Long-term Outcomes of Sentinel Lymph Node Biopsy Alone for Breast Cancer with Residual Axillary Nodal Disease (ypN+) following Neoadjuvant Chemotherapy: A Systematic Review and Meta-Analysis.

Mariam Rana MBBS MPH FRCSC[1], Anna Weiss MD[2], Alison Laws MD MPH[3], Carol Mita MS[4], and Tari King MD FASCO FSSO[5]

[1]Department of Surgery, University of Saskatchewan, Canada [2]Department of Surgery, University of Rochester, New York [3]Department of Surgery, University of Calgary, Canada [4]Harvard Medical School, Boston, MA [5]Department of Surgery, Winship Cancer Institute of Emory University, Atlanta, GA

Introduction

- The optimal management of the axilla following neoadjuvant chemotherapy (NAC) for initially node-positive breast cancer (cN+) remains contentious.
- Recent consensus by experts in St. Gallen [Ditsch et al, 2025] suggest sentinel lymph node biopsy (SLNB) alone may be acceptable for low volume residual axillary nodal disease (ypN1) following NAC.
- Data to support the oncologic safety of this approach are limited.
- The aim of this meta-analysis was to evaluate the long-term oncologic outcomes of SLNB alone for residual axillary nodal disease (ypN+) following NAC.

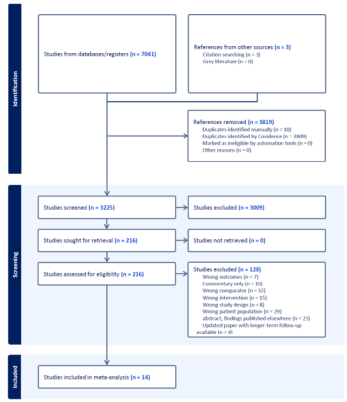


Figure 1: PRISMA diagram showing selection of studies in this review.

Methods and Materials

- Systematic review and meta-analysis was conducted.
- Medline (Ovid), Embase, and Cochrane Central Registry were searched for studies comparing women undergoing SLNB vs ALND following NAC for initially clinically node-positive breast cancer.
- Primary outcome: axillary recurrence (AR).
- Secondary outcomes: locoregional recurrence (LRR); distant recurrence (DR); overall survival (OS).
- Random effects meta-analyses were used to calculate weighted pooled effect estimates (risk ratios, RR).
- Variability across studies due to heterogeneity was estimated using I^2 statistics.

Study	Country	Study Design	Participants (N)	Median / Mean Follow-up (months)	Outcomes
Almahariq et al, 2021	USA	Observational, NCDB	1617	40	OS
Barker et al, 2023	USA	Observational, NCDB	475	47	OS
Cabioglu et al, 2023	Turkey	Prospective trial, multicentre	408	28	AR, LRR
Chun et al, 2021	South Korea	Observational	676	59.4	OS, ARFS, DMFS
Dux et al, 2023	USA	Observational	142	34	ARFS, DFS, OS
Jimenez-Gomez et al, 2022	Spain	Observational	68	60	AR
Kozak et al, 2020	USA	Observational	70	43.5	AR, LRR, DR, OS
Lim et al, 2023	South Korea	Observational	133	66	ARR, DFS, OS
Ling et al, 2020	USA	Observational	161	28.8	AR, LRR, DR, BCSS, DFS
Martelli et al, 2022	Italy	Observational	95	108	AR, DFS, OS
Naffouje et al, 2021	USA	Observational, NCDB	1109	NR	OS
Naffouje et al, 2022	USA	Observational, NCDB	2953	39.5	OS
Park Y et al, 2023	South Korea	Observational, multicentre	1273	75.3	AR, DFS, OS
Piltin et al, 2020	USA	Observational	338	34	LRR, RFS

*AR = axillary recurrence; ARR = AR rate; LRR = locoregional recurrence; DR = distant recurrence; DFS = disease-free survival; OS = overall survival; ARFS = axillary recurrence-free survival

Table 1: Characteristics of included studies.

