Current Status of Radiotherapy for the Management of Regional Nodes in Breast Cancer

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Abstract

Worldwide, breast cancer is the most common invasive cancer in women. Breast cancer constitutes about 23% of invasive cancers in women. The management of breast cancer depends on various factors, including the cancer stage and patient age. Breast cancer is usually treated with surgery, which can be followed by chemotherapy or radiation therapy, or both. Until recently, the standard procedure for axillary study was axillary dissection. Sentinel lymph node biopsy has been validated as a less-aggressive axillary treatment without an impact on survival. In the present report, we review the current management of the axillary lymph nodes, especially from the viewpoint of an oncology radiotherapist.

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Introduction

Lymphatic drainage of the breast is preferably produced by the axillary lymph nodes. It has been estimated that about 15% of the drainage ends up in the lymph nodes located in the internal mammary gland and the remaining 85% in the territory of the axilla. Although both the internal mammary lymph nodes and those located in the axilla receive drainage from the entire breast, drainage in internal mammary lymph nodes occurs more frequently in tumors located in the medial part of the breast.[1]

From the start of breast cancer treatment, the action on the regional lymph nodes flows inseparably from the local treatment of the tumor in the breast. Until recently, breast cancer surgery always involved axillary lymph node dissection (ALND) as a part of the surgical procedure.

Discussion

For the practical management of the axilla, 3 levels have been distinguished according to the location of the lymph nodes with respect to the minor pectoralis muscle. Level I encompasses those located below and outside the muscle; level II, those located at the same height; and level III (or the infraclavicular), those inside and above it (Figure 1). The nodal drainage level, beyond level III, is the supraclavicular area. The effect on the supraclavicular chain is restricted to tumors with extensive effects in the axillary area and is frequently associated with disseminated disease. The internal mammary chain extends to the fifth intercostal space; however, its effect is more common in the lymph nodes in the first 3 levels.

The risk of axillary dissemination depends on different factors. Among the best known and most widely studied are the size of the primary tumor, its histologic grade, the histologic tumor type, the presence of lymphovascular invasion (LVI), and the location of the primary tumor in the breast.

Tumor Size

Large tumors have been associated with an increased risk of axillary dissemination, and various studies have shown that as the size of the primary tumor increases, the odds of positive axillary lymph nodes increases.[2,3] A greater risk has also been demonstrated in patients who require repeat excision of residual tumor with positive margins after surgery compared with those with enlargement but negative margins after the first surgery.[4] This effect has been attributed to an underestimation of the initial tumor size.

Histologic Characteristics

The greater the histologic grade, the greater the risk of lymph node invasion.[5] Tumors with a focus of infiltration < 5 mm, those

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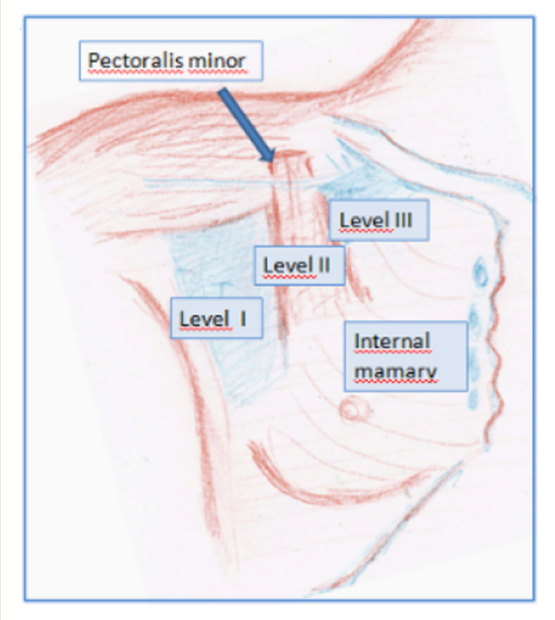
Figure 1 Axillary Lymph Node Levels I, II, and III



that are grade 1 without LVI, and tumors with pure mucinous or tubular features < 1 cm have a risk of lymph node positivity of < 5%. The same is true for intraductal carcinoma.[6]

Tumor Localization

The risk of axillary dissemination is increased for tumors located in the outer quadrants of the breast and there is a greater tendency of internal mammary tumors in the internal quadrants to drain.[7]

Assessment of the Axilla

As stated, since the start of treatment for breast cancer, a surgical approach to the axilla has been the norm. With the advent of radiation therapy (RT), hormonal treatment, and chemotherapy (CT), knowledge of the status of the axillary lymph nodes has become critical for the indication of such procedures. Furthermore, with advances in early diagnosis, the discovery of patients without nodal involvement has been greater. Thus, these patients can avoid radical surgical treatment, such as ALND, which are not without morbidity.

