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Is Lobular Histology a Predictor of Sentinel Node Positivity in Early Breast Cancer? An Integrated Analysis of Histological Subtype and Preoperative Imaging

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Abstract

Lobular histology did not independently predict sentinel lymph node biopsy positivity in early-stage cN0 breast cancer. In a retrospective cohort of 661 patients, tumor size >20 mm and vascular invasion were the main predictors of nodal involvement. Axillary ultrasound and MRI showed high specificity and negative predictive value, supporting axillary de-escalation in selected patients, including those with invasive lobular carcinoma.

Purpose: To assess whether lobular histology independently predicts sentinel lymph node biopsy (SLNB) positivity in early-stage clinically node-negative (cN0) breast cancer (BC), to identify other predictive factors of SLNB positivity, and to evaluate the diagnostic performance of preoperative axillary imaging. The cumulative incidence of local and distant recurrences were also evaluated. **Methods:** We retrospectively analyzed 661 patients with early-stage, cN0 BC undergoing surgery with SLNB. Clinical, pathological, and radiological data were assessed. Univariate and multivariate analyses were performed to identify predictors of SLNB positivity. The cumulative incidence of axillary and distant recurrences were calculated including only patients with at least 2 years follow up, for a total of 495 patients. **Results:** ILC was present in 16.9% of cases. SLNB positivity occurred in 16.1% of invasive lobular cancers (ILC) and 20% of nonspecial type tumors (NST) ($P = .3$). No significant differences in axillary lymph node dissection (ALND) rates or nodal upstaging were found between histologies. Tumor size > 20 mm and vascular invasion were independent predictors of SLNB positivity. Axillary ultrasound and magnetic resonance (MRI) showed high specificity (95% and 79%) and negative predictive value (80% and 98%) in identifying node-negative patients. No axillary recurrences occurred after a median follow-up of 49.3 months. **Conclusions:** ILC does not independently predict SLNB positivity or nodal upstaging. Tumor size and vascular invasion remain the strongest predictors. Axillary ultrasound and MRI are reliable tools to guide de-escalation. SLNB omission in well-selected cN0 patients, including those with ILC, may be considered in tailored and selected patients.

Clinical Breast Cancer, Vol. 26, No.xxx, 9–16 © 2026 The Authors. Published by Elsevier Inc.
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Keywords: Breast cancer surgery, Lobular breast cancer, Sentinel node biopsy, Axillary surgery

Introduction

Breast cancer (BC) is the most commonly diagnosed malignancy among women.[1] In early-stage disease, locoregional treatment usually consists of breast-conserving surgery (BCS) followed by radiotherapy or mastectomy. Systemic adjuvant therapies—including hormone therapy, chemotherapy, HER2-targeted agents, and CDK4/6 inhibitors—are considered based on disease stage, tumour biology, and patient comorbidities, to reduce recurrence and mortality risk.[2,3]

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Submitted: Nov 14, 2025; Revised: Dec 22, 2025; Accepted: Jan 5, 2026; Epub: 6 January 2026

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https://doi.org/10.1016/j.clbc.2026.01.002

Sentinel lymph node biopsy (SLNB) remains the standard procedure for axillary staging in clinically nodenegative (cN0) patients.[4] It is typically guided by lymphoscintigraphy using technetium-99 m or peritumoral injection of blue dye, or a combination of both, to identify the first draining lymph node.[5] However, while SLNB provides important prognostic information, it has no direct therapeutic benefit and can result in complications such as lymphedema, infection, and restricted arm mobility.[6]

In recent years, several prospective randomized trials have questioned the necessity of SLNB in low-risk patients undergoing BCS.[7-9] The ACOSOG Z0011 trial demonstrated no survival benefit from axillary lymph node dissection (ALND) in patients with limited sentinel lymph node (SLN) metastases, paving the way for further de-escalation.[7] More recently, the SOUND and INSEMA trials showed that SLNB omission in selected cT1–T2, cN0 patients with negative axillary ultrasound (US) was noninferior to SLNB in terms of invasive or distant disease-free survival.[8,9]

