Selective sentinel lymph node biopsy associated with primary systemic chemotherapy in breast cancer

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ABSTRACT

Introduction: Primary systemic chemotherapy is used in inoperable, locally advanced, or inflammatory (neoadjuvant chemotherapy) breast cancer, and when a reduction in tumor size is sought in order to offer conservative surgical treatment as an option. Its advantages include early onset of systemic treatment, possible conversion of initially non-surgical breast cancer into operable disease, an increase in conservative surgeries, and the possibility of in vivo assessment of chemosensitivity.

Objective: To assess the usefulness of selective sentinel node biopsy (SSNB) in patients with breast cancer treated with primary systemic chemotherapy.

Materials and methods: Retrospective study carried out from January 2006 to December 2015 at the Breast Pathology Department of the Complejo Hospitalario Universitario Insular-Materno Infantil de Canarias. Patients with infiltrating breast cancer (T1-4/N0-2), who were treated with neoadjuvant or primary systemic chemotherapy, plus trastuzumab in the cases with Her2/neu positive carcinoma, underwent a SSNB.

Assessment of axillary lymph nodes was performed by physical examination, axillary ultrasound, and cytological or histological study of the suspicious nodes. If the axilla was negative, before starting the primary systemic treatment, pre-chemotherapy SSNB was performed. If a positive axilla was diagnosed, SSNB was performed at the end of systemic chemotherapy, at the same time as surgical treatment.

Axillary lymphadenectomy (AL) was performed according to the protocol established at that time. The sentinel node (SN) was analyzed by hematoxylin-eosin, immunohistochemistry, or one- step nucleic acid amplification. The SN detection rate, number of axillary nodes when lymphadenectomy was performed, evolution of the disease, local and systemic recurrences, disease-free time, and survival rates were determined.

Results: Group I: pre-chemotherapy SSNB in patients with cN0 at onset. The SN was detected in 184 patients (97.8%). Group 2: post-chemotherapy SSNB in cN1-2 patients or those with locally advanced carcinoma. The SN was detected in 79 patients (79.7%).

Conclusion: Sentinel node detection is safe both before and after systemic treatment. Performing fewer axillary lymphadenectomies does not lead to an increase in local or systemic recurrences. Conservative surgical treatment of the breast and axilla has good outcomes in stages II-III. A low recurrence rate was detected locally and systemically. 25% of ALs performed due to non-migration of the contrast had more than three affected nodes. These results were obtained by applying a multidisciplinary diagnostic and therapeutic strategy.

KEYWORDS

Selective sentinel node biopsy, breast cancer, axillary lymph nodes, axillary lymphadenectomy.

Introduction

Primary systemic chemotherapy is used in inoperable, locally advanced, or inflammatory (neoadjuvant chemotherapy) breast cancer, and when a reduction in tumor size is sought in order to offer conservative surgical treatment as an option. Its advantages include early onset of systemic treatment, the possibility of converting initially non-surgical breast cancer into operable disease, an increase in conservative surgeries, and the possibility of in vivo assessment of chemosensitivity ^[1,2].

SSNB is the gold standard procedure for axillary staging of breast cancer, and it has become the standard for therapeutic of the axilla in this pathology ^[3].

Article history

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The possibility of performing SSNB before or after chemotherapy, together with its advantages and disadvantages, is discussed in the literature ^[4,5]. The use of SSNB has changed the local management of the axilla, leading axillary lymphadenec-



tomy to be abandoned in cases of positive sentinel lymph node based on the ACOSOG 2011 study that included more than 800 patients^[6]. The AMAROS trial, published in 2014, which included 4823 patients, concluded that in T1 and T2 breast cancers with positive sentinel node, sentinel node biopsy obtained the same outcomes as axillary lymphadenectomy (AL) or axillary radiotherapy, and with significantly less morbidity.

