Axillary Nodal Upstaging in T1N0 Invasive Lobular Carcinoma: Evaluating Applicability of SOUND Trial Results

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Introduction

- The SOUND and INSEMA trials support the omission of sentinel lymph node biopsy (SLNB) among stage 1, cN0 HR+/HER2- breast cancer patients with negative pre-operative axillary US (AxUS).[1,2]
- Invasive lobular carcinoma (ILC) has a **biologically unique and discohesive** growth pattern and comprises less than 15% of patients in trials which has resulted in uncertainty regarding frequency of **nodal upstaging**.[3,4,5]
- **Applicability of SLNB-omission to ILC patients remains uncertain**

Objective

To evaluate the **rate and predictors of axillary nodal upstaging** among HR+/HER2- ILC patients meeting **SOUND eligibility** criteria.

Methods

- Retrospective dataset: **cT1, cN0 HR+/HER2- pure ILC patients** with **normal pre-operative AxUS** who had upfront surgery including **SLNB and/or ALND** between 2009 and 2024.

N=639

- Clinicopathologic characteristics and nodal burden were examined
- Descriptive statistics and logistic regression analysis was performed using software R 4.4.2.

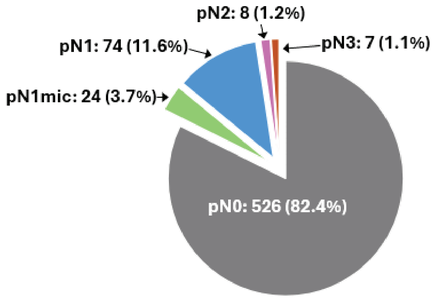
Results

Clinicopathologic features

	Total (n=639)	pN0 (n=526)	pN1-3 (n=113)	p-value
Age, years (median [IQR])	60 (51, 68)	61 (52, 68)	58 (49, 66)	0.054
Menopausal status				
Premenopausal	180 (28%)	139 (26%)	41 (36%)	0.035
Postmenopausal	459 (72%)	387 (74%)	72 (64%)	
Race/Ethnicity				
Asian/Indian	30 (4.7%)	29 (5.5%)	1 (0.9%)	0.13
Black	46 (7.2%)	36 (6.8%)	10 (8.8%)	
Other	22 (3.4%)	19 (3.6%)	3 (2.7%)	
White	523 (82%)	427 (81%)	96 (85%)	
Not reported	18 (2.8%)	16 (3.0%)	3 (2.7%)	
Histology				
Classic	539 (84%)	441 (84%)	98 (87%)	0.7
Non-classic	100 (16%)	76 (16%)	14 (13%)	
Grade				
1	53 (8.3%)	45 (8.6%)	8 (7.1%)	0.062
2	565 (88%)	468 (89%)	97 (86%)	
3	21 (3.3%)	13 (2.5%)	8 (7.1%)	
Lymphovascular invasion	38 (5.9%)	17 (3.2%)	21 (19%)	<0.001
Pathologic tumor size, centimeters (median [IQR])	1.3 (0.9, 2.0)	1.2 (0.8, 1.8)	2.0 (1.2, 2.7)	<0.001
pT stage				
pT1	488 (76%)	428 (81%)	60 (53%)	<0.001
pT2	133 (21%)	91 (17%)	42 (37%)	
pT3	18 (2.8%)	7 (1.3%)	11 (9.7%)	
Pathologic stage				
I	428 (68%)	428 (81%)	12 (10%)	<0.001
II	176 (28%)	98 (19%)	78 (77%)	
III	23 (3.7%)	0	23 (23%)	

Nodal burden

N = 113 (17.6%) had nodal metastasis



Predictors of Nodal Upstaging

UVA			
	OR	95% CI	p-value
Premenopausal	1.59	1.03, 2.43	0.036
Grade 3	3.46	1.08 11.3	0.036
LVI	6.83	3.48, 13.6	<0.001

- On MVA, **only LVI** was significantly associated with pN+ (OR 6.17; OR 95%, CI 3.10, 12.4; p<0.0001)
- MVA could not be performed among cases of extensive nodal metastasis (pN2-3) due to few upstaging events (n=15, 2.3%).

Discussion

Comparison to nodal upstaging in SLNB-omission trials

	ILC (n=639)	SOUND[1] (n=701)	INSEMA[2] (n=3,896)
pN+	17.6%	13.7%	15.1%
pN1mic	3.7%	5.1%	3.5%
pN1	11.6%	8.0%	11.4%
pN2-3	2.3%	0.6%	0.2%

Conclusions

- In this cohort of SOUND-eligible ILC patients, **17.6%** were node-positive but only **2.3%** had extensive nodal disease (pN2-3)
- These findings are comparable to the node-positive rates reported in SOUND (13.1%) and INSEMA (15.7%) trials.
- **ILC patients with a combination high-risk features such as LVI and high grade should be considered for SLNB**

References

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