Physical examination of the axilla is not a reliable method for assessing lymph node involvement in this area. Many of the positive lymph nodes for breast cancer are not clinically palpable. Also, other benign pathologic features can produce an enlarged lymph node. The positive predictive value has varied from 61% to 84%, and the probability of no involvement after normal examination findings has been 50% to 60%.[8]

Axillary Ultrasonography

In the presence of suspicious lymph nodes found on an ultrasound scan, an axillary echo scan allows for fine needle aspiration (FNA) or biopsy, which will lead to an accurate diagnosis of lymph node involvement. The morphologic alterations found on ultrasound scanning have a low predictive value in themselves.[9] Thus, surgical staging with a histologic examination of resected lymph nodes is necessary to accurately diagnose the existence of involvement in the axilla, especially because additional treatment also depends on these findings.

Until recently, the standard procedure for axillary lymph node study was ALND. ALND includes the removal of level I and II axillary lymph nodes, which has diagnostic, prognostic, and therapeutic purposes, and is the most accurate and secure method of diagnosing axillary lymph node involvement. However, this treatment is not without morbidity, such as lymphedema and neurologic damage. The latter can result in a deficit in mobility and sensitivity, which results in a compromise in functionality and quality of life.[10]

The development of the sentinel lymph node biopsy (SNB) has allowed for less-aggressive axillary surgery. The American College of Surgeons Oncology Group (ACOSOG) Z10 study showed that it is possible to identify the sentinel lymph node (SLN) in ≥ 95% of cases. Factors that could decrease the percentage of identification include an increased body mass index, patient age, and studies with < 50 patients.[11]

Several studies have shown that SNB is a safer and less morbid procedure.[12-14] These studies have shown that if the SLN is negative, the likelihood of further axillary lymph node involvement will be very low (5%-10% false-negative results), with very low values of recurrence in the axilla (range, 0%-4.5%), eliminating the necessity for lymphadenectomy. A condition for entry in the studies was that the axilla would be clinically negative.

In a recent review of axillary treatment because of breast cancer,[15] the morbidity in patients after SNB was compared with that in those who had undergone ALND. The risk of lymphedema, pain and numbness of the arm, and quality of life scores were clearly favorable for the SNB, with the values showing a doubling or tripling of complications for treatments involving lymphadenectomy.

In 2005, the first American Society of Clinical Oncology (ASCO) guide for performing SNB in cases involving early-stage breast cancer was published.[16] This guide acknowledged SNB as an acceptable treatment of stage T1 and T2 tumors, when these are treated with conservative surgery and RT to the entire breast. The ASCO guidelines allow performance of the procedure in cases involving multicentricity, cases of intraductal carcinoma with the risk of microinvasion, and cases for which mastectomy was scheduled. SNB is not recommended if the patient has undergone previous surgery in the axilla or previous CT. The axillary lymph nodes should always be clinically negative. The update published in 2014 allows for SNB after neoadjuvant systemic treatment and in patients with previous surgical procedures in the axilla or breast.[17] Treatment guidelines, such as the National Comprehensive Care Network (NCCN) guide and the Consensus of St Gallen,[18] also introduced the option of SNB as a standard treatment in these patient groups, without ALND necessary in the case of negative SNB findings.

Furthermore, the possibility of more detailed study of the lymph nodes significantly increases the detection of small tumor deposits not detected in the initial pathologic study (occult metastasis). These can be isolated tumor cells (ITCs), micrometastasis, and, infrequently, macrometastasis.

In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B32 study, 15.9% of occult metastases were detected. The differences in prognosis were small, with a difference in overall