Despite these promising results, essential concerns remain. Guidelines still use nodal status to guide adjuvant therapy, including radiotherapy and systemic treatments.[10,11] For instance, SLNB positivity may influence the indication for regional nodal irradiation and for the use of CDK4/6 inhibitors such as abemaciclib, which showed benefit in nodepositive high-risk hormone receptor (HR) positive/Human Epidermal Growth Factor Receptor 2 (HER2) negative patients in the monarchE trial, or olaparib in patients with mutation of BRCA 1-2 genes.[3,12,10] The omission of axillary surgery could therefore risk undertreatment in these selected cases.[13] Additionally, tumour histology may influence nodal spread patterns. Invasive lobular carcinoma (ILC), although underrepresented in de-escalation trials (8.5% in the SOUND trial, 12% in the INSEMA trial), shows different biological behavior compared to nonspecial type tumors (NST), including noncohesive growth and a higher rate of nonsentinel node involvement.[8,9,14,15] This behavior may compromise staging accuracy and impact treatment decisions if SLNB is omitted. Moreover, some studies have shown how ILC has a higher likelihood of multiple axillary metastases, more frequently leading to upstaging to N2 or N3 compared to tumors with NST histology. Still results are conflicting.[16,17]

In this context, the accuracy of preoperative imaging plays a crucial role in identifying positive axillary nodes correctly.[18]

Given the ongoing evolution in axillary management and the need to balance oncologic safety with reduced surgical morbidity, further investigation is warranted.

This study aims to assess the association between histologic subtype—particularly comparing ILC and NST—and SLNB positivity in early-stage cN0 BC patients undergoing BCS or mastectomy and SLNB.

Secondary objectives include evaluating nodal upstaging in clinically nodenegative (cN0) patients undergoing subsequent ALND due to SLN positivity, comparing NST and ILC tumors, and evaluating tumour-related predictive factors for SLNB positivity. The diagnostic performance of preoperative axillary imaging in identifying nodenegative patients has also been assessed, our research was focused on axillary US and magnetic resonance imaging (MRI).

The cumulative incidence for local and distant metastasis was evaluated.

Methods

All the patients underwent breast and axillary surgery at the Academic Department of Obstetrics and Gynaecology of "Umberto I" Hospital in Torino between January 01, 2014 and March 31, 2025. The Institutional Ethics Committee approved the study protocol (Prot. No. 0003599, date of approval: August 01, 2025). Informed consent was obtained from all participants included in the study.

We retrospectively included 661 patients with early BC with tumour size $\leq$ 50 mm and cN0 status before surgery. In cases of suspected lymph node involvement on preoperative imaging (US or MRI), a fine-needle aspiration (FNA) of the suspicious lymph node was performed, with a negative cytological result.

Patients who have received neoadjuvant therapy, patients with clinically nodepositive (cN+) status prior to surgery or positive fine-needle aspiration cytology of the lymph node were excluded. Prior BC or recurrences represented exclusion criteria.

Data regarding the patients' medical history, age, menopause, current surgery, and biological characteristics of the tumour, and follow-up data were obtained from prospectively maintained, nonopen-access institutional databases.

All the specimens had been tested for estrogen (ER) and progesterone receptors (PgR) by immunohistochemistry (IHC). Cancers were considered hormone-receptor-positive if at least 1% of the cells tested expressed ER. Otherwise, the tumor was considered hormone receptor-negative.[19] HER2 overexpression was evaluated with IHC staining 3 +, amplification in situ hybridization (FISH) test was performed in the case of IHC equivocal results (2 +).[20] IHC surrogates were used to classify BC as follows: luminal A (ER and/or PgR positive and HER-2 negative; ki67 < 20%), luminal B (ER and/or PgR positive, HER-2 positive and ki67 > 20%), HER-2 (ER and PgR negative and HER-2 positive) and basal-like (ER, PgR and HER-2 negative).[21]

Breast and axillary imaging (US and MRI) were performed by 3 expert breast radiologists. US were carried out with a high-resolution, electronically focused, high-frequency linear transducer of at least 12 MHz.[22]

Surgical and adjuvant medical treatment decisions were based on current international guidelines at the time of surgery.[23-27]

The cumulative incidence of axillary and distant recurrences were calculated including only patients with at least 2 years follow up, for a total of 495 patients.

