Evaluating nodal burden in T1a–T2 HR+HER2– breast cancer: Implications for SLNB omission in patients ≥50 years

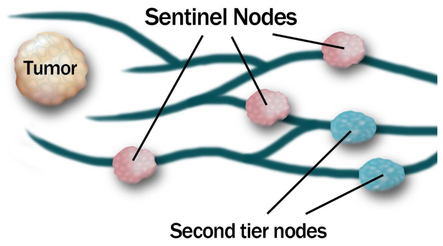
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Rates of nodal positivity are **not insignificant** for early-stage breast cancer. In women over the age of 50 where SLNB omission may be considered, **rates of nodal positivity increased from 5% for T1a lesions to 24% for T1c lesions.** Most of the nodal burden was N1 disease.

INTRODUCTION

The recent INSEMA and SOUND randomized trials support sentinel lymph node biopsy (SLNB) omission in postmenopausal patients ≥50 years with clinically node-negative T1-T2 hormone receptor-positive (HR+) HER2– breast cancer and negative axillary ultrasound.



We used real-world data to evaluate pathologic nodal positivity rates by tumor size for HR+HER2– breast cancer to assess the appropriateness of SLNB omission.

METHODS

We performed a population-based retrospective cohort study using ICES administrative databases.

Inclusion Criteria:

Population
- Biological females
- Age ≥18 yrs

Diagnosis
- First diagnosis of invasive breast cancer
- Stage I-III, T1-T2, HR+/HER2-

Time Frame
- Diagnosed between Jan 1, 2000 and Dec 31, 2019

Pathologic nodal positivity rates across T1a–T2 were calculated for the full cohort and stratified by age group (<50, 50-69, ≥70). Multivariable logistic regression adjusting for age, T stage, and hormone receptor subtype was performed. All analyses were conducted using SAS® software.

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Table 1a. Regional nodal burden among patients <50 years old, reported as frequency and proportion (%)

	Total *N* = 4895	Node-Negative *N* = 2951	Node-Positive *N* = 1944	N1 *N* = 1590	N2 *N* = 278	N3 *N* = 76
T1a	210	189 (90)	21 (10)	20 (95)	1 (5)	0 (0)
T1b	530	455 (86)	75 (14)	69 (92)	5 (7)	1 (1)
T1c	1840	1258 (68)	582 (32)	507 (87)	60 (10)	15 (3)
T2	2314	1049 (45)	1266 (55)	994 (79)	212 (17)	60 (5)

Table 1b. Nodal burden among patients 50–69 years old, reported as frequency and proportion (%)

	Total *N* = 16,987	Node-Negative *N* = 12,231	Node-Positive *N* = 4756	N1 *N* = 3905	N2 *N* = 634	N3 *N* = 217
T1a	916	871 (95)	45 (5)	40 (89)	3 (7)	2 (4)
T1b	3226	2920 (91)	306 (9)	281 (92)	17 (6)	8 (3)
T1c	7369	5594 (76)	1775 (24)	1585 (89)	151 (9)	39 (2)
T2	5479	2846 (52)	2630 (48)	1999 (76)	463 (18)	168 (6)

Table 1c. Nodal burden among patients ≥70 years old, reported as frequency and proportion (%)

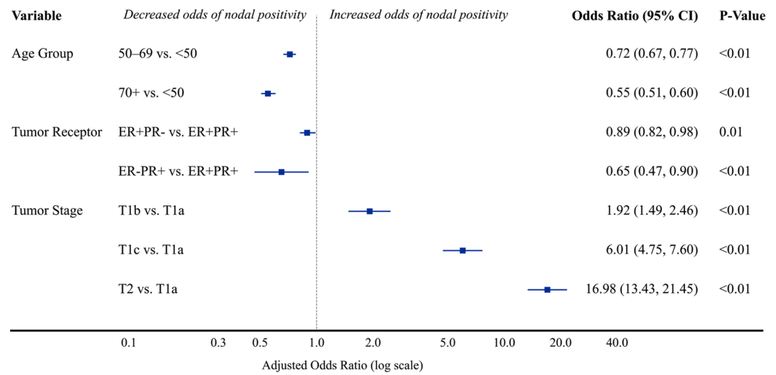
	Total *N* = 9087	Node-Negative *N* = 6792	Node-Positive *N* = 2295	N1 *N* = 1890	N2 *N* = 298	N3 *N* = 107
T1a	373	363 (97)	10 (3)	8 (80)	1 (10)	1 (10)
T1b	1529	1429 (93)	100 (7)	93 (93)	6 (6)	1 (1)
T1c	3716	2961 (80)	755 (20)	667 (88)	75 (10)	13 (2)
T2	3469	2039 (59)	1430 (41)	1122 (78)	216 (15)	92 (6)

RESULTS (cont.)

There were 30,969 HR+HER2– tumors, including 4895 (16%) patients <50 yrs, 16,987 (55%) 50–69 yrs, and 9087 (29%) ≥70 yrs. SLNB was omitted in 288 (3%) patients ≥70 yrs.

Nodal positivity rates reached 40% in <50 yr olds, and was lower in ≥50 yr olds (28% of 50–69 yr olds, 25% of ≥70 yr olds) (**Table 1a-c**). Across all age groups, 82% of node-positive patients had N1 disease. Most N2-3 disease occurred in T2 tumors (<50 yr olds: 76% N2, 79% N3. 50–69 yr olds: 73% N2, 77% N3. ≥70 yr olds: 73% N2, 86% N3).

Figure 1. Forest plot depicting multivariable logistic regression for factors associated with pathologic nodal positivity among patients with T1a–T2 hormone receptor positive (HR+), HER2-negative (HER2–) breast cancer.



On multivariable regression, **tumor size** was the strongest predictor of nodal positivity (**Figure 1**). Compared to T1a, odds were significantly higher for T1b (aOR 1.92), T1c (aOR 6.01), and T2 (aOR 16.98) [*P*<0.01 all]. **Age** was also inversely correlated with nodal positivity. Compared to patients <50 yrs, odds were significantly lower for patients 50–69 yrs (aOR 0.67) and ≥70 yrs (aOR 0.55) [*P*<0.01 all]. **Hormone receptor subtype** was also associated with nodal positivity. Compared to ER+PR+ tumors, odds were significantly lower for ER+PR– (aOR 0.89, *P*=0.01) and ER–PR+ (aOR 0.65, *P*<0.01).

DISCUSSION & CONCLUSION

Rates of nodal positivity are not insignificant for early-stage breast cancer. In women ≥50 yrs old where SLNB omission may be considered, rates of nodal positivity increased from 5% for T1a lesions to 24% for T1c lesions. Most of the nodal burden was N1 disease.

This suggests that SLNB omission would not have impacted systemic therapies, as most of these patients would receive genomic assay testing. However, **radiotherapy decisions would be impacted** as the identification of nodal disease is an indication for locoregional radiation. These findings need to be considered in the era of surgical and radiotherapy de-escalation.