Regarding the performance of pre-chemotherapy or postchemotherapy SSNB, the SENTINA study, published in 2013 and including 1737 patients, confirmed the high detection rate of the sentinel node (98.1%) when pre-chemotherapy SSNB was performed. Meanwhile the SSNB performed after primary chemotherapy presented false negative rates of 24.3% when one node was removed and 18.4% when two nodes were removed.

The Spanish Society of Senology and Breast Pathology (SESPM), in a consensus review on SSNB carried out in 2013, considered that in patients with clinically and sonographically negative axilla, the procedure can be performed before or after primary systemic treatment. In patients initially cN1/N2 with no clinical or ultrasound disease of the axilla after neoadjuvant chemotherapy, SSNB can be performed avoiding axillary lymphadenectomy.

Objective

The objective of the study was to review the results of axillary management in patients with breast cancer in whom a SSNB was performed in the context of primary systemic treatment with chemotherapy. AL has been decreasing over the years based on scientific evidence and our experience.

Materials and methods

This was a retrospective study carried out from January 2006 to December 2015 at the Breast Pathology Department of the Complejo Hospitalario Universitario Insular- Materno Infantil de Canarias.

Patient selection

We included women diagnosed with infiltrating and non-metastatic breast cancer (T1- 4/N0-2 according to the TNM staging system) from the Breast Pathology Department of this hospital.

Patients with a diagnosis of Tis/N3/M1 (TNM system) were excluded.

Breast cancer was staged using clinical examination, mammography, echography, and fine needle aspiration biopsy or core needle biopsy.

Patients were classified into two groups:

- **Group 1** (SSNB Pre-C): pre-chemotherapy SSNB, performed in patients initially with a clinically and sonographically negative axilla;
- **Group 2** (SSNB Post-C): SSNB performed after chemotherapy in patients initially with N1 stage and with a negative axilla after that treatment.

Gammagraphic and intraoperative detection of the sentinel node

On the day of the surgery, 74-111 MBq of 99mTc albumin nanocolloid was injected into the subareolar area and a lympho-gammagraphy was performed to locate the sentinel node. During the surgery the sentinel node was identified thanks to a gamma radiation probe and the node was extracted from the surgical site.

Pathology study

In the pathology study, estrogen receptors (ERs), progesterone receptors (PRs), human epidermal growth factor receptor 2 (HER2) status, p53 protein, Ki-67 protein, and cytokeratin 19 (CK19) were studied.

The patients were classified according to the following molecular classification of breast cancer:

- Luminal A (ER+/HER2-/Ki-67 <20%/PR+)
- Luminal B/HER2-negative (ER+/HER2-/Ki-67> 20% or PR <20%)
- Luminal B/HER2-positive (ER+/HER2+/any of Ki-67 or ER)
- HER2-positive (HER2 +/ER-/PR-) and triple negative (ER-/ PR-/HER2-).

The histological analysis of the sentinel node was done by hematoxylin-eosin stain and immunohistochemistry with anti-keratin antibodies AE1/AE3, or OSNA (one-step nucleic acid amplification), according to the technique used at the time of the study.

A sentinel node was defined positive when it presented macrometastasis (more than 5000 copies/ μ L mRNA CK-19 or was greater than 2 mm in diameter) or micrometastasis (250-5000 copies/ μ L mRNA CK19 or measured 0.2-2 mm in diameter). A negative sentinel node was one presenting isolated tumor cells (100-250 copies/ μ L RNA-CK19 or measuring less than 0.2 mm) or no metastatic tumor cells (fewer than 100 copies/ μ L mRNA-CK 19) ^[6]. Lymphadenectomy specimens were also studied, with hematoxylin-eosin and immunohistochemistry by pathologists.