Statistical Analysis

The Kolmogorov–Smirnov test was used to assess the distribution (normal vs. non-normal) of the quantitative variables under investigation. Correlation analysis was performed using the chi-square test for categorical variables and the Mann–Whitney U test for continuous variables.

To evaluate the performance of axillary ultrasound in predicting preoperative SLN negativity, specificity and negative predictive value (NPV) were calculated using a contingency table. Due to the study design, which excluded patients with positive findings on both preoperative US and FNA, sensitivity could not be assessed.

The chi-square test was also employed to compare axillary upstaging rates (N2/N3) between NST and ILC histological subtypes in clinically nodenegative (cN0) patients.

The association between SLN positivity and clinicopathological variables was assessed through univariate and multivariate analysis. Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were reported. Model goodness-of-fit was assessed using the Hosmer–Lemeshow test.

Axillary and distant cumulative recurrences incidences were estimated accounting for censored observations, with patients censored at last follow-up if no recurrence occurred. Differences in recurrence rates between histological subtypes (NST vs. ILC) were assessed using the log-rank test

A *P*-value $< .05$ was considered statistically significant. Data were analyzed using SPSS software, version 29.0 for macOS (IBM Corp, Armonk, NY).

Results

Population

Six hundred sixty one patients with early BC with tumor size $\leq$ 50 mm and cN0 status prior to surgery were included.

About 82.3% of the patients underwent BCS, while 17.7% mastectomy. All the patients had SLNB done, of whom, 35 patients received ALND due to SLN positivity.

Clinical and Histological Characteristics

At the time of diagnosis, mean age of the study population was 65.2 (sd 13.1), with most patients being postmenopausal. However, around one fifth of the women in our sample were premenopausal.

In line with the study's inclusion criteria, tumors were early-stage, with only around one fourth of them being more than 2 cm in size.

The most common histological subtype was NST, found in 78.2% of cases, followed by ILC subtype (16.9%).

As for tumor grade, around half of the tumors were G2.

BCS was the predominant treatment (82.3%), which aligns with the early-stage status and tumor size ($\leq$ 50 mm) of the study population. Consequently, the rate of mastectomy was significantly lower.

The clinical and histopathological characteristics of the patients included in the study are detailed in Table 1.

All patients underwent preoperative clinical examination and axillary imaging by US, while 34.8% of women also received MRI.

As regards axillary surgery, all women received SNLB as the first treatment. At the final pathological exam, SLN was negative in 80% of patients, while micrometastases (pN1mi) and macrometastases (pN1a) were found in 5.9% and 14% of cases, respectively.

Based on SLNB findings and individual patient characteristics, ALD was performed in 5.9% of cases.

Comparison Between NST and ILC Tumors

The differences between the NST and ILC histological subtypes are highlighted in Table 2.

According to the histological subtype, age distribution, and menopausal status, there were no significant differences between the 2 groups. However, premenopausal women were around one-third of ILC and around one-fifth of NST.

