

Sentinel lymph node micrometastases and isolated tumor cells in breast cancer: an evolving field

Fang Fan

Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160, USA

Corresponding to: Fang Fan, MD, PhD. Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160, USA. Tel: 913-588-7070. Email: ffan@kumc.edu.



Submitted Apr 03, 2012. Accepted for publication Apr 30, 2012.

DOI: 10.3978/j.issn.2227-684X.2012.04.04

Scan to your mobile device or view this article at: <http://www.glandsurgery.org/article/view/601/633>

Controversy still remains regarding appropriate surgical management and prognostic implications of micrometastases and isolated tumor cells (ITCs) in sentinel lymph nodes (SLNs) of breast cancer patients. There are two issues: First, is the follow-up completion axillary lymph node dissection (ALND) necessary after a diagnosis of ITCs or micrometastases in sentinel lymph node? Second, does sentinel lymph node micrometastases or ITCs carry any prognostic significance? A multicenter cohort study conducted in The Netherlands addressed the second issue in a previously published paper (1). The same group now published from the same study in a recent issue of *Annals of Surgery* (Pepels MJ, de Boer M, Bult P, *et al.*, *Ann Surg* 2012;255:116-121) addressing the first issue. In their study, they found that compared with patients who underwent axillary treatment, the adjusted hazard ratio (HR) for regional recurrence in patients who underwent only an SLN procedure was 1.08 (95% CI, 0.23-4.98) for node-negative disease, 2.39 (95% CI, 0.67-8.48) for patients with ITCs in the SLN, and 4.39 (95% CI, 1.46-13.24) for patients with micrometastases in the SLN. Basically, they did not observe an increased risk of regional recurrence in SLN negative cases if axillary treatment was omitted, which is in agreement with results seen in randomized trials. They considered the relevance of ITCs in SLN with respect to the risk of regional recurrence to be of uncertain significance and not supporting routine use of axillary treatment. In patients with micrometastases in the SLN, axillary treatment is recommended. In this group, doubling of tumor size, histologic grade 3, and negative hormone receptor status were significantly associated with regional recurrences.

Completion ALND for women with micrometastases

or ITCs in sentinel lymph nodes remain controversial because of their uncertain clinical implications and the low-yield of additional positive lymph nodes. The reported rate varies for additional positive lymph nodes in patients with micrometastases or isolated tumor cells (2-5). Although the American Society of Clinical Oncology recommended ALND for patients with sentinel lymph nodes micrometastases or ITCs (6,7), this concept has been re-examined in selected patients due to the published study of the American College of Surgeons Oncology Group Z0011 Randomized Trial (8) that compared local and regional recurrence in patients with positive SLND with or without follow up ALND. In this study, 37.5% of patients in the ALND group and 44.8% of patients in the SLND only group had sentinel nodes micrometastases. The study demonstrated that there were no statistically significant differences in locoregional recurrence after SLND with or without ALND in selected patients with sentinel lymph node metastases (including macrometastases and micrometastases). It is to be noted that the Z0011 study was performed in patients with early-stage breast cancer treated with breast conserving therapy. All patients received whole breast irradiation and over 95% of patients received adjuvant systemic therapy. The results of this study definitely raised further doubt of the necessity of completion ALND in patients with micrometastases or ITCs.

This large Dutch MIRROR (Micrometastases and Isolated tumor cells: Relevant and Robust or Rubbish?) cohort study is a recent large study examined the impact of ALND on 5-year regional recurrence rate in breast cancer patients with ITCs or micrometastases in the SLNs. The analysis corrected all the confounding factors that might have influenced the data including age, tumor

size, histologic grade, hormone receptor status, adjuvant systemic therapy, and irradiation of the breast. They clearly demonstrated that omitting axillary treatment in patients with SLN micrometastases resulted in a significantly increased 5-year regional recurrence rate of 5.6% with an adjusted HR of 4.39. Regional recurrence was also strongly associated with tumor size, grade, and hormone receptor status. Systemic therapy and breast radiation as part of breast conservation therapy may reduce the risk of local recurrence. A surgeon has to take all these factors into account to offer the most optimal and personalized axillary management strategy for a patient with SLN micrometastases or ITCs.

Acknowledgements

Disclosure: The author declares no conflict of interest.

References

1. de Boer M, van Deurzen CH, van Dijk JA, et al. Micrometastases or isolated tumor cells and the outcome of breast cancer. *N Engl J Med* 2009;361:653-63.
2. Calhoun KE, Hansen NM, Turner RR, et al. Nonsentinel node metastases in breast cancer patients with isolated tumor cells in the sentinel node: implications for completion axillary node dissection. *Am J Surg* 2005;190:588-91.
3. Gipponi M, Canavese G, Lionetto R, et al. The role of axillary lymph node dissection in breast cancer patients with sentinel lymph node micrometastases. *Eur J Surg Oncol* 2006;32:143-7.
4. van Rijk MC, Peterse JL, Nieweg OE, et al. Additional axillary metastases and stage migration in breast cancer patients with micrometastases or submicrometastases in sentinel lymph nodes. *Cancer* 2006;107:467-71.
5. Patani N, Mokbel K. The clinical significance of sentinel lymph node micrometastasis in breast cancer. *Breast Cancer Res Treat* 2009;114:393-402.
6. Lyman GH, Giuliano AE, Somerfield MR, et al. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. *J Clin Oncol* 2005;23:7703-20.
7. Schwartz GF, Giuliano AE, Veronesi U, et al. Proceedings of the consensus conference on the role of sentinel lymph node biopsy in carcinoma of the breast, April 19-22, 2001, Philadelphia, Pennsylvania. *Cancer* 2002;94:2542-51.
8. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. *Ann Surg* 2010;252:426-32; discussion 432-3.

Cite this article as: Fan F. Sentinel lymph node micrometastases and isolated tumor cells in breast cancer: an evolving field. *Gland Surg* 2012;1(1):5-6. DOI: 10.3978/j.issn.2227-684X.2012.04.04