients, two in two, three in two, six in one, and 13, 14, 15, and 19 in one patient each. The remaining 10 candidates (47.6%) had no non-SLN metastasis, so that their final pN stage was identical to the stage that would have been assigned on the basis of SLNB alone.

Number of positive SLNs	n	Any non-SLN metastasis, n (%) [95% CI]	≥4 non-SLN metastases, n (%) [95% CI]	≥4 total positive nodes (pN2 or higher), n (%) [95% CI]
1	17	8 (47.1) [23.0-72.2]	2 (11.8) [1.5-36.4]	4 (23.5) [6.8-49.9]
2	4	3 (75.0) [19.4-99.4]	3 (75.0) [19.4-99.4]	3 (75.0) [19.4-99.4]
Omission candidates (1-2)	21	11 (52.4) [29.8-74.3]	5 (23.8) [8.2-47.2]	7 (33.3) [14.6-57.0]
≥3 (not omission candidates)	5	3 (60.0) [14.7-94.7]	1 (20.0) [0.5-71.6]	3 (60.0) [14.7-94.7]
0 (frozen-section false negative)	1	1 (100)	1 (100)	1 (100)

TABLE 2: Nodal burden according to the number of positive SLNs.

95% CIs were calculated by the Clopper-Pearson exact method. Fisher's exact test, 1 versus 2 positive SLNs (exploratory): any non-SLN metastasis P = 0.59; ≥4 non-SLN metastases P = 0.028; ≥4 total positive nodes P = 0.088. "Total positive nodes" denotes positive SLNs plus positive non-SLNs and determines the pN stage; "non-SLN metastases" denotes the nodal disease that would have remained had ALND been omitted. ALND: axillary lymph node dissection; CI: confidence interval; SLN: sentinel lymph node.

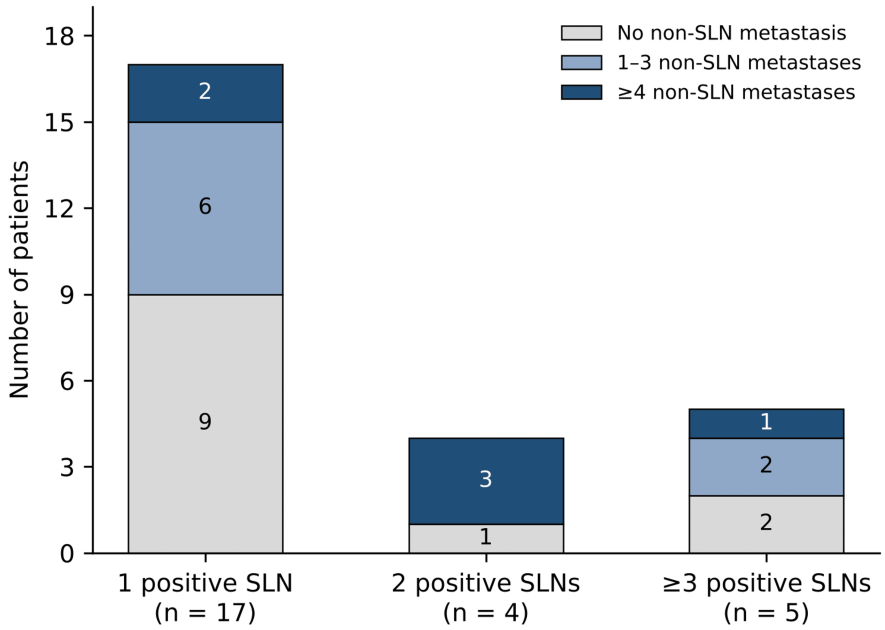


FIGURE 2: Non-sentinel lymph node metastatic burden according to the number of positive sentinel lymph nodes.

Bars show the number of patients with no non-SLN metastasis, one to three non-SLN metastases, and four or more non-SLN metastases in each group. The patient with a frozen-section false-negative SLN is not shown.
SLN: sentinel lymph node.