Systemic treatment

Two chemotherapy protocols were used in accordance with practice at the general hospitals where the drugs were administered. At the Hospital Universitario Doctor Negrín: 5-fluorouracil, epirubicin and cyclophosphamide (FEC) 600/90/600 21 days for four cycles, followed by paclitaxel 100/M2 weekly for eight cycles \pm trastuzumab + paclitaxel weekly, followed by trastuzumab 6 mg/kg every three weeks until a complete year. At the Hospital Universitario Insular de Gran Canaria the protocol was the following: FEC every 15 days x 4 cycles, followed by docetaxel every 21 days for 4 cycles.

If a tumor was Her2/neu positive, trastuzumab was administered weekly starting with the first dose of paclitaxel and finishing with the last cycle of this drug. After oncological surgery, trastuzumab was given every 21 days until a complete year of treatment.

After systemic treatment, the patients were evaluated with clinical examination, mammography, and ultrasound.

In the breast specimen, the pathological response after systemic treatment was studied, classifying the tumors into:

- 1) Pathological complete response if there was no infiltrating tumor or presence of residual carcinoma *in situ*
- 2) Pathological response greater than 50%
- 3) Pathological response less than 50%
- 4) Absence of response
- 5) Progression.

Results

We included 263 SSNB procedures done at the hospital between January 2006 and December 2015. Figure 1 shows the evolution of SSNB procedures performed at our hospital after primary systemic treatment between the years 2006 and 2015.

In group 1 (SSNB before systemic treatment), 184 procedures were done, starting from 2006. In the second group (SSNB after systemic treatment), 79 procedures were done starting from 2008.

Patients' characteristics:

In the first group, 69.6% of the patients (128) were not menopausal, and 30.4% were menopausal (56). In the second group, 64.6% (51) of the women were not menopausal, and 35.4% were (28).

Table 1 shows the ages of the women and the procedures performed; 67.55% of the women were not included in the breast

Table 1 Age of the patients and the procedures performed.

Age	Mean and Range	<40	40-50	50-70	>70
SSNB	47.6	37	80	65	2
Pre-C	(21 – 75)	(20.1%)	(44.7%)	(35.3%)	(1.1%)
SSNB	48.9	14	32	31	2
Post-C	(30 – 77)	(17.7%)	(40.5%)	(39.2%)	(2.5%)
SSNB Pre-C: Selective single node biopsy before systemic treatment (chemotherapy):					

SSNB Pre-C: Selective single node biopsy before systemic treatment (chemotherapy, SSNB Post-C: Selective single node biopsy after systemic treatment cancer population screening provided by the public health system of the Canary Islands.

Tumor characteristics

Location

In Group 1, 98 patients had (53.3%) the tumor located in the right breast. Left breast cancer was diagnosed in 86 cases (46.7%).

In Group 2, 36 cases (45.6%) had the tumor in the right breast, 42 in the left breast (53.2%), and in one case (1.3%) the tumor was bilateral.

The breast quadrant most affected in our study group was the upper outer quadrant; in this group of patients, the SSNB was done before systemic treatment in 37.5% of cases, and after chemotherapy in 38% (Table 2).

Location of the tumor	SSNB Pre-C n=184	SSNB Post-C n=79
Upper outer quadrant	69 (37.5%)	30 (38%)
Upper inner quadrant	28 (15.2%)	9 (11.4%)
Union of upper quadrants	29 (15.8%)	15 (18.9%)
Lower outer quadrant	14 (7.6%)	4 (5.1%)
Lower inner quadrant	5 (2.7%)	2 (2.5%)
Union of lower quadrants	4 (2.2%)	6 (7.6%)
Union of outer quadrants	22 (12%)	0 (0%)
Union of inner quadrants	4 (2.2%)	1 (1.3%)
Subareolar	9 (4.9%)	10 (12.6%)

Table 2 Location of the breast tumor.

Figure 1 Evolution of SSNB performed at our hospital after primary systemic treatment.



TNM stage

According to the TNM clinical staging system, the most frequent T stage in the first group was T2 (151, 82.1%) and all these patients had a clinically and radiologically negative axilla. In the second group, the T3 stage was the most frequent (38 cases, 48.1%) with only 2 cases (2.5%) with a negative axilla (Table 3).

