



Original article

Feasibility and oncological safety of sentinel node biopsy in breast cancer patients with a local recurrence

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ARTICLE INFO

Article history:

Received 27 January 2018

Received in revised form

16 May 2018

Accepted 6 June 2018

Available online 7 June 2018

KEYWORDS:

Breast cancer

Recurrence

Sentinel lymph node biopsy

Migration rate

Aberrant lymphatic migration

Outcome

ABSTRACT

Objectives: To investigate the role and feasibility of sentinel lymph node biopsy (SLNB) in breast cancer patients with a local recurrence and no clinically positive axillary lymph nodes.**Materials and Methods:** A total of 71 patients underwent SLNB for breast cancer recurrence. At first surgery, they had received SLNB (46.5%), axillary lymph node dissection (ALND) (36.6%) or no axillary surgery (16.9%).**Results:** Lymphatic migration was successful in 53 out of 71 patients (74.6%) and was significantly higher in patients with previous SLNB or no axillary surgery than in those with previous ALND (87.9% vs. 53.8%; $p = 0.009$). Aberrant lymphatic migration pathways were observed in 7 patients (13.2%). The surgical SLNB was successfully performed in 51 patients (71.8%). In 46 patients (90.2%) the SLN was histologically negative, in 3 patients (5.9%) micrometastatic and in 2 patients (3.9%) macrometastatic. The 2 patients with a macrometastases in SLN underwent ALND. In 4 out of the 18 patients with failure of tracer migration ALND, performed as surgeon's choice, did not find any metastatic node. After a median follow-up period of 39 months (range: 2–182 months), no axillary recurrence has been diagnosed.**Conclusion:** A SLNB in patients with locally recurrent breast cancer, no previous ALND and negative axillary lymph nodes is technically feasible and impacts on the ALND rate. In patients who at primary surgery received ALND, migration rate is significantly lower, aberrant migration is frequent and no clinically useful information has been obtained.

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1. Introduction

Sentinel lymph node biopsy (SLNB) is now considered the standard technique for axillary staging in patients with clinically node-negative primary breast cancer [1]. SLNB is characterized by high identification rates, low false-negative rates and it is associated with less arm morbidity (lymphedema, pain, movement restriction) than axillary lymph node dissection (ALND) [2].

The role of nodal staging in breast cancer has been radically changing over the last years. The evolution towards less aggressive surgery has led to the adoption of SLNB as the only procedure in the majority of women with a primary clinically node negative breast

cancer and on-going studies are testing whether SLNB in this setting is necessary at all [3].

However the results from trials conducted in the adjuvant setting may not be directly applicable to patients with a local recurrence. For example, in the primary setting the persistence of positive axillary nodes when ALND is omitted after a positive SLNB only minimally impairs regional control in absolute terms (0.5% vs 1.5% in the ALND vs no ALND arms; $P = 0.28$) [4], but the same may not be true in the recurrent setting where radiotherapy is not usually delivered and the risk of uncontrolled locoregional progression is both higher and associated with a very poor prognosis [5].

Approximately 5–10% of breast cancer patients develop a local recurrence in the ipsilateral breast after breast-conserving treatment (BCT) or on the chest wall after mastectomy [6,7]. Axillary staging in patients with local recurrence may have a prognostic and local control value and be of help when deciding the administration of further treatments. Patients with local recurrence who had previously not undergone ALND were usually treated with

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resection of the recurrence and ALND.

The management of locoregional nodes at local relapse is controversial and current guidelines, although suggesting that a repeated SLNB is feasible, do not expressly recommend it, especially in patient who underwent a mastectomy for the primary tumor [8,9]. Furthermore, no surgery is suggested if the sentinel lymph node cannot be identified, or if the sentinel node is located outside the ipsilateral axilla [9]. Another argument against nodal staging at local relapse is that it may not change the indication to post-operative therapies. Indeed, a recent study suggests that the use of subsequent radiation and systemic therapy is similar between patients treated and not treated with axillary surgery [10] and that randomised trials support the value of systemic therapy in patients with invasive local recurrence based on tumor biology and not nodal status [11,12].

Over the last few years there has been a growing interest in SLNB for patients with locally recurrent breast cancer and clinically negative axillary lymph nodes, with several studies showing acceptable SLN identification rates in this setting [13,14]. The advantage of repeating SLNB in patients who underwent SLNB at primary surgery is the possible avoidance of ALND and its associated arm morbidity, while SLNB in patients with a previous ALND may detect aberrant drainage pathways and thus improve axillary staging.

The aim of this study is to investigate retrospectively the feasibility, the impact on therapeutic decision and axillary control of SLNB in a consecutive series of patients with breast cancer recurrence and clinically negative axillary lymph nodes.

