Association of Long-term Oncologic Prognosis With Internal Mammary Sentinel Lymph Node Biopsy In Breast Cancer Patients

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Abstract

Internal mammary sentinel lymph node biopsy (IMSLNB) is a minimally invasive diagnostic technique for assessing regional lymph nodes, which provides precise lymph node staging and informs adjuvant treatment decisions. However, its prognostic impact remains uncertain, resulting in ongoing debate regarding its clinical application. This study aims to investigate the long-term prognostic outcomes of IMSLNB in patients with early-stage breast cancer.

Introduction

Breast cancer is the most common malignant tumor in females and a leading cause of cancer-related mortality. The status of regional lymph nodes is crucial for breast cancer staging and influences prognostic evaluation and treatment planning. Both the internal mammary lymph node (IMLN) and axillary lymph node (ALN) are key in breast lymphatic drainage, and their diagnosis has been a focus of research[1]. While axillary sentinel lymph node biopsy (SLNB) is widely recommended and personalized in clinical practice[2], the clinical use of IMSLNB remains controversial. The lack of histological diagnosis for IMLN often leads to inaccurate staging and potential under-treatment or over-treatment of breast cancer[3]. Recent studies suggest that IMSLNB provides more accurate regional lymph node staging, influencing adjuvant treatment decisions, particularly radiotherapy[4,5]. However, its clinical adoption is limited by insufficient follow-up data on its long-term impact on survival and prognosis. To date, no study has comprehensively assessed the long-term safety and efficacy of IMSLNB in breast cancer patients.

Methods and Materials

This study performed a retrospective cohort analysis involving 10,923 breast cancer patients who visited our hospital between January 1, 2013, and December 31, 2022. Following propensity score matching, the patients were categorized into two groups: the IMSLNB group and the no-IMSLNB group. The prognostic outcomes of these two groups were compared. The primary endpoint of this study was disease-free survival (DFS), while secondary endpoints included overall survival (OS), regional recurrence-free survival (RRFS), local recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS).

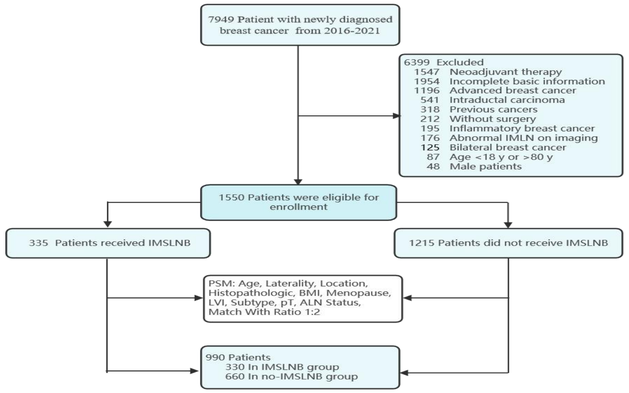


Figure 1. Flow Diagram of Participant Selection

Abbreviations: IMSLNB, internal mammary sentinel lymph node biopsy; BMI, Body Mass Index; LVI, lymphatic vessel infiltration; ALN, axillary lymph node; PSM, propensity score matching.

Results

A total of 1608 patients were included in the final analysis, with 536 in the IMSLNB group and 1072 in the no-IMSLNB group. In the IMSLNB group, 93 patients were identified with IMSLN metastasis, yielding a metastasis rate of 17.4%. Among these, 82 had concurrent ALN metastasis, while 11 exhibited isolated IMSLN metastasis. The median follow-up duration was 60.9 months.

The findings demonstrated that the 5-year DFS (95.9% vs. 93.9%; HR, 0.562; 95% CI, 0.364–0.869; P=0.010) was significantly higher in the IMSLNB group compared to the no-IMSLNB group. However, there was no statistically significant difference in the 5-year OS between the two groups (98.9% vs. 98.5%; HR, 0.487; 95% CI, 0.208–1.141; P=0.098).The 5-year RRFS (99.4% vs 98.4%, HR, 0.360; 95% CI, 0.145-0.890; P=0.027) and LRFS (99.6% vs 98.5%, HR, 0.380; 95% CI, 0.118-0.800; P=0.016) in the IMSLNB group were significantly superior to those in the no-IMSLNB group; however, there was no statistically significant difference observed in the 5-year DMFS (96.8% vs 97.0%, HR, 0.843; 95% CI, 0.472-1.508; P=0.565) between the two groups.