Histological type

The most frequent histological type was the infiltrating ductal carcinoma (Table 4). No significant difference between the study groups was found when the histological grade of the tumor was analyzed (Table 5). The immunohistochemistry characteristics of the tumors are shown in Table 6. The most frequent molecular type in our study was the Luminal B (Table 7).

Table 3 TNM stages and procedures.

Stage	SSNB Pre-C n=184	SSNB Post-C n=79
T1	0 (0%)	4 (5.1%)
T2	151 (82.1%)	28 (35.4%)
T3	29 (15.7%)	38 (48.1%)
T4	4 (2.2%)	9 (11.4%)
NO	184 (100%)	2 (2.5%)
N1	0 (0%)	27 (34.2%)
N2	0 (0%)	50 (63.29%)

Table 4 TNM stages and procedures.

Pathology	SSNB Pre-C n=184	SSNB Post-C n=79
Infiltrating ductal carcinoma	161 (87.5%)	70 (88.6%)
Infiltrating lobular carcinoma	18 (9.8%)	8 (10.1%)
Tubular carcinoma	3 (1.6)	0 (0%)
Papillary carcinoma	2 (1.1%)	0 (0%)
Medullary carcinoma	0 (0%)	1 (1.3%)

Table 5 Tumor histological grades and procedures.

Histologic grade	SSNB Pre-C n=184	SSNB Post-C n=79
GI	64 (34.8%)	16 (20.2%)
G II	74 (40.2%)	37 (46.8%)
G III	46 (25%)	26 (32.9%)

Table 8 Types of response according to the procedure.

Clinical and radiological response due to chemotherapy

Table 8 details the clinical and radiological responses according to chemotherapy. The clinical and radiological response was higher in patients in whom the SSNB was performed after systemic treatment (Group 2); it is to be noted that complete clinical response was obtained in 43 cases (54.4%), complete mammographic response in 25 cases (31.6%) and complete sonographic response in 23 cases (29.1%). Table 9 shows the pathological responses after the oncological surgery.

Pathological complete responses were reached in 32 cases (18.3%) when the SSNB was performed before systemic treatment (Group 1), and in 17 cases (21.5%) when the SSNB was performed after chemotherapy. After systemic treatment, conservative surgical treatment could be done in most of the cases (Table 10).

Table 6 Immunohistochemistry characteristics of the tumors ad	ccording
to the procedure.	

	SSNB Pre-C n=184	SSNB Post-C n=79	
ER < 1%	35 (19.02%)	24 (30.4%)	
ER ≥ 1%	149 (80.9%)	55 (69.6%)	
PR < 20%	62 (33.7%)	27 (34.2%)	
PR ≥ 20%	122 (66.3%)	52 (65.8%)	
Ki67 < 20%	51 (27.7%)	11 (13.9%)	
Ki67 ≥ 20%	133 (72.3%)	68 (86.1%)	
p53 > 50%	73 (39.7%)	33 (41.8%)	
Vascular invasion	22 (12%)	12 (15.2%)	
HER2 +	51 (27.7%)	21 (26.6%)	
ER: estrogen receptor; PR: progesterone receptor.			

Table 7 Molecular types of breast cancer according to the procedure.

Molecular types	SSNB Pre-C n=184	SSNB Post-C n=79
Luminal A	17 (9.2%)	5 (6.3%)
Luminal B	96 (52.1%)	40 (50.6%)
Luminal B HER 2 +	37 (20.1%)	11 (13.9%)
HER 2 +	14 (7.6%)	9 (11.3%)
Basal like	20 (10.8%)	14 (17.7%)