Table 1 Clinical and Histological Characteristics of Our Cohort

Variable	Number of Patients (N = 661, %)
Age (years)	
< 40	17 (2.6)
40-49	104 (15.7)
50-69	258 (39)
> 70	282 (42.)
Menopausal status	
Premenopausal	145 (21.9)
Postmenopausal	516 (78.1)
Tumor size	
≤ 20 mm	505 (76.4)
20-50 mm	156 (23.6)
pT	
1mi	3 (0.5)
1a	32 (4.8)
1b	165 (25)
1c	299 (45.2)
2	162 (24.5)
Grading	
G1	141 (21.3)
G2	370 (56)
G3	150 (22.7)
Histological type	
NST	517 (78.2)
ILC	112 (16.9)
Others	32 (4.8)
Vascular invasion	
Present	294 (44.5)
Absent	367 (55.5)
Molecular subtypes	
Luminal A	333 (50.4)
Luminal B	250 (37.8)
HER 2-positive	53 (8)
Triple negative	25 (3.8)
Breast surgery	
Conservative	544 (82.3)
Mastectomy	117 (17.7)

Abbreviations: ILC = invasive lobular carcinoma; NST = nonspecial type.

Tumour size greater than 20 mm was observed in around one-third of patients with ILC and in 22.4% of NST; however, this difference was not significant.

Regarding tumour grading, no significant correlation with histological subtype was observed; however, most ILC were intermediate grade.

As for molecular subtype, ILC showed a clear predominance of the Luminal A phenotype (70.5%), whereas NST displayed a more balanced distribution between Luminal A and Luminal B subtypes, along with a higher proportion of HER2-positive (9.7% vs. 2.7%)

Table 2 Comparison Between NST and ILC Tumors

Variables		NST (N = 517, 82.2%)	ILC (N = 112, 17.8%)	*P* Value
Age (years)	< 40	16 (3.1)	1 (0.9)	.27
	40-49	79 (15.3)	22 (19.6)	
	50-69	201 (38.9)	46 (41.1)	
	> 70	221 (42.7)	43 (38.4)	
Menopausal status	Premenopausal	108 (20.9)	33 (29.5)	.06
	Postmenopausal	409 (79.1)	79 (70.5)	
Tumoral size	≤ 20 mm	401 (77.6)	79 (70.5)	
	> 20 mm	116 (22.4)	33 (29.5)	.14
pT	1mi	1 (0.2)	0 (0.0)	.49
	1a	24 (4.6)	6 (5.4)	
	1b	133 (25.7)	22 (19.6)	
	1c	237 (45.8)	50 (44.6)	
	2	122 (23.6)	34 (30.4)	
Grading	1	109 (21.1)	20 (17.9)	.53
	2	273 (52.8)	81 (72.3)	
	3	135 (26.1)	11 (9.8)	
Molecular subtype	Luminal A	234 (45.3)	79 (70.5)	< .05
	Luminal B	212 (41.0)	30 (26.8)	
	HER2-positive	50 (9.7)	3 (2.7)	
	Triple negative	21 (4.1)	0 (0.0)	
Vascular invasion	Absent	258 (49.9)	85 (75.9)	< .05
	Present	259 (50.1)	27 (24.1)	
Multifocality	Absent	436 (81.5%)	76 (68)	< .05
	Present	81 (18.5)	36 (32)	
Breast surgery	Conservative	440 (85.1)	77 (68.7)	< .05
	Mastectomy	77 (14.9)	35 (31.3)	

Abbreviations: ILC = invasive lobular carcinoma; NST = nonspecial type.

and triple-negative cases (4.1% vs. no cases) compared to ILC. This difference in the distribution of molecular subtypes between the 2 histological types was significant ($P < .001$).

Vascular invasion, an important prognostic factor, was also evaluated. It was more frequently observed in NST (50.1%) than in ILC (24.1%), ($P < .05$).

Multifocality was significantly more common in ILC (29.5%) compared to NST (15.7%) ($P = .001$), with a consequent higher frequency of mastectomy rates (31.3% in ILC vs. 14.9% in NST) ($P < .05$).

