Axillary Management Strategies in Breast Cancer Patients With ypN0 After Neoadjuvant Therapy

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Purpose

For breast cancer patients achieving nodal pathologic complete response (ypN0) after neoadjuvant therapy (NAT), the optimal axillary management remains controversial, especially for those presenting with cN2–3 disease. While sentinel lymph node biopsy (SLNB) is increasingly adopted, the survival impact compared to axillary lymph node dissection (ALND), as well as the necessity of adjuvant axillary radiotherapy in this setting, remain unclear in real-world populations.

Methods

Using the National Cancer Database (2018–2022), we identified female patients with clinical stage I–III invasive breast cancer who presented with cN1–3 disease, received NAT, and achieved ypN0. Patients were grouped according to the type of axillary surgery (SLNB or ALND). Propensity score weighting was applied to adjust for baseline imbalances. Overall survival (OS) was compared using Kaplan–Meier curves and Cox regression. Subgroup analyses were conducted according to clinical nodal stage (cN1–cN3), and the impact of adjuvant axillary radiotherapy was also evaluated.

Table 1. Baseline Characteristics

	Unweighted			Weighted		
Characteristics	**SLNB**	**ALND**	**SMD**	**SLNB**	**ALND**	**SMD**
Number	6437	3215		9759.95	9586.57	
Age (mean (SD))	52.51 (12.76)	53.51 (12.94)	**0.077**	52.98 (12.86)	52.95 (13.01)	**0.003**
Race (%)			**0.074**			**0.008**
White	4834 (75.1)	2352 (73.2)		7280.6 (74.6)	7129.4 (74.4)	
Black	915 (14.2)	519 (16.1)		1455.3 (14.9)	1455.9 (15.2)	
Asian	464 (7.2)	207 (6.4)		666.1 (6.8)	646.7 (6.7)	
Other	224 (3.5)	137 (4.3)		358.0 (3.7)	354.5 (3.7)	
Insurance Status (%)			**0.183**			**0.009**
Private Insurance	4209 (65.4)	1849 (57.5)		6038.5 (61.9)	5951.8 (62.1)	
Medicaid	722 (11.2)	494 (15.4)		1268.4 (13.0)	1222.1 (12.7)	
Medicare	1194 (18.5)	668 (20.8)		1927.1 (19.7)	1904.6 (19.9)	
Other Government	99 (1.5)	47 (1.5)		143.2 (1.5)	138.2 (1.4)	
Not Insured	163 (2.5)	132 (4.1)		314.4 (3.2)	302.1 (3.2)	
Unknown	50 (0.8)	25 (0.8)		68.4 (0.7)	67.8 (0.7)	
Median Income (%)			**0.211**			**0.012**
<$46,277	797 (12.4)	571 (17.8)		1441.7 (14.8)	1384.1 (14.4)	
$46,278-$57,856	1212 (18.8)	690 (21.5)		1902.9 (19.5)	1895.9 (19.8)	
$57,857-$74,062	1532 (23.8)	802 (24.9)		2360.8 (24.2)	2335.6 (24.4)	
>$74,063	2896 (45.0)	1152 (35.8)		4054.6 (41.5)	3970.9 (41.4)	
Histology (%)			**0.177**			**0.010**
IDC	6082 (94.5)	2908 (90.5)		9082.2 (93.1)	8945.2 (93.3)	
ILC	150 (2.3)	80 (2.5)		228.0 (2.3)	219.2 (2.3)	
other	205 (3.2)	227 (7.1)		449.8 (4.6)	422.2 (4.4)	
Clinical N Status (%)			**0.440**			**0.024**
cN1	5615 (87.2)	2240 (69.7)		7809.1 (80.0)	7758.1 (80.9)	
cN2	411 (6.4)	431 (13.4)		928.0 (9.5)	859.3 (9.0)	
cN3	411 (6.4)	544 (16.9)		1022.8 (10.5)	969.1 (10.1)	
Clinical T Status (%)			**0.646**			**0.027**
cT1	1312 (20.4)	422 (13.1)		1728.6 (17.7)	1709.5 (17.8)	
cT2	3465 (53.8)	1229 (38.2)		4684.7 (48.0)	4657.4 (48.6)	
cT3	1300 (20.2)	674 (21.0)		1968.4 (20.2)	1956.2 (20.4)	
cT4	360 (5.6)	890 (27.7)		1378.3 (14.1)	1263.5 (13.2)	
Pathological T Status (%)			**0.143**			**0.022**
pT0	4707 (73.1)	2397 (74.6)		7170.4 (73.5)	7050.8 (73.5)	
pT1	1456 (22.6)	641 (19.9)		2106.8 (21.6)	2058.5 (21.5)	
pT2	230 (3.6)	107 (3.3)		342.9 (3.5)	356.8 (3.7)	
pT3	31 (0.5)	38 (1.2)		75.5 (0.8)	71.2 (0.7)	
pT4	13 (0.2)	32 (1.0)		64.3 (0.7)	49.3 (0.5)	
Hormone Receptor Status (%)			**0.047**			**0.007**
Positive	3361 (52.2)	1603 (49.9)		5031.7 (51.6)	4907.7 (51.2)	
Negative	3076 (47.8)	1612 (50.1)		4728.3 (48.4)	4678.9 (48.8)	
HER2 Status (%)			**0.115**			**0.019**
Positive	5096 (79.2)	2689 (83.6)		7886.0 (80.8)	7675.1 (80.1)	
Negative	1341 (20.8)	526 (16.4)		1874.0 (19.2)	1911.5 (19.9)	
Adjuvant Chemotherapy (%)			**0.023**			**0.002**
No	6324 (98.2)	3168 (98.5)		9601.7 (98.4)	9428.3 (98.3)	
Yes	113 (1.8)	47 (1.5)		158.3 (1.6)	158.3 (1.7)	
Adjuvant Radiation (%)			**0.001**			**0.002**
No	1510 (23.5)	754 (23.5)		2367.9 (24.3)	2318.2 (24.2)	
Yes	4927 (76.5)	2461 (76.5)		7392.1 (75.7)	7268.4 (75.8)	