One versus two positive sentinel lymph nodes (exploratory)

In the 17 patients with one positive SLN, non-SLN metastases were present in eight (47.1%; 95% CI 23.0-72.2%), four or more non-SLN metastases in two (11.8%; 95% CI 1.5-36.4%), and pN2-or-higher disease in four (23.5%; 95% CI 6.8-49.9%). In the four patients with two positive SLNs, non-SLN metastases were present in three (75.0%; 95% CI 19.4-99.4%), all of whom had four or more non-SLN metastases and therefore pN2-or-higher disease. In the exploratory comparison, the proportion with four or more non-SLN metastases differed between the one- and two-SLN groups (P = 0.028), whereas the difference in pN2-or-higher disease did not reach statistical significance (P = 0.088); the confidence intervals for the two-SLN group are very wide. Among the five patients with three or more positive SLNs, who would not be omission candidates, non-SLN metastases were found in three (60.0%).

Descriptive characteristics of omission candidates with a high nodal burden

The seven omission candidates with pN2-or-higher disease are listed individually in Table *3*. Four of the seven had invasive lobular carcinoma, one had mixed ductal and lobular carcinoma, one had invasive ductal carcinoma with a micropapillary component, and one had invasive ductal carcinoma. Three patients had very large primary tumors (85, 95, and 120 mm), each with 13 or more positive non-SLNs; conversely, two patients with small primary tumors (4 and 8 mm) harbored three and 14 non-SLN metastases, respectively. Six of the seven tumors were luminal type; the remaining tumor (Case 3) was the only triple-negative tumor in the cohort. In exploratory comparisons within the omission candidate group, pN2-or-higher disease was found in four of six patients (66.7%) with lobular histology versus three of 15 (20.0%) with other histologies (P = 0.12), and in three of five patients (60.0%) with tumors larger than 50 mm versus four of 16 (25.0%) with smaller tumors (P = 0.28). Among patients with a single positive SLN, both patients in whom the only SLN removed was positive (1/1) had non-SLN metastases (13 and two nodes), compared with six of 15 patients (40.0%) in whom one of two or more SLNs was positive. These observations are descriptive; given the number of events, no multivariable analysis was attempted.

Case	Age, years	Surgery	Histology	pT, mm	Positive SLNs / SLNs removed	Positive non-SLNs	Total positive nodes	pStage
1	53	Total mastectomy	ILC	120	1/1	13	14	IIIC
2	44	Total mastectomy	IDC with micropapillary component	8	1/3	14	15	IIIC
3	76	Total mastectomy	ILC (triple-negative)	4	1/3	3	4	IIIA
4	42	Total mastectomy	Mixed IDC/ILC	27	1/2	3	4	IIIA
5	53	Total mastectomy	ILC	95	2/2	19	21	IIIC
6	44	SSM	IDC	21	2/3	6	8	IIIA
7	53	NSM converted to SSM	ILC	85	2/2	15	17	IIIC

TABLE 3: Omission candidates (one or two positive SLNs) with four or more positive axillary nodes on final pathology.

IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; NSM: nipple-sparing mastectomy; SLN: sentinel lymph node; SSM: skin-sparing mastectomy; pT: pathological T category (based on the invasive tumor size); pStage: pathological stage. All other tumors were luminal type.

Discussion

In this retrospective series of mastectomy patients with a positive SLN who all underwent completion ALND, more than half of those who would qualify for ALND omission under the 2026 JBCS guideline had residual non-SLN metastases, and one in three had four or more positive nodes in total. Had ALND been omitted, these patients would have been staged as pN1 rather than pN2 or pN3. The proportion with a high nodal burden was higher among patients with two positive SLNs than among those with one, but the two-SLN subgroup contained only four patients, and this comparison should be regarded as hypothesis-generating. The study was designed as an exploratory description of a single institutional cohort, and its findings should be read in that light.

Comparison with randomized trial populations

The rate of non-SLN involvement in our cohort (52.4%) is considerably higher than that reported in the ALND arms of the landmark trials: 27.3% in ACOSOG Z0011 [19], 33% in AMAROS [3], and 34.5% in SENOMAC, in which the final nodal stage was pN2-3 in 12.5% of patients who underwent completion ALND [8,16]. Our corresponding figure for pN2-or-higher disease was 33.3%, with a 95% CI (14.6-57.0%) whose lower bound approaches the SENOMAC estimate. Several features of our cohort may explain this difference. First, Z0011 and AMAROS were restricted to cT1-2 tumors, whereas 18.5% of our patients had tumors larger than 50 mm and three had tumors of 85-120 mm; in Japan, mastectomy is often selected precisely because the disease is extensive, so a mastectomy cohort is enriched for larger and more locally advanced tumors. Second, lobular carcinoma accounted for 26% of our cohort and for four of the seven patients with a high nodal burden. Third, our series was small, and all patients were treated under a policy of universal ALND, so the figures carry wide confidence intervals and cannot be generalized to other populations. Nevertheless, the direction of the finding is consistent with trial data: a non-negligible minority of patients eligible for ALND omission harbor pN2-3 disease.