As regards the assessment of the correlation between histological subtype and SLNB positivity at the final pathological report, no significant differences between ILC and NST were found (16.1% vs. 20% respectively). Also, the rate of AD was similar between the 2 groups. A total of 35 patients who underwent AD following SLNB were included in the analysis. Upstaging after ALND—defined as a re-evaluation of the clinical stage to a more advanced level compared to staging based on SLNB findings—was similar between the 2 groups (14.8% in NST histology and 12.5% in ILC) (Table 3).

Other Predictive Factors for SLN Positivity

Age between 40 and 49 years old, premenopausal status, tumoral diameter > 20 mm, vascular invasion, high tumoral grade, and luminal B subtype were significant predictive factors for SLN positivity at univariate analysis (Table 4A).

Multivariate analysis confirmed tumoral dimension > 20 mm and vascular invasion as independent predictive factors. Histological type was not an independent factor predicting SLN positivity in our study (Table 4B).

Performance of Axillary Imaging

Axillary US demonstrated a high negative predictive value (NPV) (0.803) and specificity (0.95). About 80% of patients with negative findings on axillary US were confirmed to have no axillary involvement.

Similarly, MRI showed a good preoperative accuracy with a specificity of 0.79 and a negative predictive value of 0.98.

Stratifying by histological type, axillary US showed a specificity of 94.8% for NST and 96.8% for ILC, with an NPV of 79.8%

Table 3 Comparison Between NST and ILC Tumors With a Focus on Nodal status. No Differences Were Seen Between the 2 Histotype in Terms of SLN Positivity, ALND, and Nodal Upstaging After ALND

Variables		NST (N = 517, 82.2%)	ILC (N = 112, 17.8%)	*P* Value
pN	0	409 (79.1)	94 (83.9)	.30
	1mi	33 (6.4)	3 (2.7)	
	1a	75 (14.5)	15 (13.4)	
ALND	No	489 (94.6)	104 (92.9)	.94
	Yes	27 (5.2)	8 (7.1)	
Nodal upstaging after ALND ($n = 35$)	No	23 (85.2)	7 (87.5)	.45
	Yes	4 (14.8)	1 (12.5%)	

Abbreviations: ALND = axillary lymph nodes dissection; ILC = invasive lobular carcinoma; NST = nonspecial type.

Table 4 Univariate (A) and Multivariate Analysis (B)

Variables	A) Univariate Analysis		*P*-Value	B)Multivariate Analysis	
		Odds Ratio (IC)		Odds Ratio (IC)	*P*-Value
Age	> 70 y	Reference			
	50-69 y	0.87 (0.56-1.34)	.526	1.07 (0.65-1.76)	.79
	40-49 y	1.84 (1.1-3.06)	.019	1.46 (0.47-4.55)	.52
	< 40 y	*0.42 (0.05-3.35)*	.41	0.24 (0.02-2.60)	.24
Menopause	*Yes*	*Reference*			
	No	1.59 (1-2.50)	.04	1.58 (0.58-4.29)	.37
Tumor size	< 20 mm	*Reference*			
	> 20 mm	2.57 (1.70-3.89)	< .05	2.15 (1.31-3.51)	.002
Grading	1	*Reference*			
	2-3	1.92 (1.19-3.59)	.023	0.96 (0.51-1.81)	.9
Vascular invasion	Absent	*Reference*			
	Present	5.57 (3.59-8.65)	< .05	5.87 (3.47-9.93)	< .05
Ki-67	< 20	*Reference*			
	≥ 20	1.46 (0.99-2.15)	.054	0.49 (0.07-3.27)	.46
Molecular subtype	Luminal A	*Reference*			
	Luminal B	1.65 (1.10-2.47)	.016	1.92 (0.28-13.2)	.51
	HER2+	0.89 (0.39-1.99)	.776	1.38 (0.23-8.43)	.73
	Triple Negative	0.67 (0.19-2.31)	.522	0.68 (0.09-5.19)	.71
Histological type	NST	*Reference*			
	ILC	0.73 (0.42-1.25)	.30	0.82 (0.43-1.55)	.53

Abbreviations: ILC = invasive lobular carcinoma; NST = nonspecial type.

and 84.3%, respectively. As for MRI, specificity was 97.6% for NST and 100% for ILC; NPV was 77.1% for NST and 82.3% for ILC.