	SSNB Pre-C n=184		SSNB Post-C n=79			
	Clinically	Mammography	Ultrasound	Clinically	Mammography	Ultrasound
Complete response	71 (39.6%)	32 (17.8%)	24 (13.4%)	43 (54.4%)	25 (31.6%)	23 (29.1%)
Response >50%	69 (38.5%)	76 (42.4%)	100 (55 %)	30 (38%)	35 (44.3%)	42 (53.2%)
Response<50%	33(18.4%)	67(37.4%)	51(28.4%)	6(7.6%)	19(24%)	14(17.7%)
Progression	6 (3.3%)	4 (2.2%)	4 (2.2%)			

	SSNB Pre-C n=174	SSNB Post-C n=79
Mean tumoral size	1.8 cm	1.4 cm
Complete response	32 (18.3%)	17 (21.5%)
Pathological response > 50%	95 (54.5%)	34 (43%)
Pathological response < 50%	46 (26.43%)	28 (35.4%)
Progression	1 (0.5%)	0 (0%)

Table 9 Pathological responses after oncological surgery.

Table 10 Types of oncological surgery.

	SSNB Pre-C n=174	SSNB Post-C n=79
Conservative surgery	151 (86.7%)	75 (94.9%)
Mastectomy	23 (13.2%)	4 (5.1%)

Sentinel node

The sentinel node (SN) was identified in 180 patients (97.8%) when SSNB was performed before systemic treatment, and in 55 cases (69.6%) when the procedure was done after chemotherapy. In this second group, in 16 cases the SN was not identified (20.3%) and there were 8 cases (10.1%) of persistent positive axilla. The highest percentage of positive SN was identified in the first group with 92 cases (50%), while in the second, there were 23 cases (41.8%). The mean number of positive SN was not higher than 2, which is important for planning the complementary treatment (Table 11).

Figure 2 shows the evolution of axillary lymphadenectomy performed during the study years. Over the years, 104 axillary lymphadenectomies were performed according to the protocol in force during that time, with a decrease while SSNB rates rose.

The increase in ALs until 2008 was due to the validation period of SSNB procedure after systemic treatment. Six pa-

tients out of 184 who underwent SSNB before chemotherapy did not continue with complementary treatment for the following reasons: alternative medicine, personal decision, death, or surgery in another hospital; in another 4 patients, SN was not identified. Therefore, in 174 patients in total, oncologic surgery was done after hemotherapy.

Table 12 shows that a higher number of ALs was done when the SSNB was performed after chemotherapy (70.9%). In this study we also analyzed the ALs performed during the period of the study, highlighting those performed because the contrast did not migrate to allow location of the SN, and the numbers of nodes affected (Table 13). In the SSNB Pre-C group, 48 ALs were performed (26.15%). The average number of nodes removed was 13.9, with 1.6 positive nodes. After chemotherapy, 56 ALs (70.9%) were performed, including 16 (28.57%) due to non-migration of the contrast.

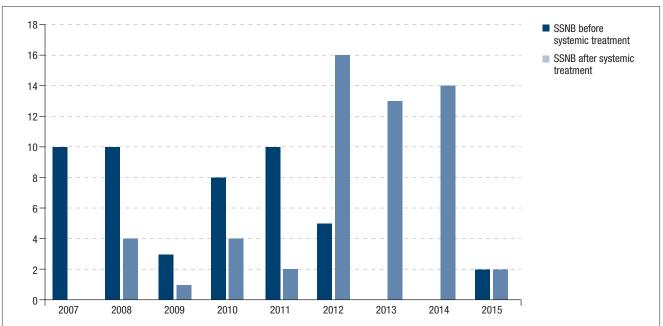
Table 11 Sentinel nodes identified and analysis.

	SSNB Pre-C n=184	SSNB Post-C n=79
SN identification	180 (97.8%)	55 (69.6%)
Negative SN	88 (47.8%)	32 (58.2%)
Positive SN	92 (50%)	23 (41.8%)
Mean positive SN	1.6 (1 – 9)	1.5 (1 – 6)
SN: sentinel node.	1	

Table 12 Axillary lymphadenectomy.

