THE AMERICAN SOCIETY OF Breast Surgeons

Resource Guide

Axillary Management for Patients With In-Situ and Invasive Breast Cancer: A Concise Overview

Purpose

To outline axillary management of patients with in situ and invasive breast cancer.

Associated ASBrS Statements, Guidelines, or Quality Measures

1. Consensus Statement: Consensus Guideline on the Management of the Axilla in Patients With Invasive/In-Situ Breast Cancer – *Approved September 19, 2019*
2. Performance and Practice Guidelines for Sentinel Lymph Node Biopsy in Breast Cancer Patients – *Revised November 25, 2014*
3. Performance and Practice Guidelines for Axillary Lymph Node Dissection in Breast Cancer Patients – *Approved November 25, 2014*
4. Quality Measure: Sentinel Lymph Node Biopsy for Invasive Breast Cancer – *Approved November 4, 2010*

Methods

A literature review inclusive of recent randomized controlled trials evaluating the use of sentinel lymph node surgery and axillary lymph node dissection for invasive and in-situ breast cancer as well as the pathologic review of sentinel lymph nodes and indications for axillary radiation was performed. This is not a complete systematic review but rather, a comprehensive review of recent relevant literature. A focused review of non-randomized controlled trials was then performed to develop consensus guidance on management of the axilla in scenarios where randomized controlled trials data are lacking. The ASBrS ALND Work Group developed a consensus document, which was reviewed and approved by the ASBrS Board of Directors.

Summary of Data Reviewed

Background

Axillary management for breast cancer has become increasingly complex and multidisciplinary. The surgical options are no surgery vs sentinel lymph node biopsy (SLNB) vs axillary lymph node dissection (ALND). The medical oncologist has many choices for systemic therapy, adjuvant vs neoadjuvant. The radiation oncologist can offer no radiotherapy (RT) vs breast/chest wall RT, vs breast/chest wall/node field RT. This

complexity is compounded by progress in each subspecialty, with advances in systemic therapy and RT allowing selective de-escalation in the extent of surgery. Finally, clinicians must draw on extensive literature comprising observational studies, randomized trials (RCTs), systematic reviews, and meta-analyses.

Many ASBrS Official Statements (Consensus Guidelines, Quality Measures, and Performance and Practice Guidelines) address the axilla, the most recent and detailed in 2019 (Chair: Lee G Wilke). Here, the objective was for an independent panel of experts to provide a single "Quick Access" position statement combining all of these, a departure from our usual guideline process.

Similar to earlier ASBrS guidelines on axillary management, we did not aim to satisfy the demanding requirements of formalized guideline development, and to this end provide links to the recent and comprehensive Ontario ASCO Guideline[1] for a deep dive into the topic. We aimed to provide a practical, data-based, and concise summary of the current literature and an outline of our group consensus on axillary management (no axillary surgery vs SLNB vs ALND). This document is therefore not intended to be prescriptive; there is room for multidisciplinary collaboration throughout.

Recommendations

Indications for no surgical axillary lymph node staging

1. When surgical nodal staging will not affect adjuvant therapy recommendations.
    - Axillary staging is of little value in the setting of advanced age, serious comorbidities, or when it will not affect decisions regarding adjuvant therapy.[2]

2. Pure DCIS undergoing breast-conserving surgery.
    - Patients with DCIS and no clinical or radiologic suspicion of invasion do not require axillary staging. The overall risk of nodal metastasis for DCIS is approximately 1-2%.[3]

3. ≥70 years of age with cT1-2N0 hormone receptor positive breast cancer
    - 62% of patients in the CALGB 9343 RCT did not have axillary staging. Survival was unaffected, and only 3% developed axillary recurrence. This trial is the basis of the current SSO Choosing Wisely guideline recommendation against routine SLNB in patients age 70+ with HR+/HER2- invasive breast cancer.[4]

4. Prophylactic mastectomy
    - Axillary staging is not recommended for prophylactic mastectomy, as the likelihood of incidentally finding invasive cancer is about 2% and about 1% for nodal metastases.[5]

5. Primary breast sarcoma or phyllodes tumor
    - The risk of nodal metastasis for breast sarcoma - including angiosarcoma and malignant phyllodes tumor - is negligible.