These differences were not statistically significant ($P > .05$).

Local and Distant Recurrences

Four hundred ninety five patients were included in the analysis, of which 389 were NST and 106 were ILC. Mean follow-up was 49.3 months (25-162). No axillary recurrences were observed in our cohort. Distant recurrences occurred in 6 out of 495 patients (1.21%).

By stratifying for histological type, 4 recurrences were NST (0.9%) and 2 were ILC (1.8%). The difference is not statistically significant ($P = .29$).

Discussion

This retrospective study examined a cohort of 661 patients diagnosed with early-stage BC (pT1-2) and clinically nodenegative status (cN0) before surgery. The cohort was characterized in terms of clinical, histological, and molecular features, as well as radiological profile, therapeutic management, and follow-up timing.

The study aimed to identify predictive factors for SLN positivity and to evaluate the diagnostic accuracy of preoperative imaging

in predicting SLN involvement. Given the ongoing trend of surgical de-escalation in axillary management, the rationale of the study aligns with current literature exploring the potential to omit SLNB in selected patients in the near future.

Particular focus was given to the role of histologic subtype, especially in comparing NST versus ILC as a predictive factor for nodal status.

SLNB in early-stage BC remains a topic of considerable interest, and it has been investigated in clinical trials for its potential omission in well-selected early-stage patients.[8,9] Identifying predictive markers of SLN status is central to optimizing treatment and minimizing surgical morbidity.

The 2025 St. Gallen International Breast Cancer Conference addressed this topic in light of recent data from the SOUND and INSEMA trials, underscoring that de-escalation strategies such as SLNB omission should not be universally applied to all BC patients regardless of age, histological subtype, molecular profile, or tumor size. Notably, 53.6% of experts considered tumor sizes below 20 mm as appropriate for omission, with 15.9% suggesting the threshold be lowered to < 15 mm.[8,9,26]

Among the 661 patients included in our study, age at diagnosis ranged from 30 to 90, with a mean age of 65.2, slightly higher than the SOUND trial population (mean age ≈ 60 years).[8] This difference may stem from differing inclusion criteria, as our cohort was not selected based on age. Indeed, in our cohort the majority were postmenopausal, while 21.9% were premenopausal.

Consistent with the literature, in our sample population NST was the most frequent histological subtype.[2] The majority of tumors were intermediate grade, and BCS was more common than mastectomy.[28]

A comparative analysis of the 2 most prevalent histological subtypes, NST and ILC, revealed several differences. Consistent with prior reports, ILC demonstrated higher HR expression and lower Ki-67 levels compared to NST, resulting in a greater prevalence of Luminal A tumors in the ILC group.[14]

Although tumor grade was not statistically associated with histotype, most ILC were low-to-intermediate grade—also observed in the studies by Farrokh et al.[29] and by Barroso-Sousa et al.[30] However, the grading system may not fully capture ILC's biological behavior due to their lack of tubular formation, leading to frequent G2 classification.[31]

Multifocality was observed in over one-third of ILC, consistent with literature indicating their noncohesive growth pattern and loss of E-cadherin expression,[32,33] contributing to infiltrative behavior and imaging occultation.