	SSNB Pre-C n=174	SSNB Post-C n=79
AL according to the protocol	48 (27.5%)	40 (50.6%)
AL due to no migration of the SN	88 (47.8%)	32 (58.2%)
AL: Axillary lymphadenectomy.		

Figure 2 Number of axillary lymphadenectomy by year according to the guide protocol.



In this group, the nodes removed during the AL numbered 14.4, the average number of positive nodes being 2.7 both in the ALs indicated by protocol and in those performed due to non-migration of the contrast. After systemic treatment and on-cological surgery, the breast cancer treatment was completed with radiotherapy and hormonal therapy (Table 14).

The local and systemic recurrence rates and survival rates can be observed in Table15.The median follow-up time was between 5 and 10 years depending on the time of diagnosis. The survival rate was 91.3% in the patients with SSNB performed before chemotherapy, with a mortality rate of 8.7%. There was one death not related to breast cancer. In the second group, the survival rate reached the 94.9% with 4 deaths.

Discussion

The initial systemic treatment for women with locally advanced breast cancer, T2 stage or with a positive axilla, is based on chemotherapy ^[7,8]. It is important to note that breast cancer is usually characterized by a long evolution and therefore the preclinical, clinical, and metastatic phases of the disease can last for years or decades. The biological behavior of breast cancer, as developed primarily by Fisher [9], led us to consider the disease as systemic from the very early stages of development. The potential benefits of adjuvant therapies depend on the patient's risk of recurrence, their functional status, and the coexistence of other conditions. At older age, functional capacity decreases, and comorbidity increases. Although the number of elderly patients with breast cancer is increasing, relatively few patients aged 65 years or older are included in clinical trials^[9]. Even so, age is considered a determining factor in the treatment of breast cancer, which differs according to the age of the patient [10]. In addition, there is a huge debate about the nature of breast cancer in elderly patients, and it seems to be less aggressive in this context^[11].

The primary systemic treatment in women with locally advanced breast cancer is based on chemotherapy ^[7,8]. Randomized studies show that the overall survival rate and disease-free rate for neoadjuvant treatment are similar to those recorded for adjuvant chemotherapy ^[7,12].

It should be pointed out that over the period of this study we have modified our way of managing the SSNB. We currently do not perform AL when a SSNB is positive; AL is only performed when there is no migration of the contrast, making it impossible to identify the SN, or when a positive axilla persists despite systemic treatment. This is important for the definition of pathological complete response, as this definition has varied in the literature. It has been extensively shown that the rate of survival in patients treated with sentinel lymph node dissection alone is non-inferior to the overall survival of those treated with axillary lymph node dissection ^[13-15].

In the large series of 11955 patients reported by Cortazar *et al.* ^[16], initially only the breast was assessed to identify the response; subsequently, the axilla was included, in accordance with the concept currently accepted, as it was shown that patients with affected nodes after systemic treatment have a worse prognosis ^[17]. The pathological complete response rate

Table 13 Axillary	lymphadenectomy.	Number	of	nodes	retrieved	and
positive nodes.						

Axillary lymphadenectomy	Number of nodes retrieved Mean ± SD	Positive nodes Mean ± SD
SSNB Pre Cn=48	13.9 ± 7.9	1.6 ± 7.9
SSNB Post CN=40	14.6 ± 5	2.7 ± 4.1
SSNB Post- Cnon-migrating contrast n=16	14.4 ± 4.9	2.7 ± 4
SD: standard deviation		

Table 14 Types of adjuvant treatment.

	Radiotherapy	Hormone therapy
SSNB Pre Cn=174	169 (97.1%)	140 (79.5%)
SSNB Post Cn=79	79 (100%)	56 (79%)

Table 15 Recurrence and survival rates.

