Nomogram incorporating axillary ultrasound characteristics can identify a subgroup of breast cancer patients unlikely to benefit from sentinel lymph node biopsy

Hanh-Tam Tran, MD; Daina Pack, MD; Charles Mylander, PhD; Laura Martino, BS; Martin Rosman, MD; Lorraine Tafra, MD; Rubie Sue Jackson, MD, MPH

The Rebecca Fortney Breast Center, Anne Arundel Medical Center, Annapolis, Maryland

Anne Arundel Medical Center
Fortney Breast Center

INTRODUCTION

- For clinically node-negative patients, surgical sentinel lymph node biopsy (SLNB) is the standard of care to definitively assess axillary lymph node (ALN) status. However, SLNB conveys a 4% risk of lymphedema and 10% risk of permanent paresthesias[1].
- In the CALGB 9343 subset analysis, omission of radiation and axillary staging was associated with a 3% axillary recurrence rate in patients >70 years old with cT1N0M0 hormone positive breast cancer (BC) treated with lumpectomy[2].
- The authors concluded that "if the results of sentinel node biopsy are not likely to change the choice of systemic treatment, it is questionable whether this 3% decrement warrants the use of sentinel node biopsy in this population"[2].
- It would be useful to identify patients at very low likelihood of ALN metastasis, to consider omission of SLNB in such patients.
- Qiu et al. developed the **Shantou nomogram** to predict probability of ALN metastasis using preoperative prognostic factors and axillary ultrasound (axUS) characteristics[3].
- The purpose of this study is to validate the Shantou nomogram in the AAMC breast cancer population, which is more heterogeneous and has lower prevalence of metastasis than the Shantou population.

METHODS

- This is a retrospective analysis of female BC patients at a single center between February 2011 to October 2014 with (1) invasive BC, (2) an axUS, and (3) had a SLNB or ALN dissection.
- Patients with locally advanced BC, neoadjuvant treatment, or bilateral BC were excluded.
- The clinical tumor size, ER status, grade, cortical thickness and longest axis of the most suspicious ALN, and ALN hilum appearance (present/absent) on axUS were used to calculate the likelihood of ALN metastasis, referred to as the probability of nodal metastasis (PNM).
- PNM was correlated with actual pathology from surgical staging, using metastasis >0.2 mm to define a positive node.
- We determined the actual proportion with ALN metastasis (i.e. false negative rate) for each PNM threshold.

REFERENCES
[1] DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: A systematic review and meta-analysis. *Lancet Oncol*. 2013;14(6):500-515. doi:10.1016/S1470-2045(13)70076-7
[2] Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343. *J Clin Oncol*. 2013;31(19):2382-2387. doi:10.1200/jco.2012.45.2615.
[3] Qiu SQ, Zeng HC, Zhang F, et al. A nomogram to predict the probability of axillary lymph node metastasis in early breast cancer patients with positive axillary ultrasound. *Sci Rep*. 2016;6(February):1-12. doi:10.1038/srep21196
[4] Jackson RS, Mylander C, Rosman M, et al. Normal Axillary Ultrasound Excludes Heavy Nodal Disease Burden in Patients with Breast Cancer. *Ann Surg Oncol*. 2015;22(10):3289-3295. doi:10.1245/s10434-015-4717-7

RESULTS

- 357 patients met study criteria. The mean age was 61.9 years.
- 80% of the patients were Caucasian, 14% were African American, 1% were Asian, and 5% were not recorded.
- The mean clinical tumor size was 1.9 cm. 68% had invasive ductal carcinoma. 72% were node negative on SLNB.
- The median ALN cortical thickness and longest axis were 2.2 mm and 16 mm.
- 96% of patients had ALN fatty hilum present on axUS.
- The AUC for the Shantou nomogram in the study cohort was 0.70 (95% CI 0.64, 0.76).
- **19.6% of the study cohort had a PNM <9.2%, which correlated with an actual proportion of ALN metastasis of 8.7% (Table).**

Table 1. Performance of the Shantou nomogram in the study group. Results for various probability of nodal metastasis (PNM) thresholds are displayed, showing how test characteristics varied based on the threshold used to define a PNM. In the study group (n=357), 100 patients (28%) had nodal metastasis. ALN: axillary lymph node.

PNM threshold	Cumulative patient number & percentage (%)	Cumulative number of patients with ALN metastasis	Sensitivity (%), e.g. the likelihood of a true positive ALN status having PNM equal to or above the indicated threshold	Specificity (%), e.g. the likelihood of a true negative ALN status having a PNM below the indicated threshold	% with pathological ALN metastasis (false negative rate)
<4.6%	22 (6.2%)	0	100.0%	8.6%	0.0%
<5.3%	31 (8.7%)	1	99.0%	11.7%	3.2%
<9.2%	69 (19.6%)	6	94.0%	24.5%	8.7%
<10%	73 (20.4%)	8	92.0%	25.3%	11.0%
<20%	152 (42.6%)	30	70.0%	47.5%	19.7%
<30%	224 (62.7%)	48	52.0%	68.5%	21.4%
<40%	268 (75.1%)	57	43.0%	82.1%	21.3%

CONCLUSION

- The Shantou nomogram, although developed in a Chinese population, nevertheless showed fair predictive ability in AAMC's more heterogeneous suburban population.
- Using a predicted likelihood of nodal metastasis of 9% as a cut-off, the nomogram was able to identify 1 in 5 of our patients as being likely node negative, with a low (8.7%) false negative rate.
- This is an improvement over axUS alone, as we have previously shown that cases with a negative axUS still have an 18% risk of nodal metastasis[4].
- For patients with a PNM value of <9%, multidisciplinary discussion is warranted to determine if SLNB is likely to alter adjuvant therapy. If chemotherapy is not an option, or if multigene assay is planned in the setting of node-positive disease, it is unlikely that omission of SLNB would meaningfully affect survival.

ID 580621