2. Materials and methods

The medical records of the patients who underwent surgery because of a breast cancer recurrence at the Mauriziano Hospital and at Candiolo Cancer Institute, in Turin, Italy, between 1997 and 2016, have been analysed. Patients with clinical regional lymph node metastases, proven by ultrasound and fine needle aspiration (FNA), and those with distant metastases were excluded from the analysis because the SLNB procedure was not indicated. All women with operable locally recurrent breast cancer, defined as biopsy-proven reappearance of carcinoma in the ipsilateral breast with clinically negative lymph nodes, and who received SLNB at the time of recurrence were included in the study. All patients underwent preoperative mammography plus breast and axillary ultrasound as locoregional staging, plus chest X-ray, liver US and bone scintigraphy as systemic staging. A PET-TC scan was performed in selected patients. Axilla was evaluated clinically and by ultrasound. FNA was performed in case of doubt. All the patients signed informed consent to the anonymous use of their clinical data for scientific purposes and the Institutional Review Board approved the study.

The standard procedure for lymphatic mapping was lymphoscintigraphy with radioactive-labeled technetium; in few cases, at surgeon's choice, blue dye was injected when lymphoscintigraphy was not able to identify a node. During surgery, the sentinel lymph node (SLN) was identified using the gamma probe or by the visualization of the blue-stained lymph drainage pathway and sent for histopathologic examination.

Systemic treatments were prescribed by a multidisciplinary team on the basis of the prognostic and predictive factors according to the protocols in force at the time. All the patients were clinically examined at 4 month intervals for the first two years, at 6 months intervals up to the fifth year and then annually.

All significant variables regarding both the primary tumor (histopathologic characteristics, type of breast surgery, axillary procedures and adjuvant treatments) and the local recurrence (histopathologic characteristics, breast surgery and axillary

procedures, systemic treatments, migration rate, surgical removal rate, percentage and site of extra-axillary migration, pathologic status of the SLN) were retrieved from the medical records and follow up status was updated when incomplete.

2.1. Statistical analysis

Contingency tables were created for comparison of categorical variables between groups and the Chi square test was used to test the statistical significance. Disease free survival (DFS) was calculated in months between the date of recurrence and the date of first cancer diagnosis. The median time to recurrence was estimated by the Kaplan Meier Method. The level of significance was set to 5% two tailed. Statistical analysis was carried out with SPSS software version 17 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Tumor characteristics and treatments

Between 1997 and 2016, 194 patients were diagnosed with a locoregional recurrence of breast cancer. Thirty one were clinically "node positive" and received ALND, 163 had a breast recurrence with no clinical regional lymph nodes metastases; out of them 71 (43.5%) received SLNB, 20 (12.3%) received ALND and 72 (44.2%) did not receive axillary surgery at all (Fig. 1).

Seventy-one patients with local recurrence of breast cancer who received SLNB were included in the study. The median time to recurrence was 108 months (range 13–316) from the primary surgery. The histopathological features of the primary and recurrent tumors are described in Table 1.

As to the treatment of the primary tumor, 66 patients (93%) had received breast-conserving surgery (BCS) and 5 (7%) had undergone a mastectomy. At primary surgery, SLNB was performed in 33 patients (46.5%) whereas 26 patients (36.6%) received ALND. Twenty patients (16.9%), mainly because of a diagnosis of DCIS, received no axillary treatment at primary surgery. All patients after BCS received radiotherapy (RT); 1 patient received post-mastectomy RT.

At recurrence, 29 patients (40.8%) received BCS, while 42 (59.2%) underwent a mastectomy. Ten patients received RT, of which 7 (24.1%) after BCS and 3 (7.1%) after mastectomy.

The treatment of the primary and recurrent breast tumors is described in Table 2.

3.2. Lymphatic migration

Overall, lymphatic migration, leading to SLN identification, was successful in 53 out of 71 patients (74.6%). In the remaining 18 patients (25.4%) tracer migration was considered unsuccessful; in 3 of these patients blue dye was also injected, but with a negative result. SLN identification was significantly higher in patients who at primary treatment underwent SLNB or no axillary surgery as compared to those who received ALND (87.9% vs. 53.8%; $p = 0.009$) (Table 3). A non significant higher success rate was observed in those women with less than 10 nodes removed at previous axillary dissection (3 out of 4 with less than 10 nodes vs. 11 out of 22 with more than 10 nodes). The migration was successful in all the 5 patients previously treated with mastectomy (4 with SLNB and 1 with 36 lymphnodes removed at first surgery). The time to recurrence was not significantly associated with a different migration rate in our study.

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