	SSNB Pre Cn=174	SSNB Post Cn=79
No recurrences	152 (87.3%)	69 (87.3%)
Local recurrence	4 (2.29%)	2 (2.5%)
Axillary recurrence	0 (0%)	0 (0%)
Contralateral breast cancer	1 (0.57%)	1 (1.3%)
Systemic recurrence	20 (11.4%)	10 (12.6%)
Survival	168 (91.3%)	75 (94.9%)

differs in the literature, being dependent not only on different tumors and patient cohorts, but also on the different types of chemotherapy, doses, cycles, and target therapies, such as the different anti-Her 2 drugs and hormone treatments. Published complete pathological response rates range from 8% (Alvarado-Cabrero et al.) [18] to 51% (Mittendorf et al.) [19] in Her 2+ patients. Our Breast Pathology Department works with two general hospitals, where our patients receive chemotherapy treatment. We obtained a complete pathological response rate of 18.3% in patients who underwent SSNB before chemotherapy, and 21.5% in those who underwent SSNB after systemic treatment. To evaluate the response, we used the RECIST and WHO criteria; however, we currently evaluate the response with the Miller and Payne criteria. In our center we proceeded with a high percentage of conservative surgeries: 94.9% in the SSNB Post-C group, and 86.7% in the SSNB Pre-C group. Conservative surgery has been associated with lower morbidity, better cosmetic results, and better body image. It is known that conservation of the breast does not depend solely on the tumor size, but also on the tumor size in relation to the size of the breast. We consider our breast conservative surgery rates to be highly satisfactory if compared with those recorded in other centers and series treated with chemotherapy [11].

In a North American study, which included 770 patients from eight National Cancer Institutes, the conservative surgery rate was 45% ^[11]. In our SSNB Pre-C group, we identified the

axillary SN in 97.8% of the cases, finding a positive SN in 50% of them (92), with an average of 1.6 positive SNs. Of the 174 cases that continued through to complete treatment, AL was performed in 48 cases (27.5%). Lymphadenectomy was not performed if micrometastases were identified due to a protocol change; it was done if the SN was positive. The protocol was subsequently updated, so that if the SN is positive, and after the systemic treatment the axilla becomes negative, AL is not performed, but the treatment of the axilla is complemented with radiotherapy. In the AL procedures performed in the SSNB Pre-C group, an average of 13.9 nodes was obtained with an average of 1.6 nodes found to be affected, as in the post-chemotherapy group. In the patients who were candidates for post-chemotherapy SNNB, we identified axillary SNs in 55 cases (69.6%), and failed to identify it in 16 (20.3%). These results coincide with those of other publications in which the positive axillary status at diagnosis decreases the ability to identify the SN by biopsy [20,21]. There was persistence of a positive axilla in 8 cases (10.1%).

The SN was negative in 32 cases (58.1%) and positive in 23 with an average positive node rate of 1.5. These data correspond to those published previously, where there is a higher SN detection rate in pre-chemotherapy SSNB with respect to post-chemotherapy SSNB, and there is a higher rate of positive SN in pre-chemotherapy SSNB. Out of the 79 patients who were candidates for post-chemotherapy SSNB, AL was performed in 56 cases, in 40 cases (50.6%) due to post-chemotherapy positive sentinel node, and in 16 (20.3%) due to non-migration of the contrast to identify the sentinel node.

The average number of nodes removed was 14.6 and 14.4 respectively. The mean number of positive nodes was 2.7, so we propose not to perform AL after a positive SN identified after chemotherapy since the mean of positive nodes is the same, with never more than three axillary nodes found to be affected.

Conclusions

Identification of the SN is safe before and after systemic treatment. Performing fewer axillary lymphadenectomies does not lead to an increase in local or systemic recurrences. Conservative surgical treatment of the breast and axilla has good outcomes in stage ll-III cases. A low rate of recurrence was detected locally and systemically. 25% of axillary lymphadenectomies performed due to non-migration of the contrast had more than three affected nodes. These results were obtained by applying a multidisciplinary diagnostic and therapeutic strategy.

