International Journal of Surgery 35 (2016) 58–63

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Application of a predictive model of axillary lymph node status in patients with sentinel node metastasis from breast cancer. A retrospective cohort study

Salvatore Vieni, Giuseppa Graceffa, Roberta La Mendola, Stefania Latteri, Adriana Cordova, Mario Adelfio Latteri, Calogero Cipolla*

Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo, Italy

HIGHLIGHTS

- In about 60% of patients with metatstic SLN, there is no further axillary neoplastic involvement.
- MSKCC nomogram is a valid tool available to select the patients for axillary lymphadenectomy.
- The nomogram has a high reliability and a remarkable utility in clinical practice.

ARTICLE INFO

Article history:
Received 7 June 2016
Received in revised form
8 September 2016
Accepted 11 September 2016
Available online 12 September 2016

Keywords:
Breast neoplasms
Sentinel lymph node biopsy
Lymphatic metastasis
Axilla
Lymph node excision

ABSTRACT

Background and objectives: The Axillary Lymph Node Dissection (ALND) is the standard treatment in patients with invasive breast cancer and sentinel node metastasis, but in 60% of the cases there is no further axillary neoplastic involvement, so this invasive intervention represents an overtreatment. The purpose of the study is to identify patients with low risk of additional nodal metastases, to omit ALND.
Methods: The MSKCC *Additional nodal metastasis nomogram* was applied on a sample of 175 patients with invasive breast cancer who underwent ALND after detection of macrometastasis with the extemporaneous examination of the sentinel lymph node. Patients were classified as "low risk" when the result of the nomogram was $\leq$50%. Sensitivity, specificity, positive and negative predictive values and AUC (Area Under Curve) of the ROC curve of the nomogram were then calculated.
Results: A cut-off by 50% yielded 92.3% sensitivity, 81,4% specificity, 80% positive predictive value and 92.9% negative predictive value. The ROC curve AUC in these patients was 0.885.
Conclusions: The MSKCC nomogram has proven to be an effective tool in estimating the axillary lymph node status and it can potentially be used to better select the patients with sentinel node macrometastasis who can actually benefit from ALND.

1. Introduction

In patients with invasive breast cancer and clinically negative axilla, the sentinel lymph node biopsy (SLNB) is considered to be a safe and reliable tool in the estimation of the neoplastic involvement of axillary lymph nodes and, if it results positive for metastasis, the treatment currently provided in clinical practice is the axillary lymph node dissection (ALND). However, recent evidences show that only in 40% of the cases the sentinel lymph node metastases are associated with a further involvement of the axilla [1] and that the omission of ALND in patients with tumors characterized by favourable histopathological features, no palpable adenopathy and 1 to 2 metastatic sentinel lymph nodes is not associated with a worse prognosis [2,3]. In fact in breast cancer patients with clinically negative lymph nodes, SLNB alone often seems to represent a sufficient treatment together with an effective systemic therapy [4–9]. This leads to the actual need to perform such a demolitive intervention as ALND, with the risk of complications, only basing on neoplastic colonization of the sentinel lymph node (SLN), considering that after surgery patients often undergo adjuvant therapy, which is an effective tool to ensure adequate

* Corresponding author. Department of Surgical, Oncological and Oral Sciences, University of Palermo, Via del Vespro 129, 90127, Palermo, Italy.
E-mail address: calogerocipolla@virgilio.it (C. Cipolla).

http://dx.doi.org/10.1016/j.ijsu.2016.09.015
1743-9191/

locoregional control of disease and to reduce the risk of recurrence [10].

To make surgery more conservative and to customize treatment as much as possible basing on histopathological and biological features of breast cancer [11], many predictive models have been developed in order to identify patients who actually benefit from ALND among those with metastatic SLN. The *Additional nodal metastasis nomogram* elaborated by Memorial Sloan- Kettering Cancer Center (MSKCC) [12] provides a percentage corresponding to the risk of non-SLN metastasis in SLN-positive patients. Considering the maneuverability of the nomogram and the easily accessible information that it requires, the nomogram was applied to a sample of patients with invasive breast cancer and positive SLN to assess its sensitivity, specificity, positive and negative predictive values. In particular, the possibility of using MSKCC nomogram in daily clinical practice has been taken into consideration for those patients at high risk of additional axillary metastasis who undergo ALND at the same surgical time with tumor excision, distinguishing them from those to whom ALND can be reasonably omitted because further axillary involvement is negligible.

