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Is sentinel lymph node biopsy indicated in multicentric or multifocal breast cancer?

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Abstract

For a long period of time it has been considered that multicentric/ multifocal breast cancer represents a formal contra-indication for sentinel node biopsy. However, recent studies have showed that sentinel node biopsy is both accurate and feasible in these particular situations. Moreover, performing this technique will minimize the proportion of patients submitted to un-necessary complete axillary lymph node dissection. This is a literature review of the most recent studies which evaluated the role of sentinel node biopsy in multicentric and multifocal breast cancer patients.

Keywords: *multicentric, multifocal, breast cancer, sentinel node biopsy*

Introduction

Sentinel lymph node biopsy (SLNB) has become the standard of care in the last decades for breast cancer patients with clinically negative axilla. The wide applications of this method leaded to a significant diminish of the rate of un-necessary axillary lymph node dissection; in consequence, the morbidity of the procedure significantly decreased while the quality of life improved[1]. However few contraindications have been initially stated for SLNB, the most commonly reported being related to breast tumor characteristics or axillary status; therefore, prior mastectomy or prior excisional breast biopsy, advanced stage tumors (T3 or T4), prior axillary surgery including prior SLNB, palpable adenopathic masses, male breast cancer, multifocal and multicentric lesions as well as neoadjuvant chemotherapy have been considered for a long period of time as contraindications for SLNB[2,3]. However, more recent studies came to demonstrate that certain criteria represent only relative contraindications, in certain cases SLNB being feasible and providing for the patient the same benefit of avoiding an unnecessary complete lymph node dissection and its' secondary comorbidities such as chronic lymphedema of the upper limb[4].

Multifocal versus Multicentric Breast Cancer

Multifocal breast cancer refers to the presence of two or more foci of invasive breast cancer arising in the same quadrant while multicentric breast cancer is defined by the presence of two or more malignant tumors located in different breast quadrants or in the same quadrant but at least 5 cm apart[2]; the reported incidence of these conditions range between 11% and 16 %[5]. The main reason for contraindicating SLNB in multicentric or multifocal breast cancer relates to the fact that it was considered that there is no guarantee that all tumors will drain at the level of the same lymph node stations; therefore, it was thought that each tumor might have its proper lymphatic drainage and its proper sentinel lymph node; therefore injecting one tumor will lead to the discovering of its SLNB while no information about the lymphatic pattern of the other tumors could be achieved[4,6]. Therefore, traditional surgical therapy in cases with multicentric/multifocal breast cancer consisted of modified radical mastectomy[7]. Moreover, most studies regarding SLNB excluded multicentric/multifocal breast cancer patients considering that SLNB would predispose to a higher rate of false negative results in association with an inadequate lymph node staging[2,8].

The Role of SLNB in Multicentric/Multifocal Breast Cancer Patients

Once the first anatomy studies reporting the fact that practically the whole breast drains through a constant, limited number of lymphatics were published, the utility of SLNB in multicentric or multifocal lesions was revised. Therefore, it seems that the breast has a deep and a superficial lymphatic pattern and a subareolar plexus draining to the axillary lymph nodes via one or two main lymphatic channels[9,10].

However, once the observation that one peri-areolar injection is equivalent to a peri-tumoral injection in sentinel lymph node identification for uni-centric breast cancer raised the hypothesis that a single peri-areolar injection could be also enough in order to identify the sentinel lymph node for multicentric or multifocal lesions[4,6]. An interesting study which demonstrated the equivalence between peri-areolar and peri-tumoral injection was conducted by Tuttle and contributors and published in 2002. The authors included in their study 159 patients with uni-centric breast tumors submitted to SLNB in which 99mTc was

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injected into the subareolar area while 1% isosulfan blue dye was injected in the breast parenchyma; the authors observed that in every case at least one radioactive sentinel lymph node was identified while a blue sentinel lymph node was identified in 97% of cases. Moreover the blue lymph node was also radioactive in 98% of cases, indicating that the peri-areolar injected radioactive compound as well as the blue dye (which had been injected in the breast parenchyma) drained through the same channels, in the same axillary lymph nodes[11]. Therefore probably, a small number of lymphatics provide the entire drainage of the breast parenchyma.

