

Original Article

Selective biopsy of the sentinel lymph node in breast cancer: Without axillary recurrences after a mean follow-up of 4.5 years[☆]Luis Bañuelos Andrió^{a,*}, Gil Rodríguez Caravaca^b, Miguel Argüelles Pintos^c, Mercedes Mitjavilla Casanova^d^a Unidad de Medicina Nuclear, Hospital Universitario Fundación Alcorcón, Madrid, Spain^b Servicio de Medicina Preventiva, Hospital Universitario Fundación Alcorcón, Madrid, Spain^c Servicio de Anatomía Patológica, Hospital Universitario Fundación Alcorcón, Madrid, Spain^d Servicio de Medicina Nuclear, Hospital Universitario Puerta de Hierro, Majadahonda, Madrid, Spain

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ABSTRACT

Objective: To analyze the rate of axillary recurrences (AR) in patients with early breast cancer who had not undergone an axillary node dissection (ALND) because of a negative sentinel lymph node biopsy (SLNB). **Material and methods:** The study includes 173 patients operated on for breast cancer and selective node biopsy. Thirty-two patients with positive SLNB underwent ALND. We followed up 141 patients with negative SLNB without LDN, with a median follow-up of 55 months (range 74–36 months).

Results: The detection rate of SLN was 99.42%. After a median follow-up of 4.5 years, there were no axillary recurrences. Two patients developed local recurrence, other two patients developed distant metastases and four patients developed a metachronous tumor. Four patients died, none of them because of breast cancer.

Conclusions: The results obtained support the SLNB as an accurate technique in the axillary stratification of patients with breast cancer, offering in the cases of negative SLNB a safe axillary control after 4.5 years of follow-up.

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Biopsia selectiva del ganglio centinela en cáncer de mama: sin recurrencias axilares tras un seguimiento medio de 4,5 años

RESUMEN

Palabras clave:

Cáncer de mama

Ganglio centinela

Linfadenectomía axilar

Recurrencias axilares

Objetivo: Analizar la tasa de recurrencias axilares (RA) en pacientes con cáncer de mama en estadios iniciales y biopsia selectiva del ganglio centinela negativa (BSGC) sin linfadenectomía (LDN) posterior.

Material y métodos: Se han incluido un total de 173 pacientes a quienes se aplicó la BSGC tras diagnóstico de cáncer de mama en estadios iniciales. En 32 pacientes la BSGC fue positiva y estas pacientes fueron sometidas a LDN. Se han seguido 141 pacientes con BSGC negativa sin LDN, por un periodo medio de 55 meses (rango 74–36).

Resultados: La tasa de detección del GC fue del 99,42%. Después de un periodo de seguimiento medio de 4,5 años no se han detectado RA. Dos pacientes desarrollaron recidiva local, otras 2 desarrollaron metástasis a distancia y 4 desarrollaron un cáncer intercurrente. Se produjeron 4 muertes, ninguna de ellas asociadas al cáncer de mama.

Conclusiones: Los resultados obtenidos apoyan la BSGC como una técnica exacta en la estadificación axilar de los pacientes con cáncer de mama en estadios iniciales, ofreciendo en los casos de BSGC negativa un control axilar seguro después de 4,5 años de seguimiento medio.

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Introduction

Axillary lymph node status continues to be an important prognostic factor in patients with breast cancer. In the last years notable changes have been produced in the treatment of the axilla in patients with breast cancer with no clinical evidence of lymph

node involvement. Selective sentinel lymph node biopsy (SLNB) has replaced axillary lymph node dissection (ALND) in the staging of axillary lymph nodes in patients with breast cancer since it has shown to be as precise as ALND.¹

Recent studies have demonstrated equivalent rates of overall survival, disease-free survival and regional control among patients undergoing ALND and those in whom only SLNB was performed in cases with a negative sentinel lymph node (SLN) result.^{2,3} Some recent studies have concluded that ALND is not always necessary when SLNB provides a positive result based on the effectiveness of new systemic treatment and greater knowledge of tumor behavior and metastasis.^{4,5}

In this regard, patients developing axillary recurrence (AR) following a negative SLNB are of special interest since they are a group

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* Corresponding author.

E-mail address: lbañuelos@fhalcorcon.es (L. Bañuelos Andrió).

of patients who have not received additional treatment of the axilla and definitively reflect the validity of the technique. The objective of this study was to analyze the rate of AR in 173 consecutive patients with early stage breast cancer undergoing SLNB as the method of staging, with a mean follow-up of 55 months.

Material and methods

We included 173 consecutive patients with T1-T2 breast cancer and negative axilla by clinical and ultrasound examination who underwent surgical treatment using SLNB as the procedure for axillary staging in the Fundación Alcorcón University Hospital. The diagnosis of breast carcinoma was made by mammography, ultrasonography, MR and histological study in all the patients. In most of the cases (96.8%) the diagnosis was performed by ultrasound-guided thick needle biopsy. The ultrasound study also included axillary examination, with aspiration puncture with thick needle of adenopathies with suspicion of infiltration. The study period was from October 2006 to December 2009 during which time patients with a positive SNL underwent ALND.