2. Materials and methods

2.1. Inclusion criteria of the study

Data on patients who underwent SLNB between January 2009 and June 2015 were collected. All patients received a preoperative diagnosis of breast cancer confirmed by clinical and instrumental examinations (mammography and ultrasound) and core biopsy. 200 women with SLN macrometastasis, found with the intra-operative examination, were selected and subjected to ALND at the same operative time of tumor resection. 25 patients were eliminated from the sample because 20 of them were characterized by histological types of invasive breast cancer that are not included in the nomogram (mucinous, tubular, papillary, mixed types) and the other 5 for incompleteness of the pathological report. The nomogram was then applied to a total of 175 patients, who meet the following criteria: invasive ductal or lobular breast cancer preoperatively diagnosed by mammography, ultrasound and core biopsy; clinically negative axillary lymph nodes (N0); detection of macrometastases (neoplastic aggregates >2 mm) at intraoperative examination of SLN performed by frozen section; execution of complete ALND by the surgeon.

2.2. Patient characteristics

Patient characteristics are different (Table 1). They are all female and aged between 32 and 86 years for a median age of 55.12 years. 164 of them (93.7%) were subjected to quadrantectomy, the remaining 11 (6.3%) to mastectomy, both accompanied by SLNB and subsequent ALND. The histological features of the different cancers were obtained from a preoperative core biopsy performed on breast lesions. In all cases, core biopsy provided information that was fully confirmed by histopathological examination performed on a surgical specimen, establishing itself as a reliable tool for preoperative characterization of breast cancers [13,14]. 157 tumors (89.7%) were ductal type, while only 18 (10.3%) were classified as lobular. As regards the histological grade, 12 breast cancers were G1 (6.9%), 121 G2 (69.1%) and 42 (24%) were G3.

Core biopsy also provided the gene expression pattern of each tumor: 158 patients (90.3%) had ER-positive tumors and 17 (9.7%) of them ER-negative; 148 cancers (84.6%) were PR-positive, 27 (15.4%) lost PR expression; in 87 cases (49.7%) tumors showed HER2/neu overexpression, 88 cancers (50.3%) didn't show it.

The last information supplied by core biopsy, then confirmed by the analysis of the surgical specimen, is the presence of lymphovascular invasion, that is the detection of neoplastic cells within lymphatic and/or blood vessels. 107 tumors of the sample (61.1%) had lymphovascular invasion, 68 (38.9%) did not.

The dimensions of the tumors, obtained from pre-operative ultrasound, varies between 0.2 and 7 cm, for a median of 2 cm. Finally, in 27 patients (15.4%) preoperative imaging showed a multifocal breast cancer.

Table 1
Patient characteristics.

Characteristic	Number of patients and percent
Age	
≤50	66 (37,7%)
>50	109 (62,3%)
Operation	
Quadrantectomy	164 (93,7%)
Mastectomy	11 (6,3%)
Number of positive SLNs	
1	123 (70,3%)
2	43 (24,6%)
3	7 (4,0%)
>3	1 (0,6%)
Number of negative SLNs	
0	86 (49,1%)
1	56 (32,0%)
2	26 (14,9%)
>2	8 (4,6%)
Cancer histotype	
Ductal	157 (89,7%)
Lobular	18 (10,3%)
Histological grade	
G1	12 (6,9%)
G2	121 (69,1%)
G3	42 (24,0%)
ER-status	
Positive	158 (90,3%)
Negative	17 (9,7%)
PR-status	
Positive	148 (84,6%)
Negative	27 (15,4%)
HER2/neu overexpression	
Yes	87 (49,7%)
No	88 (50,3%)
Lymphovascular invasion	
Yes	107 (61,1%)
No	68 (38,9%)
Multifocality	
Yes	27 (15,4%)
No	148 (84,6%)
Tumor size	
T1 (≤2 cm)	88 (50,3%)
T2 (>2 cm e ≤ 5 cm)	81 (46,3%)
T3 (>5 cm)	6 (3,4%)

2.3. Diagnostic and therapeutic procedures and SLN identification

Patients in the sample received a preoperative diagnosis of breast cancer using imaging techniques (mammography and ultrasound) and core biopsy which was performed by Lorad® digital stereotatic table or ultrasound guidance.

The absence of suspicious lymphadenopathy, which is a basic requirement in order to perform the sentinel lymph node biopsy, was then checked by means of the clinical and ultrasound examination of the axilla.

The identification of SLN was preoperative and intraoperative. The day before surgery, all patients underwent lymphoscintigraphy by means of a subareolar injection of Nanocoll (^{99}Tc labelled human serum albumin), which is a very accurate procedure to identify of the sentinel lymph node [15,16]. Anterior and anterior-oblique scans