Importantly, the detection of additional nodal disease by ALND does not translate into a survival benefit from ALND itself. SENOMAC demonstrated non-inferior recurrence-free survival [7] and, in its 2026 update, non-inferior overall survival in a population that included 919 mastectomy patients, nearly all of whom received postoperative radiotherapy [8]. Regional recurrence rates were below 1% in both arms. The question raised by our data is therefore not whether ALND should be performed for local control, but how the loss of staging information should be managed when ALND is omitted after mastectomy. Our study did not collect recurrence or survival data and cannot address whether omission would have altered outcomes.

One versus two positive sentinel lymph nodes

In our series, four or more non-SLN metastases were found in three of four patients with two positive SLNs

compared with two of 17 with one (P = 0.028). With only four patients in the two-SLN group, three of whom had very large or lobular tumors, this difference may reflect the tumor characteristics of those individual patients rather than the SLN count itself, and the confidence interval for the two-SLN estimate (19.4-99.4%) spans almost the entire range. The observation is nonetheless biologically plausible: the number of positive SLNs is a component of every validated nomogram for non-SLN metastasis and for having four or more positive nodes [20,21]. In SENOMAC, 84.6% of participants had a single macrometastatic SLN, so the evidence base for omitting ALND with two positive SLNs rests on a smaller subgroup [8], although the trial results were reported to be consistent across subgroups. We therefore do not propose that patients with two positive SLNs be managed differently on the basis of our data; rather, we suggest that the SLN count, the SLN ratio (positive SLNs/SLNs removed), tumor size, and histology be considered together when ALND omission is discussed, and that this hypothesis be examined in larger series.

Potential consequences of nodal understaging after mastectomy

The clinical consequences discussed below were not measured in this study; we did not record which adjuvant treatments were given, nor whether treatment would have differed had ALND been omitted. The following considerations are therefore theoretical and are intended to illustrate why the staging information lost with ALND omission may matter after mastectomy.

First, adjuvant abemaciclib is indicated for hormone receptor-positive, HER2-negative disease with four or more positive nodes, or with one to three positive nodes and either a tumor of 5 cm or larger or histological grade 3 [11]; in Japan, Ki-67 of 20% or higher in the setting of one to three positive nodes is also accepted, following the monarchE cohort 2 definition. In our cohort, 26 of 27 tumors were luminal type. Of the six luminal pN2-or-higher patients in Table *3*, two (Cases 2 and 4) had tumors of 3 cm or less, histological grade 1, and Ki-67 below 20% and would not have met any of the one-to-three-node criteria; whether they would have received abemaciclib on the basis of pN1 staging alone is uncertain. The SENOMAC post hoc analysis estimated that 104 completion ALNDs would be required to prevent one invasive disease-free survival event through abemaciclib eligibility, at the cost of severe arm impairment in approximately nine patients, and concluded that ALND should not be performed solely to establish this indication [16]. Our data do not contradict that conclusion. They suggest only that in a mastectomy population with larger and more often lobular tumors, the proportion of omission candidates with pN2-3 disease may be higher than in SENOMAC, which would alter the arithmetic of that trade-off; whether it does so to a clinically meaningful degree cannot be determined from 21 patients.

Second, the 21-gene recurrence score is validated for patients with up to three positive nodes [12] and is reimbursed in Japan only for pN0-N1 disease. If a patient who truly has pN2 disease is staged as pN1, a recurrence score may be obtained and chemotherapy withheld on the basis of a low score, although the RxPONDER evidence does not extend to four or more positive nodes. Conversely, the 2026 JBCS guideline conditions ALND omission after mastectomy on “appropriate radiotherapy,” which in practice means chest wall and regional nodal irradiation for all omission patients. In our cohort, 10 of 21 omission candidates (47.6%) had no non-SLN metastases and a final pN1 status with one or two nodes, a group for whom the absolute benefit of postmastectomy radiotherapy is smaller and more debated [13-15]. Omitting ALND therefore trades surgical morbidity for a uniform radiotherapy recommendation that may overtreat some patients, and that is not acceptable to all; in our experience, some older patients choose mastectomy specifically to avoid radiotherapy, and such patients cannot satisfy the guideline’s precondition for omission.