Results

Among 9,652 patients, 66.7% underwent SLNB and 33.3% underwent ALND. Consistent with previous studies (ACOSOG Z0011、SENTINA、ACOSOG Z1071), for patients initially diagnosed as cN1, SLNB achieved comparable or even better OS compared with ALND (weighted HR 1.63, 95% CI 1.26–2.10, p < 0.001).For cN2–cN3 patients, no significant OS difference was observed between SLNB and ALND after adjustment (cN2: weighted HR 0.79, 95% CI 0.41–1.53, p = 0.61; cN3: weighted HR 0.94, 95% CI 0.53–1.67, p = 0.91). However, the wide 95% CI and curve separation beyond 36 months suggest potential long-term risk that warrant further investigation. Axillary radiotherapy did not significantly impact OS in either surgical group.

Conclusion

- For cN1 patients who achieve ypN0 after NAT, SLNB can safely replace ALND,
- For cN2–3 patients with high axillary tumor burden, long-term regional or distant recurrence risk remains.
- Axillary de-escalation should be cautious, guided by imaging downstaging, targeted axillary dissection (TAD), and radiotherapy planning for individualized management.
- Adjuvant RNI did not reduce overall survival risk in patients with ypN0 after NAT.

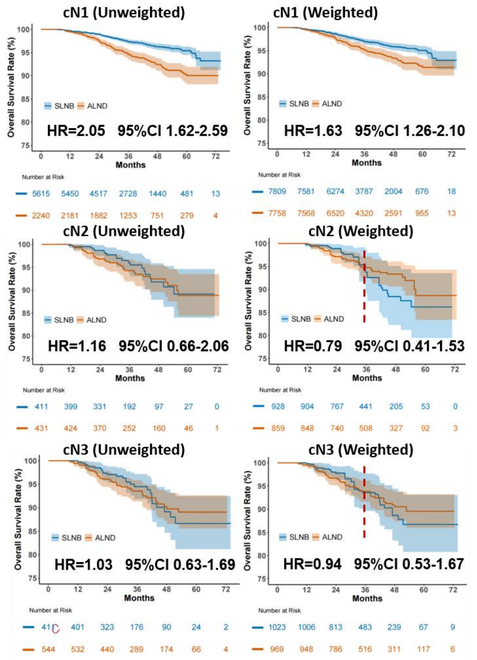


Fig.1 Subgroup analysis of overall survival by axillary surgery type in ypN0 patients, stratified by clinical nodal status at diagnosis (cN1-cN3).

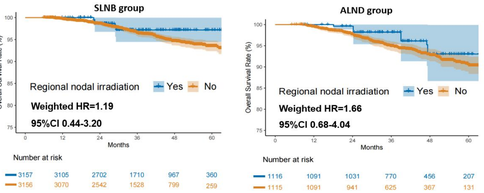


Fig.2 Overall survival by axillary radiotherapy status in patients with ypN0 disease following neoadjuvant treatment.

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