



EDITORIAL

The value of surgical staging of the axilla

El valor de la estadificación quirúrgica de la axilla



It is an honor to have my comments accompany the excellent consensus of the Sociedad Española de Senología y Patología Mamaria for sentinel node biopsy and management of the axilla for breast cancer. Axillary management has become far more complicated over the years. As late as the 1970's and early 1980's, axillary management was quite simple. Every patient with any form of breast cancer was treated with axillary dissection as part of a modified radical mastectomy. Even patients with DCIS or LCIS were treated with modified radical mastectomy. After axillary dissection was appropriately eliminated for the noninvasive malignancies, sentinel node biopsy became the first major advance in axillary surgery and remains the cornerstone of axillary management. But even the use of this procedure has evolved a great deal since it was first introduced. I first attempted sentinel node biopsy as a diagnostic test in 1991 merely to determine whether a patient was node negative and could be spared the morbidity of an axillary dissection.¹ Currently the use of sentinel node biopsy has expanded, and the management of the axilla has become nuanced. Variations in axillary operations and the use of radiation therapy as well as the increasing use of neoadjuvant chemotherapy have added to the complexity and difficulty of axillary management.

Accurate evaluation of the axilla is essential to the assessment of the patient with breast cancer. Axillary staging begins with a careful physical examination followed by axillary ultrasonography. All patients with invasive breast cancer benefit from sonographic examination of the axilla, infraclavicular and supraclavicular nodal regions. Nodes that appear suspicious either on imaging or palpation should be further evaluated by image-guided core needle biopsy. Women with involved nodes may require neoadjuvant chemotherapy depending on a number of clinical features. Indications for neoadjuvant hormone therapy are not yet clearly defined, and the management of the axilla after neoadjuvant hormone therapy is even less clearly defined.

Some oncologists are suggesting that axillary operations are no longer necessary. They base this statement on the fact that axillary operations do not impact overall survival

and that equivalent regional control may be achieved with axillary irradiation. These statements are not entirely true.

While it is true that axillary lymph node dissection may itself impart no survival advantage for the clinically node negative patient, those who have limited axillary nodal disease such as women who would be eligible for American College of Surgeons Oncology Group (ACOSOG) Z0011² or the AMAROS³ trial, axillary dissection may be therapeutic for women with involved lymph nodes or those whose nodes remain involved after being treated with neoadjuvant systemic therapy. The staging information provided by surgical staging often guides the selection of systemic therapy which does impact survival. No imaging modality and no procedure short of operation can provide such definitive information.

No image-guided procedures can rule out metastasis because they lack the sensitivity needed to accurately stage the axilla. A core biopsy guided by ultrasonography which indicates metastases is entirely reliable, but an ultrasound-guided biopsy showing a lack of metastasis cannot be relied upon.

Some women, in fact, may be managed without surgical axillary staging. Elderly women with small hormone receptor-positive tumors and clinically tumor-free lymph nodes can often avoid axillary staging, but even elderly women with large tumors, those who undergo neoadjuvant chemotherapy, those with suspicious nodes or hormone receptor-negative tumors or HER2-positive tumors may, in fact, require axillary staging. Axillary radiation can achieve excellent regional control similar to axillary lymph node dissection with a lower lymphedema rate for women with clinically negative lymph nodes and a low axillary burden found on sentinel node biopsy, but women with palpable nodes, more than two positive lymph nodes, or nodal involvement post-neoadjuvant chemotherapy cannot be treated with radiation alone. Ongoing studies may show the efficacy of nodal irradiation for women with residual nodal disease after neoadjuvant chemotherapy, but these studies are not yet complete.

Postmenopausal women with clinically node-negative breast cancer and genomic risk scores that are low or women with severe comorbidities for whom decisions for adjuvant therapy will not change regardless of axillary status may be managed without sentinel node biopsy. The pre-menopausal woman requires axillary staging regardless of her genomic risk score since any nodal metastasis in a pre-menopausal woman is an indication for systemic chemotherapy.

Nodal status is important for all biologic subtypes of breast cancer. In women with HER2-overexpressing tumors, the APT⁴ study demonstrated the safety of de-escalation of systemic therapy for women with T1 or small T2 tumors and pathologically tumor-free nodes. Pathologic nodal status must be determined by sentinel node biopsy in these patients. For women with HER2-overexpressing tumors treated with neoadjuvant systemic therapy, the KATHERINE⁵ trial demonstrated that residual disease in the breast or nodes warrants systemic therapy with T-DM1 rather than Trastuzumab so knowledge of status of nodes is essential for these women as well. Most patients with triple negative tumors are treated with neoadjuvant chemotherapy, and their nodal status postoperatively is necessary to rule out residual disease for management with capecitabine.

Clearly axillary surgery and sentinel node biopsy are relevant and contribute to treatment decisions and outcomes. Axillary dissection itself still remains critical in the management for women post-neoadjuvant chemotherapy with involved lymph nodes and selected women not treated with neoadjuvant chemotherapy such as those with bulky disease or multiple involved lymph nodes, perhaps even those with limited nodal disease managed with mastectomy. Future studies, of course, will always change the management algorithm for patients with breast cancer, but despite systemic therapy and imaging advances, surgical management of the axilla currently remains critical for optimal care. Sentinel node biopsy is the heart of axillary management. With these guidelines the Sociedad Española de Senología y Patología Mamaria contributes greatly to the care of patients, and this consensus should be a document often referred to by the practicing oncologist.

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Conflict of interest

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References

1. Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg*. 1994 Sep;220(3):391–8 discussion 398–401.
2. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized clinical trial. *JAMA*. 2017 Sep 12;318(10):918–26.
3. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol*. 2014 Nov;15(12):1303–10 Epub 2014 Oct 15.
4. Tolane SM, Barry WT, Dang CT, Yardley DA, Moy B, Marcom PK, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. *N Engl J Med*. 2015;372(2):134–41.
5. von Minckwitz G, Huang CS, Mano MS, Loibl S, Mamounas EP, Untch M, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. *N Engl J Med*. 2019;380(8):617–28.

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