ILC in our study population more often require mastectomy than NST, probably due to multifocality itself. In the literature, a higher rate of mastectomy for ILC is reported too, associated with both multifocality and larger tumor size.[29,34]

Vascular invasion was significantly more frequent in NST tumors. This is attributed to their greater angiogenic activity via overexpression of VEGF and HIF-1α.[35]

Several studies have evaluated the potential influence of histological subtype on SLN positivity, with controversial results. In a retrospective cohort of 6922 patients the positive rate of SLN was significantly higher in patients with NST than that in patients with ILC (19.3% in NST vs. 12.9% in ILC, $P = .008$).[36]

A similar result was obtained by Houvenaeghel et al.[37] who retrospectively evaluated patients with early BC who underwent SLNB. In this series, NST tumors presented a higher SLN positivity rate than ILC.[37]

These results can be interpreted by observing ILC biology, characterized by diffuse growth, multifocality, and E-cadherin loss, which can increase the risk of imaging misinterpretation and nodal under staging.[38]

On the contrary, many studies state a higher nodal burden in ILC than NST cancers.[36,39]

Besides, other studies showed no impact of histological type in SLN positivity. A large retrospective cohort of 2283 patients by Silverstein et al.[40] found no significant difference (30% in NST vs. 31% in ILC; $P = .8$), with ILC not being an independent predictive factor of nodal positivity.

Similarly, our study found a similar SLN positivity between NST and ILC (20.88% vs. 16.7%, respectively). In our series, ILC does not independently increase the risk of SLN metastasis. This aligns with findings by Adachi et al.[39] who found that SLN positivity was not related to the histological type. However, their findings were consistent with a positive higher rate of non-SLN in ILC.[39] Considering the biological behavior of ILC, other recent studies have investigated the lymphatic dissemination patterns in non-SLN, suggesting a higher rate of non-SLN positivity in ILC than in NST cancers.[15,41]

In a retrospective cohort of 159 patients, Cipolla et al.[15] reported significantly higher rates of non-SLN involvement in the ILC group (66.7% vs. 45%; $P = .02$), suggesting that SLN positivity in ILC may more reliably predict further axillary disease.[15] In our study, among 35 cN0 patients undergoing AD after SLNB positivity, no significant difference in nodal upstaging was found between NST and ILC. This aligns with Vandorpe et al.[41] who found ILC was not an independent risk factor for nodal upstaging in a cohort of 4292 BC patients.[41]

These discrepancies underscore the need for prospective studies with adequate ILC representation to better understand its role in nodal upstaging and its prognostic impact.

Although there are conflicting results regarding the risk of axillary lymph node involvement in ILC, it is important to highlight that this does not appear to impact the rate of locoregional recurrence. Indeed, a sub analysis of the ACOSOG-011 trial showed no axillary recurrences despite the higher proportion of SLN macro metastases for ILC.[42]

In our study, considering a minimum follow-up of 24 months, no axillary recurrences were seen, and the number of distant metastases was less than 2%. Our results are consistent with the outcomes obtained in the SOUND and INSEMA trials, suggesting the safety of omission of SLNB in selected categories of patients.[8,9]

In line with this data, a recent analysis also supported extending "Choosing Wisely" SLNB omission recommendations to patients with ILC.[43] This evidence is supported by the fact that ILC are more frequently luminal A tumors and more frequently lack vascular invasion, as also seen in our study.[44]

However, in a recent summary from the 2025 St. Gallen International Breast Cancer Conference, it has been highlighted that the possibility of such de-escalation outside of clinical trials should not be considered universally applicable to all patients with breast cancer, regardless of age, histological type, molecular profile, and lesion size.[26]

Other Predictive Factors for SLN Positivity

Age under 50 years was significantly associated with SLN positivity, consistent with previous literature.[45] Given that the average menopausal age in Italy is 51, women ≤ 50 years in this study were likely premenopausal, a state linked with higher SLN positivity.[46]

Tumors > 20 mm were significantly associated with SLN positivity. This result is consistent with most of the studies present in literature.[40,45,47]

Intermediate-to-high tumor grade was also significantly associated with SLN positivity, echoing other findings.[45,48] Similarly, vascular invasion strongly correlated with SLN positivity: 34.4% versus 8.4% in tumors without vascular invasion. As stated by Kuhn et al.[49] vascular invasion represents an important predictive factor for nodal positivity; due to its reliable prognostic capacity, it can be helpful in deciding adjuvant treatments in case of a nonconclusive genomic testing.