Indications for sentinel lymph node biopsy (SLNB)

1. cT1mi-3N0 (palpably node-negative) cancer
    - SLNB is indicated for most patients with cN0 breast cancer. This is supported by an extensive body of literature, but with variable use of axillary imaging, so is indicated even if a previously non-palpable, image-detected node was found to contain metastasis.[6,7] (see SLNB #2 below)

2. cT1-2N0 (palpably node-negative) cancer with abnormal axillary imaging and/or a positive lymph node needle biopsy
    - About 70% of patients with a normal axilla on physical examination but abnormal axillary imaging - and about 50% of those with a positive FNA/core needle biopsy – will have 1-2 SLN+ and have the option to avoid ALND.[8] (see SLNB #4 and 5 below)

3. DCIS with a mass, other suspicion of invasion, or requiring mastectomy
    - SLNB is appropriate for DCIS whenever the risk of upstaging to invasive cancer is increased. SLNB is feasible post-mastectomy, but its performance in this setting is unproven.

4. cT1-2N0 (palpably node-negative) cancer with 1-2 SLN+ having BCT with WBRT
    - SLNB without ALND is appropriate for patients undergoing BCT who meet the entry criteria of the IBCSG 23-01 and Z0011 trials and are found to have 1 or 2 positive SLN.[9,10]

5. cT1-2N0 (palpably node-negative) cancer having mastectomy, with 1-3 SLN+ and receiving axillary RT
    - SLNB without ALND is appropriate for patients undergoing mastectomy with 1-3 positive SLN who meet the entry criteria for the AMAROS and OTOASOR trials. The data for 3 SLN+ may be insufficient, in that 95% of AMAROS patients had 1-2 SLN+.[11,12]

6. cN0 (palpably node-negative) cancer post neoadjuvant therapy
    - Upfront image-guided needle biopsy is indicated for any patient with clinical or radiologic suspicion of node metastasis - SLNB should not be done prior to neoadjuvant therapy. SLNB performs well in the post-neoadjuvant setting, and axillary US can suggest treatment response but is not reliable enough to determine the surgical approach. SLNB is suitable for patients who were palpably node-negative, or biopsy-proven node-positive upfront, as long as they are palpably

node-negative post-neoadjuvant. For patients who were biopsy-proven node-positive upfront, the false-negative rate of SLNB is minimized by the retrieval of >2 SLN, by dual mapping, and by retrieval of the biopsied/clipped node. The data for patients presenting with cN2 disease may be insufficient – in ACOSOG Z1071 (below) 95% of patients had cN1 disease on presentation.[13-19] (see ALND #1 below)

7. Invasive local recurrence post-BCT with a cN0 axilla
    - SLNB is feasible for patients with prior BCT/SLNB or BCT/ALND who present with invasive local recurrence and a cN0 axilla. All patients with invasive local recurrence require systemic adjuvant therapy, so it is not yet clear if the results of a reoperative SLNB are meaningful in this setting.[20]

Indications for axillary dissection (ALND)

1. cN2-3 on presentation (palpably node-positive and biopsy-proven)
    - To avoid false-positives, needle biopsy is indicated to confirm node status in all patients with clinical or radiologic suspicion of node metastasis. Most patients with cN2-3 disease will receive neoadjuvant therapy, and since the performance of SLNB in this setting is uncertain (see SLNB #6 above), ALND is appropriate either upfront (for patients who are ineligible for neoadjuvant) or post-neoadjuvant.
    - Supraclavicular and/or internal mammary nodal disease is best treated with systemic therapy and RT.

2. cN0 with positive SLN and ineligible for IBCSG 23-01/Z0011/AMAROS/OTOASOR
    - In the setting of upfront surgery, ALND is appropriate for BCT patients with >2 SLN+ and for mastectomy patients with >3 SLN+.

3. cN1-2 (palpably node-positive and biopsy-proven) and ineligible for neoadjuvant therapy
    - ALND is appropriate for patients with cN1-2 disease who are not candidates for neoadjuvant therapy (see ALND #1 above).

4. cN1-2 (palpably node-positive) post-neoadjuvant therapy
    - ALND is indicated for patients who remain palpably node-positive following neoadjuvant therapy.

5. cN0 and SLN+ post neoadjuvant therapy
    - For upfront surgery, the oncologic outcomes of axillary RT vs ALND for patients with cN0 disease are comparable, with less morbidity for axillary RT. This has not yet been demonstrated for the post-neoadjuvant setting, and ALND is indicated for patients who are cN0 but SLN+. The Alliance A 011202 trial (a randomization of

patients with positive SLN post-neoadjuvant to ALND vs axillary RT) is evaluating axillary RT as an alternative to ALND for future patients.[21]

6. Inflammatory breast cancer
    - Limited data on the performance of SLNB post-neoadjuvant for inflammatory breast cancer indicate low success and high false-negative rates. ALND is indicatedn this setting

7. Invasive local recurrence with a cN1-2 (palpably node-positive and biopsy-proven) axilla
    - ALND is indicated for patients with invasive local recurrence and clinically positive nodes.