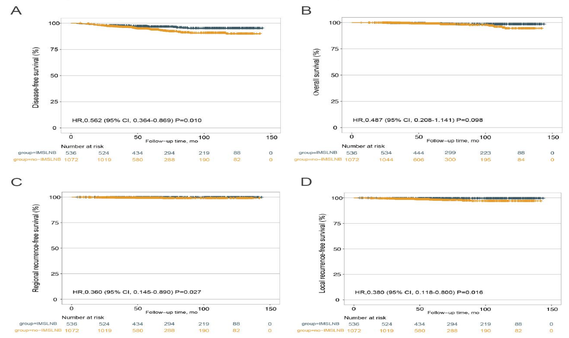
Exploratory subgroup analysis of DFS revealed that patients within specific subgroups, including diagnostic age (>50 years), mastectomy, absence of lymphovascular invasion, pathological type as invasive ductal carcinoma, and negative ALN status, demonstrated significant benefit from IMSLNB (P<0.05).

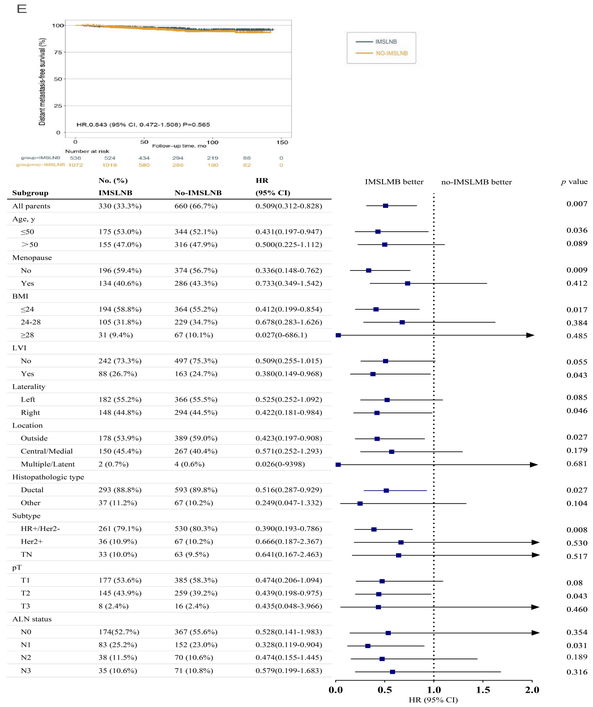
Table 1. Partial Results: Baseline Characteristics of Patients Before and After Propensity Score Matching (PSM)

Abbreviations: IMSLNB, internal mammary sentinel lymph node biopsy; LVI, lymphatic vessel infiltration; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; ALN, axillary lymph node; NA, not applicable.

Characteristic	Before PSM			After PSM		
	IMSLNB (n=537)	no-IMSLNB (n=1704)	*P value*	IMSLNB (n=536)	no-IMSLNB (n=1072)	*P value*
No.	537	1704	*NA*	536	1072	*NA*
Age,y						
≤50	308 (57.3%)	934 (54.8%)	*0.319*	307 (57.3%)	592 (55.2%)	*0.456*
>50	229 (42.7%)	770 (45.2%)		229 (42.7%)	480(44.8%)	
Breast surgery						
Mastectomy	477 (88.8%)	1432 (84.0%)	*<0.001*	477 (88.8%)	922 (86.0%)	*0.093*
Lumpectomy	60 (11.2%)	272 (16.0%)		59 (11.2%)	150 (14.0%)	
Histopathologic type						
Ductal	486 (90.5%)	1542 (90.5%)	*0.995*	485 (90.5%)	976 (91.0%)	*0.714*
Other	51 (9.5%)	162 (9.5%)		51 (9.5%)	96 (9.0%)	
Menopause						
Yes	209 (39.0%)	764 (44.8%)	*0.016*	209 (39.0%)	423 (39.5%)	*0.857*
No	328 (61.0%)	940 (55.2%)		327 (61.0%)	649 (60.5%)	
LVI						
Yes	118 (22.0%)	378 (22.2%)	*0.919*	118 (22.0%)	260 (24.3%)	*0.318*
No	419 (78.0%)	1326 (77.8%)		418 (78.0%)	812 (75.7%)	
Subtype						
HR+/HER2−	299 (55.7%)	1003 (58.9%)	*0.465*	299 (55.7%)	623 (58.1%)	*0.459*
HR+/HER2+	113 (21.0%)	311 (18.3%)		113 (21.0%)	192 (17.9%)	
HR−/HER2+	64 (11.9%)	207(12.1%)		63 (11.9%)	128 (12.0%)	
TNBC	61 (11.4%)	183 (10.7%)		61 (11.4%)	129 (12.0%)	
pT						
T1	282 (52.4%)	1083 (63.6%)	*<0.001*	281 (52.4%)	591 (58.3%)	*0.195*
T2	231 (43.1%)	539(31.6%)		231 (43.1%)	418 (39.2%)	
T3	24 (4.5%)	82(4.8%)		24 (4.5%)	63 (2.4%)	
ALN stage						
N0	249 (46.4%)	877 (51.5%)	*0.015*	248 (46.4%)	439 (41.0%)	*0.371*
N1	117 (20.7%)	394 (23.1%)		117 (20.7%)	290 (27.1%)	
N2	107 (20.0%)	244 (14.3%)		107 (20.0%)	227 (21.1%)	
N3	64 (11.9%)	189 (11.1%)		64 (11.9%)	116 (10.8%)	

