

Original Article

Breast cancer lymphoscintigraphy: Factors associated with sentinel lymph node non visualization

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ABSTRACT

Objective: To evaluate factors associated with non identification of the sentinel lymph node (SLN) in lymphoscintigraphy of breast cancer patients and analyze the relationship with SLN metastases.**Material and methods:** A single-center, cross-sectional and retrospective study was performed. Forty patients with lymphoscintigraphy without sentinel lymph node identification (negative lymphoscintigraphy – NL) were enrolled. The control group included 184 patients with SLN identification (positive lymphoscintigraphy – PL).

Evaluated factors were age, body mass index (BMI), tumor size, histology, localization, preoperative breast lesion hookwire (harpoon) marking and SLN metastases.

The statistical analysis was performed with uni- and multivariate logistic regression models and matched-pairs analysis.

Results: Age ($p=0.036$) or having BMI ($p=0.047$) were the only factors significantly associated with NL. Being ≥ 60 years with a BMI ≥ 30 increased the odds of having a NL 2 and 3.8 times, respectively.Marking with hookwire seems to increase the likelihood of NL, but demonstrated statistical significance is lacking ($p=0.087$). The other tested variables did not affect the examination result. When controlling for age, BMI and marking with the harpoon, a significant association between lymph node metastization and NL was not found ($p=0.565$).**Conclusions:** The most important factors related with non identification of SLN in the patients were age, BMI and marking with hook wire. However, only the first two had statistical importance. When these variables were controlled, no association was found between NL and axillary metastases.

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Linfogammagrafía en el cáncer de mama: factores asociados con la no visualización del ganglio centinela

RESUMEN

Objetivo: Evaluar los factores relacionados con la no identificación del ganglio centinela (GC) en la linfogammagrafía de pacientes con cáncer de mama y su relación con metástasis en el GC.**Material y métodos:** Se realizó un estudio unicéntrico, transversal y retrospectivo. Se seleccionaron 40 pacientes con linfogammagrafías sin identificación de GC (linfogammagrafía negativa - LN). El grupo control incluyó 184 pacientes con identificación del GC (linfogammagrafía positiva - LP).

Los factores evaluados fueron: edad, índice de masa corporal (IMC), tamaño, histología, localización, marcación preoperatoria del tumor con arpón e metástasis en el GC. El análisis estadístico se realizó mediante modelos de regresión logística univariante y multivariante y análisis pareado.

Resultados: La edad ($p=0.036$) y el IMC ($p=0.047$) fueron los únicos factores asociados significativamente con LN. Tener edad ≥ 60 años o IMC ≥ 30 elevaron la probabilidad de tener una LN 2 y 3.8 veces, respectivamente.La marcación con arpón parece aumentar la probabilidad de LN, pero sin significación estadística ($p=0.087$). Las otras variables no influyeron el examen. Al controlar edad, IMC y marcación con arpón, no se encontró una asociación significativa entre metástasis de ganglios linfáticos y LN ($p=0.565$).**Conclusión:** Los factores más importantes relacionados con la no identificación del GC en las pacientes fueron edad, IMC y marcación con arpón, pero, sólo los dos primeros tuvieron relevancia estadística. Cuando se controló estas variables, no se encontró asociación entre LN y metástasis axilares.

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Palabras clave:

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Introduction

It is widely accepted that sentinel lymph node (SLN) biopsy is an important procedure for the correct staging of patients with breast cancer. Furthermore, SLN biopsy allows a minimally invasive surgery, reducing the co-morbidities associated with axillary lymph node dissection. Lymphoscintigraphy is a simple and accurate method that helps identifying the sentinel lymph node.^{1–3}

In a minority of cases lymphoscintigraphic detection of SLN is not possible. Failure to visualize a SLN increases the difficulty of surgical intervention.^{2,4} In some patients the hidden SLN will be intra-operatively detected, either by gamma-probe alone or by gamma-probe combined with blue dye. When SLN is not found, axillary lymph node dissection is recommended.⁵

Some authors argue that the main reason for SLN non identification is SLN metastization because lymphatics may be blocked by cancer cells, not allowing colloid progression through lymphatic channels.^{1,6} On the other hand, there are studies that did not find significant association between negative lymphoscintigraphy and axillary metastases.⁶ During the past decade several other factors have been reported as being related to the failure of SLN identification in lymphoscintigraphy, namely, patient's age and body mass index (BMI), as well as tumor characteristics.