8. Axillary metastasis from occult breast primary
    - Most patients with axillary metastasis from an unknown breast primary are candidates for neoadjuvant therapy, but ALND is appropriate for those who are ineligible or remain node-positive post-neoadjuvant.

Sequencing treatment to minimize the odds of ALND

Tumor subtype is an important predictor of lymph node response to neoadjuvant chemotherapy, with rates of nodal pathologic complete response (pCR) ranging from about 20% for ER+/PR+/HER2- to over 90% for ER-/PR-/HER2+. Most patients with palpably node-positive axillae will be referred for neoadjuvant therapy - regardless of tumor subtype - to downstage the breast/axilla. For patients who are palpably node-negative, the rates of ALND for the unresponsive subtype ER+/PR+/HER2- (most of whom will remain node-positive post-neoadjuvant) will be minimized by a strategy of upfront surgery, in that most will have 0-2 SLN+ and can avoid ALND. For those with the responsive subtypes ER-/PR-/HER2- and ER-/PR-/HER2+, the rates of ALND will be minimized by a strategy of neoadjuvant chemotherapy.[22,23]

Prevention of lymphedema

Lymphedema is a significant complication of ALND, affecting approximately 20% of patients. The only clear risk factors are BMI and extent of axillary surgery, but chemotherapy and especially RT are additive. The benefit of standard therapies is uncertain. Newer surgical techniques, such as axillary reverse mapping, lymphatic transfer, and lympho-venous anastomosis are promising both for prevention and for treatment of established lymphedema. However, well-designed prospective studies with uniform criteria for patient selection, procedure, and outcome assessment are needed. In institutions where these techniques are available, they should be considered whenever ALND is required.[24-26]

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Working Group Members

Chairs

Hiram S. Cody III, MD, FACS, Attending Surgeon, Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, Professor of Surgery, Weill Cornell Medical College, New York, NY

Howard Snider, MD, FACS, Montgomery, AL

Section Editors

Theresa Schwartz, MD, MS, FACS, Senior Staff Surgeon, Henry Ford Health System, Detroit, MI

Kari M. Rosenkranz, MD, FACS, Associate Professor of Surgery, Geisel School of Medicine, Interim Division Chief, Surgical Oncology, General Surgery Residency, Program Director, Vice-Chair for Education, Department of Surgery, Dartmouth Hitchcock Medical Center, Lebanon, NH

Ted A. James, MD, MHCM, FACS, Associate Professor of Surgery, Harvard Medical School, Chief, Breast Surgical Oncology, Beth Israel Deaconess Medical Center, Boston, MA

Members

Michael Alvarado MD, Professor of Surgery, University of California San Francisco, San Francisco, CA

Judy C. Boughey, MD, FACS, Professor of Surgery, Mayo Clinic, W.H. Odell Professor in Individualized Medicine, Chair, Division of Breast and Melanoma Surgical Oncology, Program Director - Multidisciplinary Breast Surgery Fellowship, Mayo Clinic, Rochester, MN

Sara Javid, MD, FACS, Associate Professor of Surgery, University of Washington, Breast Surgery Section Chief, Seattle, WA

Armando E. Giuliano, MD, FACS, FRCSEd, Linda and Jim Lippman Chair in Surgical Oncology, Chief, Surgical Oncology, Associate Director, Samuel Oschin Comprehensive Cancer Institute, Co-Director, Saul and Joyce Brandman Breast Center – A Project of Women's Guild, Cedars-Sinai Medical Center, Los Angeles, CA

Julie A. Margenthaler, MD, FACS, Director of Breast Surgical Services of the Joanne Knight Breast Center at Siteman Cancer Center, Professor of Surgery, Washington University School of Medicine, St. Louis, MO

Meena S. Moran, MD, Professor, Dept. of Therapeutic Radiology, Chief, Breast Radiation Program, Yale University School of Medicine, New Haven, CT

Roshni Rao, MD, FACS, Vivian L. Milstein Associate Professor of Surgery, Chief, Division of Breast Surgery, Columbia University Medical Center, New York Presbyterian Hospital, New York, NY

Lee G. Wilke, MD, FACS, Professor of Surgery, Senior Medical Director, Clinical Oncology Services; Hendricks Chair in Breast Cancer Surgery Research, Vice Chair of Research, UW Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI

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	Lilly	Research Funding (*institution*)	Clinical Trial PI
Lee G. Wilke	Elucent Medical	Minority Stock Owner	Minority Stock Owner; Founder