



Original article

Detection of sentinel lymph node in breast cancer recurrence may change adjuvant treatment decision in patients with breast cancer recurrence and previous axillary surgery



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ABSTRACT

Use of sentinel lymph node dissection in patients with ipsilateral breast cancer recurrence is still controversial. The objective of this study is to evaluate the feasibility of the sentinel lymph node in breast cancer recurrence (SLNBR) and whether the positivity had impact in the adjuvant treatment.

Between 2008 and 2012 we performed SLNBR in patients with ipsilateral breast tumor recurrence. We included 53 patients in a prospective study. Forty-three patients (81%) had a previous axillary lymph node dissection (ALND) and ten (19%) had a previous sentinel lymph node biopsy (SLNB). Identification rate after SLNB was 50% and after ALND was 60.5% ($p = 0.4$). Nine patients (26%) had a positive SLNBR. Adjuvant systemic treatment was given to all the patients with a positive SLNBR and to 23 (85%) with a negative SLNBR ($p = 0.29$). Six patients (66%) with positive SLNBR and 4 patients (14%) with negative SLNBR underwent radiation therapy ($p < 0.01$).

As conclusions of our study we conclude that sentinel lymph node biopsy in breast tumor recurrence is feasible and significant differences were found in the use of radiation therapy in patients with a positive SLNBR.

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Introduction

Lymph node status is the most important predictive factor for primary breast cancer in clinical practice and the status of the axillary nodes has therapeutic implications. Sentinel lymph node biopsy (SLNB) is the standard treatment in axillary staging in patients with early breast cancer. It allows an accurate staging of the axilla with less morbidity than the axillary lymph node dissection (ALND) [1]. Large prospective trials have shown its accuracy and false negative rates and when the SLN is negative there is no need

to perform an ALND [2]. However, there are some indications for the use of SLNB that are still controversial and one of these indications is the use of SLNB after breast cancer recurrence.

Ipsilateral tumor recurrence (ITR) has been reported to be from 2% to 18%. Around 8.8% of patients develop an ipsilateral breast tumor recurrence (IBTR) twelve years after primary breast conservative surgery [3]. Ipsilateral mastectomy tumor recurrences (IMTR) are less frequent with an incidence of 2.3% at 20 years [3]. It is already known that locoregional failure is associated with an elevated risk of developing distant disease and of death [4,5]. The European Society of medical Oncology (ESMO) guidelines suggest that isolated tumor recurrences should be treated like a new primary, with a curative intent [6]. Treatment of local recurrences usually consists on salvage mastectomy or excision of the recurrence but there are no guidelines for the treatment of regional nodes in those cases. Axillary staging in patients with ITR is not a standard procedure, even in the last ASCO guidelines it is not

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recommended to perform a sentinel lymph node dissection in patients with previous axillary surgery [7]. One of the reasons may be that after axillary surgery, lymphatic drainage may be impaired and in the case of previous ALND no more nodes would be found.

Previous studies have reported that the sentinel node biopsy after breast recurrence (SLNBR) is feasible [8–14]. It has been demonstrated that patients who have undergone SLN biopsy with initial breast conserving treatment of breast cancer may benefit from remapping of sentinel lymphatic drainage [15]. In patients with previous ALND it has been shown that axillary surgery may alter regional lymphatic drainage and studies have reported lower rates of SLNBR detection and more extra-axillary lymphatic drainage [14,15]. However, these reports are retrospective, using hospital or national registries so there is a high heterogeneity in previous procedures, techniques, identification methods and results.

Indications for systemic treatment and radiotherapy after breast tumor recurrence are not standardized and usually depend on tumor characteristics and staging. The more information on disease staging at the time of the breast recurrence could help determining type of adjuvant treatments although there's a lack of evidence and adjuvant systemic after ITR is given according expert opinions [6]. The use of SLNBR may help staging patients with breast cancer recurrences as it can identify occult nodal metastasis that otherwise would not have been found. Whether the finding of additional occult nodal metastases may improve patient's outcome, further long term studies will address this issue.

The objective of this study was to confirm the feasibility and accuracy of the SLNBR in patients with breast cancer recurrence and previous axillary surgery (ALND or SLNB) and to determine whether the finding of a positive SLNBR would impact treatment decisions.