In our tertiary cancer center we perform around 570 lymphoscintigraphies in breast cancer patients per year. The scintigraphic SLN identification rate in our department is 98% and the concordance of SLN detection both in lymphoscintigraphy and surgery is 95%.

The primary goal of this retrospective study was to analyze which factors could influence the lymphoscintigraphic SLN non identification and to study each factor separately. As a secondary analysis, we wanted to establish the relationship between lymphoscintigraphic failure in detecting the SLN and the existence of SLN metastases, by controlling for the previously defined variables that could influence the examination result.

Material and methods

We reviewed all lymphoscintigraphies performed in breast cancer patients between January 2010 and December 2013, corresponding to a total of 2200 examinations.

Lymphoscintigraphy was classified as:

- Positive lymphoscintigraphy (PL) – lymphoscintigraphy with SLN identification.
- Negative lymphoscintigraphy (NL) – lymphoscintigraphy without SLN identification.

During this period we found 40 NL and from the remaining large amount of PL, we only included 184 PL in our study. The PL group was considered as a “control group” and corresponded to all patients with SLN identification in lymphoscintigraphy consecutively performed between January and June 2011. This period was randomly selected, because the technique was similar between 2010 and 2013.

Inclusion and exclusion criteria:

We included all female patients, with unilateral breast carcinoma and without previous chemotherapy that performed lymphoscintigraphy in our department.

Lymphoscintigraphy was performed in patients with histological confirmation of invasive carcinoma or *in situ* carcinoma with high or intermediate grade, necrosis or other aggressive

characteristics and that had no histological evidence of axillary metastases.^{1,3,7}

Our study excluded patients with bilateral breast cancer, male patients and patients treated with neoadjuvant chemotherapy prior to lymphoscintigraphy, due to the small number of patients in these groups. We wanted to have a homogenous study group, avoiding extra factors that could influence the results.

Patients with very early stage breast cancer (low-grade ductal carcinoma *in situ*) who were not proposed to mastectomy, inflammatory breast cancer, histologically confirmed positive axillary or extra-axillary lymph nodes or patients with widespread metastases beyond surgical resection did not perform lymphoscintigraphy.

Lymphoscintigraphy and surgical technique of the sentinel lymph node:

All examinations were performed in our department using a subareolar injection of 55.5 MBq (1.5 mCi) of ^{99m}Tc-albumin nanocolloid, 0.5 mL, in the same quadrant of the breast lesion.

Immediately after the injection sequential anterior, lateral and antero-oblique planar images, with the patient in supine position, were acquired using a dual-head Siemens E. Cam[®] or Philips Brightview[®] gamma-cameras with low-energy and high-resolution collimators. The first axillary hotspot identified in the lymphoscintigraphic image was considered the SLN and its projection was marked in the skin using a point source of ^{99m}Tc and further confirmed with a gamma-probe (Eurorad Europrobe[®]).

When SLN was identified in lymphoscintigraphy, it was considered PL.

When the SLN was not visible in the first set of images, patients were encouraged to do breast massage and image acquisition was sequentially repeated until up to 4 h after injection.

In our department we did not inject a second dose of radiopharmaceutical because of time and logistic aspects. In the period of time included in our study we did not have SPECT/CT available.

When SLN was not identified in lymphoscintigraphy, it was considered NL.

Usually, lymphoscintigraphy and surgery took place on the same day. In the operating room and after anesthesia, the surgeon injected blue dye in the upper-external breast quadrant. SLN biopsy was guided by our cutaneous mark and the removed SLN was the lymph node with highest counts shown by the gamma-probe (Euro-rad Europrobe[®]), the majority marked with blue dye. Occasionally, more than one lymph node was resected, namely when there were other lymph nodes with >10% of the SLN greatest activity and when clinically suspicious lymph nodes were found. The lymph nodes removed were measured with gamma detector probe to confirm that they were responsible for the activity detected during lymphoscintigraphy and surgery. After resection, the axillary region was explored with the gamma-probe to confirm that there was only residual radioactivity.

The SLN was separated and carefully identified, putted in formal and sent to the Department of Pathology, where the SLN protocol was performed. First a macroscopic study of the lymph node was made, then it was sliced following the longitudinal/vertical axis into approximately 2 mm serial sections. Afterwards the lymph node was fixed in paraffin blocks. Three-micro sections of each block were obtained, stained with hematoxylin–eosin and finally examined under the microscope. Immunohistochemical study was used in dubious cases.

Parameters analyzed:

We retrospectively collected information from the patients' medical records concerning the factors referred in the literature as being associated with SLN identification failure in

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