Third, the number of involved nodes guides radiotherapy field design, including the inclusion of the internal mammary chain [15]. Without ALND, this decision must rely on SLN findings and tumor characteristics alone. We did not evaluate radiotherapy planning in this study.

Toward selective omission of ALND after mastectomy

Our findings do not argue for retaining universal ALND, which in this series exposed roughly half of omission candidates to the morbidity of a procedure that yielded no additional positive nodes [1,16]. They are more consistent with a selective approach, in which patients at higher risk of a high nodal burden are identified before the decision to omit ALND is made. In our cohort, the patients with pN2-or-higher disease tended to have two positive SLNs, a high positive-SLN ratio, lobular histology, or a large primary tumor; these are descriptive observations from seven patients and do not constitute validated risk factors. Established nomograms that incorporate these and other variables [20,21] may help to identify patients in whom the probability of four or more positive nodes is high enough to justify ALND or, alternatively, a predefined adjuvant plan that assumes pN2-3 disease. Lobular carcinoma deserves specific mention: although Mamtani et al. found that lobular histology did not increase the need for ALND under Z0011 criteria in a breast-conserving cohort [22], lobular tumors are difficult to size accurately by imaging and were over-represented among our patients with extensive non-SLN involvement. Axillary radiotherapy, as validated in AMAROS, offers regional control equivalent to ALND and can be integrated into the postmastectomy fields [3,4]. Finally, the broader trend toward axillary de-escalation, including omission of SLNB altogether in selected cN0 patients in the SOUND and INSEMA trials [23,24], highlights that nodal staging information is being progressively removed from the adjuvant decision pathway; prospective data on

how adjuvant decisions should be made in its absence are needed.

Limitations

This study has several limitations. It is a single-center, retrospective, descriptive analysis of 27 patients, of whom 21 were omission candidates, and the subgroup with two positive SLNs contained only four patients; all subgroup comparisons are exploratory, were not adjusted for multiplicity, and are susceptible to chance. The study was not designed or powered to identify predictors of a high nodal burden, and no multivariable analysis was performed. No recurrence or survival data were collected, and the actual adjuvant treatments given were not analyzed, so the clinical consequences of understaging (changes in adjuvant therapy or in outcomes) were not assessed, and the safety of ALND omission in this population cannot be inferred from our data. Several pathological variables were incomplete or unavailable: histological grade was missing in nine patients (seven with lobular carcinoma), lymphovascular invasion was recorded in only seven, and extracapsular extension and the total number of nodes retrieved by ALND were not recorded, so these components of existing nomograms could not be evaluated. Nodal metastases were assessed on HE staining alone, in accordance with the JBCS General Rules, without routine cytokeratin immunohistochemistry; this may have left occasional isolated tumor cells or small micrometastases in non-SLNs undetected, although such foci would not have altered the pN2-or-higher classification. The definition of an SLN was not standardized by radioactivity count, and the number of SLNs removed varied from one to six, which affects both the number of positive SLNs and the apparent non-SLN burden. Patients with one positive SLN were not separated by SLN ratio in the primary analysis. Finally, because the cohort was treated under a policy of universal ALND, selection for mastectomy rather than breast conservation may itself have enriched the series for advanced disease, and the proportions reported here should not be extrapolated to other populations.

Conclusions

In this exploratory single-center series of mastectomy patients with one or two positive SLNs, omission of ALND would have left non-SLN metastases undetected in about half of patients and would have understaged approximately one-third from pN2-3 to pN1. A high nodal burden was observed more often in patients with two positive SLNs, lobular histology, or large primary tumors, although these descriptive observations from a small number of patients require confirmation. Because the total number of positive nodes still enters decisions on adjuvant chemotherapy, CDK4/6 inhibitor eligibility, and radiotherapy after mastectomy, our data suggest that ALND omission in this setting may be best implemented selectively, with explicit consideration of these characteristics and with a predefined adjuvant strategy for patients in whom residual nodal disease cannot be excluded. Multicenter prospective studies that link SLN findings, omission of ALND, adjuvant treatment decisions, and long-term outcomes in mastectomy patients are needed before firm recommendations can be made.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Medical Ethics Committee of Kanazawa University issued approval 2025-312 (115089). **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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