Methods

We performed a prospective study including patients with breast cancer recurrence (IBTR or IMTR) and previous axillary surgery. After institutional review board, patients were enrolled from 2006 to 2012. Patients were stratified according to previous axillary surgery: patients with a previous ALND and patients with previous SLNB. Patients with ipsilateral axillary metastasis at the time of recurrence that were confirmed by fine needle aspiration were excluded from the study. All patients signed an informed consent. There were no men included in the study.

All breast cancer recurrences were diagnosed by a core needle biopsy. Mammography, magnetic resonance imaging of the breast (MRI), breast and axillary ultrasound were performed for local staging in all patients. A bone scan and a chest-abdominal CT were performed for metastatic staging in all patients. PET-TC was not performed in any patient.

Sentinel lymph node procedure

In patients with IBTR, radioisotope ^{99}Tc -Nanocolloid was injected subareolar similar to lymphatic mapping in primary breast cancer as it has been previously reported [16]. In patients with IMTR the ^{99}Tc -Nanocolloid was injected on the mastectomy scar. All injections were performed the day before the surgery. Planar and SPECT-TC images were done in all patients as part of the SLNB protocol. If no drainage was observed, a reinjection with ^{99}Tc was performed in the same place.

During surgery, SLNBR was identified using a gamma probe (Navigator GPS, RMD instruments, Watertown, MA, USA). All nodal basins (axilla, supraclavicular, and internal mammary) were checked with the gamma probe even if no node were shown on

imaging. Excision of extra-axillary SLNBR was left at the discretion of the surgeon. The axilla was explored after the procedure and all palpable suspicious nodes were also excised. No blue dye was used in any patient.

As part of the protocol, patients with a previous SLNB underwent a subsequent ALND after the SLNBR. Also in the case that the SLNBR was not found, an ALND was performed.

SLNBR were sent fresh to Pathology. Intraoperative SLN evaluation was performed only when the results of the SLNBR implied another surgical technique as in patients with contralateral axillary drainage, in this case the surgeons decided whether or not to perform a contralateral ALND in case of a positive SLNBR in the contralateral axilla. Each sentinel node was cut in 2 mm step sections and stained with hematoxyline-eosin (H&E). If SLNBR were negative on H&E, cytokeratin staining was performed. Metastasis to the SLNBR were defined according to the seventh edition of the AJCC staging system [17].

Systemic adjuvant treatment was given according to the criteria of the oncologist as well as adjuvant radiotherapy was administered according to the criteria of the radiation oncologist. Patients were followed with physical exam and a blood test with tumor markers every 6 months. A mammography of the remaining breast was performed annually.

Statistical analysis

Patient data was captured on registration forms and a data base was filled with the information. Identification rate and localization patterns in patients with previous SLNB and previous ALND were compared with the chi-square (χ^2) test and the Fisher's exact test. Post recurrence treatments in patients with positive and negative nodes also were compared using the chi-square (χ^2) test and the Fisher's exact test. The observed differences were considered statistically significant when $p < 0.05$. SPSS for Windows, version 15.0 (SPSS; Chicago, Ill, USA), was used for all statistical analyses.

Results

Informed consent was signed by 54 patients. One patient revoked the informed consent before the contrast injection, so a total of 53 procedures were performed in patients with ITR. Forty-three patients (81%) had a previous ALND and ten patients (19%) had a previous SLNB.

Primary breast cancer tumor characteristics and treatment are summarized in Table 1. Eleven patients had not received any systemic treatment.

Recurrence tumor characteristics

Breast tumor recurrences occurred after a mean of nine years (range, 25–279 months, median 100 months). Fifteen patients (27%) had ITR during the first five years after surgery. Six patients (11%) recurred while on hormonal adjuvant treatment.

In two patients the histology of the recurrence was different than the histology of the primary tumor. One patient had an invasive lobular carcinoma (ILC) in the primary tumor and had an invasive ductal carcinoma (IDC) in the lumpectomy bed. One patient had an IDC in the primary tumor and an invasive mucinous carcinoma in the same quadrant 30 months later.

Second sentinel node procedure

Identification rate of the SLNBR after SLNB was 50% and after ALND was 60.5% ($p = 0.4$).

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