Multivariate analysis of our data confirmed that ILC was not significantly associated with positive nodal status. However, tumor size > 20 mm and vascular invasion remained strong independent predictors for SLN positivity, consistent with literature.[45]

Axillary US and MRI Performance

In the context of omitting SLNB, preoperative imaging plays a key role, as it must have high specificity to minimize the risk of false-negative results.

Due to our study design—excluding patients with preoperative US or core needle biopsy-confirmed nodal positivity—sensitivity could not be assessed. However, specificity and NPV were analyzed. Axillary US showed high specificity (0.95) and a strong NPV (0.8), confirming its usefulness in ruling out axillary involvement. These findings align with literature reporting US specificity between 93.6% and 100%.[50] Despite high specificity, the US alone lacks the sensitivity to detect axillary metastasis reliably. This is partly due to the absence of standardized sonographic criteria for nodal positivity.

As for axillary US, MRI specificity and NVP were highly reliable in detecting suspicious axillary nodes.

Both techniques showed similar performance, regardless of the histological type. This data is consistent with Topps et al.[51] who investigated the role of preoperative axillary US in NST and ILC BC.[51]

This study presents some limitations. First, the retrospective design of the study; secondly, the low number of patients who underwent ALND which can underestimate the effect of ILC in nodal upstaging and positivity of non-SLNs.

A key strength of this study is the use of a homogeneous patient cohort, all managed within a single institutional setting, thereby reducing potential variability in clinical assessment and treatment approaches. Moreover, the inclusion of a high number of cases with ILC provides a significant result, addressing an area where existing literature remains inconclusive. Finally, the study includes one of the largest sample sizes to date, focusing on preoperative imaging in different histological subtypes.

Conclusion

This study reinforces the importance of a tailored approach to axillary management in early-stage BC. While ILC presents distinct biological and clinical characteristics, it does not independently predict SLN positivity or higher risk of nodal upstaging. Tumor size > 20 mm and vascular invasion emerge as the most robust predictors of SLN involvement, highlighting the need for comprehensive preoperative evaluation.

In the era of surgical de-escalation, our findings support the growing body of evidence advocating for selective omission of SLNB in well-defined low-risk patients, an approach currently limited to clinical trials, but which may potentially become standard clinical practice in selected cases in the future.

Axillary US, with its high specificity and negative predictive value, may serve as a valuable tool in this refined decision-making process.

As the field moves toward more personalized, less invasive treatment strategies, future prospective studies—particularly those including a higher representation of ILC—will be essential in defining new standards of care that optimize both oncologic safety and quality of life.

Clinical Practice Points

- Lobular histology is not an independent predictor of SLNB positivity or nodal upstaging.
- Tumor size > 20 mm and vascular invasion remain the strongest predictors of nodal involvement.
- Preoperative axillary ultrasound and MRI demonstrate high reliability in identifying truly nodenegative patients.
- In well-selected cN0 patients, including those with ILC, SLNB omission may be considered as part of a personalized, de-escalated surgical approach

Disclosure

The authors have no relevant financial or nonfinancial interests to disclose.

CRediT authorship contribution statement

Francesca Accomasso: Writing – original draft, Methodology, Formal analysis, Conceptualization. **Gaia Ruggeri:** Investigation, Data curation. **Silvia Actis:** Writing – review & editing, Formal analysis, Conceptualization. **Elena Paradiso:** Investigation, Data curation. **Pier Giorgio Spanu:** Supervision, Conceptualization. **Luca Giuseppe Sgro:** Data curation, Conceptualization. **Annamaria Ferrero:** Writing – review & editing, Supervision. **Valentina Elisabetta Bounous:** Writing – review & editing, Supervision, Conceptualization.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to privacy concerns, but are available from the corresponding author on reasonable request.

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