Lymphoscintigraphy and the surgical technique of the sentinel lymph node

On the morning of the surgery patients with a palpable tumor underwent lymphoscintigraphy with a subdermal injection of 37MBq ^{99m}Tc nanocolloid human serum albumin (Nanocoll™) in 0.1 ml of saline solution in the breast region in which the tumor was localized. If the tumor was not palpable a subdermal injection was made in the quadrant of the lesion described in the imaging studies. After the subdermal injection the region was massaged to favor migration of the tracer by the lymphatic pathway.

A conventional dual-head Philips Skylight gamma camera with low-energy, high-resolution collimators was used for image acquisition. Images were obtained in anterior, lateral, and, if necessary, anterior oblique projections with the patient in a supine position with the arms behind the head at a 90° angle. Methacrylate filled with ^{99m}Tc was used as a flat source to draw the contour of the body and thereby obtain anatomical references for the images acquired. During the acquisition, the energy peak was 140 keV (10%) and a 256 × 256 matrix was used without applying zoom. Whenever necessary, the breast was separated from the axilla using adhesive tape to avoid contamination of the image by the injection points.

The SLN was identified obtaining the scintigraphic images in the gamma camera at 30 min after the injection of the radiotracer. In the case of no radiotracer migration in these first 30 min, a new massage was made in the zone of the injection, and images were acquired at 60–90 min. If no migration of the radiotracer was observed at this time the patient was reinjected with the same technique described above. The areas of activity corresponding to the SLN were localized on the skin of the patient with a radioactive point and marked with a cross using an indelible marker.

If the tumor was not palpable after the identification and marking of the SLN on the skin, the patient was sent to the radiology department for the placement of a metallic harpoon.

For the intraoperative localization of the SLN a gammadetector probe (Europrobe™, Eurorad, Strasbourg, France) was used by an experienced nuclear medicine physician. Prior to initiating the surgical procedure in the axilla the gamma detector was covered with a sterile drape and the radioactive activity at the injection points was measured. Thereafter, the skin at the axillary level was measured to localize the point of greatest radioactivity with the aim of orienting the surgical incision. Following the incision, the search for the SLN was begun. All the lymph nodes presenting radioactivity greater than 10% of the lymph node presenting the greatest activity

measured with the gamma detector probe were resected, with all being measured in counts per second (cps). All the lymph nodes were measured with the gamma detector probe after removal to confirm that they were responsible for the activity detected *in vivo* and to avoid the alteration of other tissues with radioactivity (injection points, other SLNs, etc.). In the cases in which more than one SLN was resected together, these were separated prior to being sent to the Department of Pathology. All the lymph nodes resected were collected separately for individualized study. To finalize the search for the SLN, a minute search for any radioactivity present in the surgical bed was made. Once it had been demonstrated that no deposit surpassed 10% of the SLN of greatest activity, the tissues were sent to the Department of Pathology. Rigorous digital examination of the axilla was also carried out after the SLNB to detect lymph nodes macroscopically suspected of metastatic infiltration susceptible to biopsy.

Pathologic analysis of the sentinel lymph node

For intraoperative examination the fresh SLN(s) were sent to the Department of Pathology. A macroscopic study of the lymph node was made by the pathologist who sliced the lymph node into sections of approximately 2 mm following the longitudinal/vertical axis based on the morphology of the lymph node. The most suspicious section from a macroscopic point of view was frozen at –20 °C and a 5–10 micro section was later sectioned and stained with hematoxylin–eosin (H&E) to assess the presence of malignancy. This procedure was carried out in a mean time of approximately 20–30 min.

The definitive histopathologic study of the SLN(s) was posteriorly carried out. To do this, they were fixed in formol and thereafter in paraffin blocks. Each lymph node was independently embedded in paraffin. Two 3-micro sections of each block were obtained with an interval of 3–5 micro section, and these were stained with H&E. In the case of no pathological findings in the H&E study, the immunohistochemical study was performed using cytokeratin AE1–AE3.

Surgical procedure

The breast cancer was resected in all the patients with a conservative approach (tumorectomy) or total mastectomy associated to SLNB. In the case of non-palpable breast lesions a metallic guide was placed at the site of the tumor under stereotactic or ultrasound guidance. All the patients in whom metastasis was detected in the frozen section (FS) underwent ALND during the same surgical procedure. If the SLN was negative in the FS but was positive for metastasis in the definitive analysis, the patients underwent ALND in a second surgical approach. Patients with a negative SLN did not undergo ALND.

Clinical follow-up

After completion of the corresponding surgical treatment and adjuvant therapy according to the protocol of our hospital, the patients were clinically followed in the Department of Gynecology by clinical examination (with breast and axillary examination), analytical tests (tumor markers) and mammography at intervals of 6–12 months. The mean follow-up of our patients was 55 months (36–74 months). On clinical suspicion of recurrence or mammographic alterations during the follow up, a directed study was performed.

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