Moreover, the guidelines of the American and European Nuclear Society state that both superficial and deep injections are valid and comparable in terms of sentinel lymph node identification[12,13].

Another question that was initially raised in regard with SLNB in multicentric or multifocal lesions was related to the possibility of identifying all the sentinel lymph nodes and to the risk of a higher risk of axillary recurrence[4]. However, recent studies came to demonstrate that SLNB is a feasible and accurate technique for both multicentric and multifocal breast cancer; moreover, the rate of axillary recurrence seems not to be significantly modified when compared to unicentric breast tumors[7].

An interesting study conducted on the theme of SNLB in multicentric/multifocal breast cancer patients was conducted by Holwitt and published in 2008[7]. The study included 41 patients with multicentric/multifocal tumors routinely submitted to axillary lymph node dissection (e.g. regardless the sentinel lymph node status) and 52 patients with the same type of tumors who were submitted to axillary lymph node dissection only if a positive sentinel lymph node was detected; in all cases both radiocolloid and blue dye were injected (i.e. while 99Tc radiocolloid was injected peri-tumorally in all patients, blue dye was injected either peri-tumorally or in the subareolar space). Although the two groups were similar in terms of clinical, demographic and histopathological characteristics, the incidence of axillary metastases was significantly higher among patients who underwent systematic axillary lymph node dissection regardless the status of SLNB when compared to those submitted to axillary lymph node dissection if positive SLNB was found (p=0.001). In the meantime, the sensitivity and specificity of SLNB among the patients from the first group were 93% and 100% respectively while the false negative rate was of 7%. Moreover, the sentinel lymph node was the only positive lymph node in 43% of patients from the first group. Among patients from the second group, six out of the 52 cases has positive sentinel lymph nodes and were further submitted to axillary lymph node dissection; however, after a median follow up of 4,8 years, none of the patients within the second group did not experience any axillary recurrence[7].

More recently, Saiz et al. conducted a study on 73 patients with multifocal breast cancer patients and 16 multicentric breast cancer patients submitted to SLNB and compared their results to the one reported by patients with unifocal lesions[14]. In all cases peri-areolar radiocolloid injection was used. In multicentric/multifocal lesions a higher percent of extra-axillary lymph nodes was observed; in the meantime in the first category of patients a significantly higher number of sentinel lymph nodes was seen when compared to unifocal lesions. Another interesting observation was the one that in multifocal breast cancer patients the rate of sentinel lymph node detection was slightly higher than in multicentric lesions while the number of extra-axillary lymph nodes was slightly lower when compared to multicentric breast cancer patients. Similarly to Holwitt's study, no axillary relapse was found during the follow up period (of 67.2 months) in multicentric or multifocal breast cancer patients[14].

Another interesting study conducted on this subject was a multicentric one, conducted in seven Dutch hospitals between January 2008 and January 2013[15]. The authors showed that SLNB in multicentric/multifocal lesions can reach a sensitivity and a negative predictive value of 100% and a false negative rate of 0%. In the meantime, after a median follow up period of 23 months no axillary recurrence was reported. Another interesting observation of this study regarded the correlation between the diameter of the primary tumor and the positivity rate of SLNB (i.e. higher tumoral diameters being associated with positive SLNB)[15].

Once certain authors demonstrated the feasibility and efficacy of SLNB in multicentric or multifocal breast cancer patients, other authors focused their attention on determining which cases should not be submitted to this technique. However, in the study conducted by Moody and contributors in 2012, the authors showed that multicentric or multifocal tumors previously submitted to neoadjuvant chemotherapy or with larger than 5 cm tumors SLNB should be formally contraindicated due to the higher risk of false negative rates[16].

Conclusions

SLNB is a safe and effective method which might provide a proper axillary evaluation in multicentric or multifocal breast cancer patients. Therefore, decreasing the number of un-necessary axillary lymph node dissection provides a significantly increase of the overall quality of life, diminishing the rate of postoperative comorbidities such as upper limb lymphedema. In regard to the site of injection, it seems that peri-areolar injection is able to identify the sentinel lymph nodes with a very good accuracy degree. However it can be concluded that performing SLNB in multicentric or multifocal lesions does not seem to increase the rate of axillary relapse. ■

Conflict of interests: The authors declare no conflict of interests.

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