References

- Redden MH, Furhman GM. Neoadjuvant chemotherapy in the treatment of breast cancer. Surg Clin North Am. 2013;93:493-9.
- Untch M, Konecny GE, Paepke S, von Minckwitz G. Current and future role of neoadjuvant therapy for breast cancer. Breast. 2014;23;526-37.
- Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EO-RTC 10981-22023 AMAROS): a randomised, multicentre, open-la-

bel, phase 3 non-inferiority trial. Lancet Oncol. 2014;15:1003-10.

 Benson JR, Jatoi I. Sentinel lymph node biopsy and neoadjuvant chemotherapy in breast cancer patients. Future Oncol. 2014;10:577-86.

- Mamounas EP. Timing of determining axillary lymph node status when neoadjuvant chemotherapy is used. Curr Oncol Rep. 2014;16:364.
- Giuliano AE, Morrow M, Duggal S, Julian TB. Should ACOSOG Z0011 change practice with respect to axillary lymph node dissection for a positive sentinel lymph node biopsy in breast cancer? Clin Exp Metastasis. 2012;29:687-92.
- Wolmark N, Wang J, Mamounas E, Bryant J, Fisher B. Preoperative chemotherapy in patients with operable breast cancer: nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. J Natl Cancer Inst Monogr. 2001:96-102.
- Bear HD, Andersen S, Smith RE, et al. Sequential preoperative or postoperative docetaxel added to preoperative doxorubicin plus cyclophosphamide for operable breast cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol 2006;24:2019-27.
- Goodwin JS, Hunt WC, Humble CG, Key CR, Samet JM. Cancer treatment protocols. Who gets chosen? Arch Intern Med.1998;148:2258-60.
- Kimmick G, Muss HB. Breast cancer in older patients. Semin Oncol. 2004;31:234-48.
- Mc Guire KP, Hwang S, Cantor A, et al. Surgical patterns of care in patients with invasive breast cancer treated with neoadjuvant systemic therapy and breast magnetic resonance imaging: results of a secondary analysis of TBCRC 017. Ann Surg Oncol 2015,22:75-81.
- Fisher B, Bryant J, Wolmark N, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol. 1998;16:2672-85.
- Veronesi P, Corso G. Standard and controversies in sentinel node in breast cancer patients. Breast. 2019;48 Suppl 1:S53-S56.
- Giuliano AE, Ballman KV, McCall L, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: The ACOSOG Z0011 (Alliance) randomized clinical trial. JAMA. 2017;318:918-26.
- Galimberti V, Cole BF, Zurrida S, et al; International Breast Cancer Study Group Trial 23-01 investigators. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. 2013;14:297-305.
- Cortazar P, Zahng L, Untch M, et al. Pathological complete response and long- term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384:164-72.
- Penault-Llorca F, Abrial C, Raoelfils I, et al. Comparison of the prognostic significance of Chevallier and Sataloff's pathologic classifications after neoadjuvant chemotherapy of operable breast cancer. Hum Pathol. 2008;39:1221-8.
- Alvarado-Cabrero I, Alderete-Vázquez G, Quintal-Ramírez M, Patiño M, Ruíz E. Incidence of pathologic complete response in women treated with preoperative chemotherapy for locally advanced breast cancer: correlation of histology, hormone receptor status, Her2/Neu, and gross pathologic findings. Ann Diagn Pathol. 2009;13:151-7.
- Mittendorf EA, Wu Y, Scaltriti M, et al. Loss of HER2 amplification following trastuzumab-based neoadjuvant systemic therapy and survival outcomes. Clin Cancer Res. 2009;15:7381-8.
- Classe JM, Bordes V, Campion L, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy for advanced breast cancer: results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French prospective multicentric study. J Clin Oncol. 2009;27:726-32.
- Buch E, Diaz S, Tajuerce M, et al. Biopsia selectiva del ganglio centinela posneoadyuvancia como herramienta en la valoración de la axila. Rev Senol Patol Mamar. 2014;27:170-5.

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