Figure 2. Kaplan-Meier Survival Curve After Propensity Score Matchin (A, B, C, D, E)





Subgroup	No. (%) IMSLNB	No. (%) No-IMSLNB	HR (95% CI)	*p* value
All parents	330 (33.3%)	660 (66.7%)	0.509(0.312-0.828)	0.007
Age, y				
≤50	175 (53.0%)	344 (52.1%)	0.431(0.197-0.947)	0.036
>50	155 (47.0%)	316 (47.9%)	0.500(0.225-1.112)	0.089
Menopause				
No	196 (59.4%)	374 (56.7%)	0.336(0.148-0.762)	0.009
Yes	134 (40.6%)	286 (43.3%)	0.733(0.349-1.542)	0.412
BMI				
≤24	194 (58.8%)	364 (55.2%)	0.412(0.199-0.854)	0.017
24-28	105 (31.8%)	229 (34.7%)	0.678(0.283-1.626)	0.384
≥28	31 (9.4%)	67 (10.1%)	0.027(0-686.1)	0.485
LVI				
No	242 (73.3%)	497 (75.3%)	0.509(0.255-1.015)	0.055
Yes	88 (26.7%)	163 (24.7%)	0.380(0.149-0.968)	0.043
Laterality				
Left	182 (55.2%)	366 (55.5%)	0.525(0.252-1.092)	0.085
Right	148 (44.8%)	294 (44.5%)	0.422(0.181-0.984)	0.046
Location				
Outside	178 (53.9%)	389 (59.0%)	0.423(0.197-0.908)	0.027
Central/Medial	150 (45.4%)	267 (40.4%)	0.571(0.252-1.293)	0.179
Multiple/Latent	2 (0.7%)	4 (0.6%)	0.026(0-9398)	0.681
Histopathologic type				
Ductal	293 (88.8%)	593 (89.8%)	0.516(0.287-0.929)	0.027
Other	37 (11.2%)	67 (10.2%)	0.249(0.047-1.332)	0.104
Subtype				
HR+/Her2-	261 (79.1%)	530 (80.3%)	0.390(0.193-0.786)	0.008
Her2+	36 (10.9%)	67 (10.2%)	0.666(0.187-2.367)	0.530
TN	33 (10.0%)	63 (9.5%)	0.641(0.167-2.463)	0.517
pT				
T1	177 (53.6%)	385 (58.3%)	0.474(0.206-1.094)	0.08
T2	145 (43.9%)	259 (39.2%)	0.439(0.198-0.975)	0.043
T3	8 (2.4%)	16 (2.4%)	0.435(0.048-3.966)	0.460
ALN status				
N0	174(52.7%)	367 (55.6%)	0.528(0.141-1.983)	0.354
N1	83 (25.2%)	152 (23.0%)	0.328(0.119-0.904)	0.031
N2	38 (11.5%)	70 (10.6%)	0.474(0.155-1.445)	0.189
N3	35 (10.6%)	71 (10.8%)	0.579(0.199-1.683)	0.316

Figure 3. Forest Plot for Subgroup Analysis of Disease-Free Survival

Abbreviations: IMSLNB, internal mammary sentinel lymph node biopsy; BMI, Body Mass Index; LVI, lymphatic vessel infiltration; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; ALN, axillary lymph node.

Conclusions

IMSLNB enables more precise regional lymph node staging for early-stage breast cancer, facilitates the optimization of adjuvant radiotherapy strategies, thereby enhancing RRFS, LRFS, and DFS outcomes. It can be recommended as a minimally invasive technique for regional lymph node staging.

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Supplementary Figure 1. Subgroup analysis of seed marking on neoadjuvant therapeutic efficacy and postoperative disease recurrence .
A: Intergroup differences in pCR rates among the overall population. B: HR+/HER2-subgroup. C: HER2+ subgroup. D: TNBC subgroup. E: The impact of ^{125}I seed marking on the 3-year iDFS in the overall population. F: Kaplei-Meier curves of 3-year iDFS stratified by ^{125}I seed marking status and pCR status.
Group A=without ^{125}I seed-marked group. Group B=^{125}I seed-marked group
*:p<0.05; **:p<0.01; ***:p<0.001; NS: No statistically significant difference

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