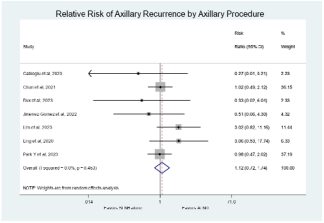


Figure 2: Forest plot for primary outcome, axillary recurrence (AR).

Results

- Fourteen observational studies were eligible for meta-analysis, providing data for 9,518 patients.
- The median age of women included in the studies ranged from 47 to 53 years.
- The rates of axillary recurrence ranged from 0.2% to 7.8% across all included studies.
- Distant recurrence rates ranged from 15.7% to 38.6%.
- No significant differences were observed in AR between patients undergoing SLNB alone versus ALND, following NAC: pooled RR 1.12 (95% CI: 0.72-1.74, $I2$=0.0%).
- Similarly, no significant differences were observed in LRR (RR 0.97, 95% CI: 0.68-1.37, $I2$=0.0%) nor overall mortality (RR 0.96, 95% CI: 0.65-1.42, $I2$=58.3%) between the two groups.
- However, the pooled risk of distant recurrence was lower for SLNB alone compared to the ALND group (RR 0.75, 95% CI: 0.60-0.95, $I2$=0.0%).

Study	Nodal Stage pre-Neoadjuvant Chemotherapy	Sentinel Lymph Node Mapping	Median / Mean Number of Sentinel Lymph Nodes Harvested	Final Nodal Status after NAC and Axillary Surgery
Almahariq et al, 2021	cN1	NR	<= 4 LNs (NCDB)	ypN1
Barker et al, 2023	cN1*	NR	<= 4 LNs (NCDB)	ypN+
Cabioglu et al, 2023	cN1-3	Single-tracer (blue dye technique); TAD	NR	ypN+
Chun et al, 2021	cN1-3	Single tracer (^{99m}Tc radiolabeled colloid)	NR	ypN1
Dux et al, 2023	cN1*	Dual tracer; TAD	3 (3-5)	ypN+
Jimenez-Gomez et al, 2022	cN1-3*	Dual tracer	2	ypN+
Kozak et al, 2020	cN1-3	NR	NR	ypN1
Lim et al, 2023	cN1	NR	6	ypN1 (includes N1mi)
Ling et al, 2020	cN1-3	NR	3 (2-4)	ypN1 (includes N1mi)
Martelli et al, 2022	cN1	Single-tracer (^{99m}Tc radiolabelled colloid)	2 (1-8)	ypN1
Naffouje et al, 2021	cN1	NR	NR	ypN1
Naffouje et al, 2022	cN1*	NR	3	ypN1
Park Y et al, 2023	cN1-3	NR	6 (5-10)	ypN+
Piltin et al, 2020	cN1-3*	NR	2	ypN+
*Biopsy-proven node-positive				

Table 2: Nodal status before and after neoadjuvant chemotherapy and axillary surgery.

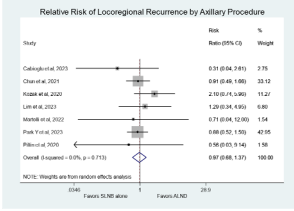


Figure 3: Forest plot for secondary outcome, locoregional recurrence (LRR).

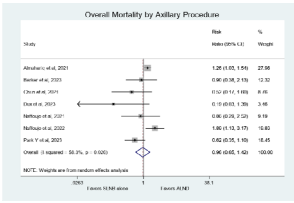


Figure 4: Forest plot for secondary outcome, overall mortality.

Conclusions

- This meta-analysis suggests that long-term outcomes of SLNB alone for breast cancer with residual axillary nodal disease following NAC are not inferior to those of ALND.
- AR rates were low across all included studies.
- The majority of recurrences were distant, questioning the need for aggressive axillary surgery for patients with low volume residual axillary nodal disease.
- We await prospective data from several randomized clinical trials, including Alliance A011202 and MAC19, to further guide axillary management in this group of patients.

Acknowledgements

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References

Ditsch et al (2025) St. Gallen/Vienna 2025 Summary of Key Messages on Therapy in Early Breast Cancer from the 2025 St. Gallen International Breast Cancer Conference. https://doi.org/10.1159/000546080

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