Management of the axilla in patients with breast cancer

Amit Goyal

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Abstract This article reviews the changes in management of the axilla in patients with breast cancer in the last decade. It discusses the recent advances, existing controversies and provides evidence-based guidelines for use in clinical practice.

Sentinel lymph node (SLN) biopsy has replaced the more morbid axillary lymph node dissection (ALND) and four node sampling for axillary nodal staging. Blue dye guided four node sampling is an acceptable alternative when radioisotope facilities are not available. ALND is reserved for patients with proven axillary lymph node involvement.

Preoperative axillary ultrasound and fine-needle aspiration cytology or core biopsy of suspicious lymph nodes reliably identifies around 30% of node positive patients. Intraoperative assessment of the SLN using frozen section or real time molecular assays enables surgeons to perform one stage ALND in node positive patients. For those patients in whom intra-operative SLN assessment is negative, but whose final pathology reveals SLN metastasis, standard treatment has been to perform a completion ALND. Predictive models can be used to identify a low-risk group of SLN-positive patients in whom routine ALND may not be necessary. In the future, completion ALND for microscopic disease will not be the standard of care but axillary radiotherapy may be an alternative with equal control and less morbidity.

Keywords Axillary lymph node dissection · Blue dye · Breast cancer · Four node sampling · Lymphatic mapping · Radioisotope · Sentinel lymph node biopsy

Introduction

Until recently, the standard approach to the axilla in patients with invasive breast cancer has been axillary lymph node dissection (ALND), which consumes considerable resources and causes both acute and late morbidities for the patient. Complications of ALND include lymphoedema, pain, numbness and limited shoulder movement [1].

Why do patients with invasive breast cancer need to undergo ALND?

The first reason to perform an ALND is nodal staging. The presence or absence of axillary lymph node involvement is the most important prognostic factor. Adjuvant treatment is advised for all node-positive patients, whereas adjuvant treatment for node-negative patients depends on the presence of other patient and tumour-related factors.

The second reason to perform an ALND is to establish the extent of nodal involvement, which might have an impact on adjuvant treatment recommendations. Tumour burden in the axilla may influence the choice of chemotherapy regimen. Patients with 4 or more involved nodes are offered chest wall and supraclavicular fossa radiotherapy to decrease the risk of loco-regional recurrence. The third reason to perform an ALND is to ensure axillary tumour control.

However, management decisions on adjuvant chemotherapy are based increasingly on primary tumour characteristics rather than on nodal status. Nodal status does not change the systemic treatment plan. The incidence
of axillary metastases has decreased because of earlier detection of the primary tumour by increased use of mammographic screening. Axillary dissection in node negative women exposes them to the complications of this procedure without any benefit. Long-term follow-up data from the NSABP B-04 study suggests that ALND does not confer any significant survival advantage [2]. These developments have prompted exploration of less invasive staging methods for establishing which patients have nodal metastases and therefore need ALND. The most recent overview by the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) revealed that one life is saved at 15 years for every four isolated locoregional recurrences prevented by radiotherapy at 5 years [3]. This implies that local recurrence has a small adverse effect on survival, and regional disease control is important.

Other methods for axillary staging

Physical examination of the axilla in patients with invasive breast cancer has poor sensitivity and specificity to detect the presence of axillary lymph node metastases. Tumour and patient-related factors are of little value in predicting axillary lymph node involvement in patients with invasive breast cancer. Tumour size has a statistically significant relationship with lymph node metastasis but nevertheless has limited predictive value. Sophisticated techniques such as scintimammography, high-resolution computed tomography (HRCT), dynamic contrast enhanced magnetic resonance imaging (MRI) and positron emission tomography (PET) have been found to be of limited use. The sensitivity and specificity of these methods is inferior to the information from ALND. In addition, early treatment of the axilla in patients with node positive invasive breast cancer ensures excellent regional control and might improve survival in some cases.

Sentinel lymph node biopsy

Over the past decade, SLN biopsy has become well established as a new standard for axillary node staging in breast cancer. Numerous observational studies of SLN biopsy validated by a completion axillary dissection (ALND) have established that SLN biopsy is feasible, accurate and safe [4]. NEW START data analyses of more than 6,000 patients has demonstrated that multiprofessional training and standard methodology can achieve sentinel node identification rate of >95% and accuracy rates of <10% [5]. NICE (National Institute of Clinical Excellence, UK) 2009 guidelines recommend that axillary staging should be performed by SLN biopsy using a combination of isotope and blue dye [6].

Patient selection

SLN biopsy is suitable for all patients with clinically node negative invasive breast cancer irrespective of tumour size. Many putative “contraindications” (including prior surgical biopsy, large tumour size and multicentricity) have been disproved, but the role of SLN biopsy following neoadjuvant chemotherapy, remains a subject of debate. Patients with T3 tumours have a relatively high-risk of nodal metastases and in the absence of intraoperative sentinel node assessment may be offered ALND at the outset in areas where access to healthcare is limited.

Approximately, 20% of patients with ductal carcinoma in situ (DCIS) diagnosed by core needle biopsy are upstaged to invasive disease at excision. Presence of a clinically palpable mass or mammographic mass increases the chances of finding an invasive component at excision by approximately 5- to 7-fold. SLN biopsy should be performed at the time of the initial procedure in this subgroup of patients to avoid a second operative procedure for axillary nodal staging [7]. In addition, SLN biopsy should be performed in patients undergoing mastectomy because mastectomy precludes SLN biopsy if invasive disease is subsequently discovered.

Isotope or blue dye

ALMANAC and NEW START data demonstrates that a combined technique maximises both the success and accuracy of SLN biopsy. The failed localisation rate increases by 3–10% if only one tracer is used to identify the sentinel node. More importantly, using the blue dye or isotope alone increases the false negative rate by 2–4% [4, 5].

Site and volume of injection

The breast tissue and its overlying skin drains to the same few axillary SLNs regardless of the injection site. Peritumoural, intradermal, subdermal or subareolar routes of injection have equally good results and a comparably low rate of false negative procedures [8–10]. Peritumoural injection is given in the breast parenchyma at four sites. Intradermal and subdermal injections are given as a single dose into the breast skin directly over the tumour or at the periareolar edge in the tumour quadrant. Subareolar injections are given into the subareolar lymphatic plexus independently of the tumour site. Superficial injection techniques require a much lower-volume of injection than the peritumoural method, and leave a much smaller “hot spot” in the breast. This facilitates the identification of SLN, especially for patients with tumours high in the axillary tail of the breast.

While superficial injections of isotope maximise the