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Breast cancer sentinel lymph node biopsy efficacy after neoadjuvant chemotherapy as an axillary staging predictor.

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Abstract

Introduction: Selective sentinel lymph node biopsy (SLNB) in breast cancer is the standard method for axillary staging in patients with clinically negative axilla. Studies indicate avoiding axillary lymphadenectomy in patients with negative SLNB, including those who previously received neoadjuvant chemotherapy (NQT). This study aims to determine the efficacy of SLNB in detecting sentinel lymph nodes after QTN in a reference cancer institute in Ecuador.

Materials and Methods: An observational, analytical, and retrospective study was conducted at Hospital SOLCA Guayaquil from January 2015 to December 2020. Eighty-one clinically negative axillary breast cancer patients who received CTN before surgery were evaluated. The variables are sentinel node biopsy, neoadjuvant chemotherapy, diagnostic accuracy, and axillary staging. An odds ratio of 95% was considered, with P <0.05.

Results: Of 81 operated patients, 52 received SLNB, with sampling detecting sentinel nodes in 92.3% of the cases. The percentage of false negatives is 21.7% after QTN. The remaining 29 patients received axillary lymphadenectomy.

Conclusion: SLNB effectively detects the sentinel node in patients with clinically negative breast and axillary cancer, even after neoadjuvant chemotherapy. However, there is a significant risk of false negatives after CTN, which may lead to the need to perform additional axillary lymphadenectomy for a more accurate assessment of axillary staging.

Keywords:
MeSH: Biopsy, Breast Neoplasms, Ganglia, General Surgery, Lymph Node Excision, Neoadjuvant Therapy, Observational Study, Odds Ratio, Patients, Sampling Studies, Sentinel Lymph Node.

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Introduction

Selective sentinel node biopsy (SLNB) is the standard method used to assess the presence of axillary lymph node metastases in patients with breast cancer who do not have clinical evidence of axillary involvement [1]. This surgery aims to control neoplastic spread in the lymph

nodes and provide valuable information to guide systemic treatment and radiotherapy. According to the international consensus in St. Gallen, avoiding axillary dissection in patients with negative results on SLNB is recommended, except in specific cases of micrometastases or isolated tumor cells in the sentinel nodes [1].

The NSABP and ACO-SOG Z0011 studies support using SLNB as the reference method for nodal staging in the early stages of breast cancer. They even suggest that axillary lymphadenectomy can be avoided in patients with lymph node involvement limited to one or two nodes as long as breast-conserving surgery is performed and radiation therapy is administered [2]. However, doubts arise about the usefulness of SLNB in cases of locally advanced disease or after receiving neoadjuvant chemotherapy (NQT). It has been observed that SLNB following CTN can lead to tumor regression in the axillary lymph nodes in a significant percentage of patients [3].

Previous research has shown that disease-free and overall survival in patients undergoing SLNB is comparable to or even superior to those undergoing axillary lymphadenectomy [4]. These findings support the idea that SLNB may be a safe and effective option for nodal staging in breast cancer, thus avoiding the risks and complications associated with axillary lymphadenectomy [2].

A prospective study in a group of patients who received CTN followed by SLNB and axillary dissection reported a false negative rate exceeding 10% [2], while Chirappapha et al., in their trial, obtained a percentage of identification of the sentinel node of 95% [5]. An analytical study presented by the MD Anderson Cancer Center of Texas revealed a 25% false negative rate and a 92.8% positive sentinel node identification rate in patients with FNA-confirmed axillary metastases who received QTN and SLNB [1].

The axillary status is vital in local breast cancer treatment, systemic therapy, and radiotherapy planning. QTN has acquired an essential role in managing breast cancer, both in locally advanced disease and early stages [5], demonstrating that QTN can achieve a complete pathological response in the breast and axilla, a predictor of overall and disease-free survival. Given the above, there is uncertainty about how SLNB influences the progression of breast cancer and the survival of patients, given the diagnostic accuracy of this procedure [6].

The present work aims to determine the efficacy of SLNB as a diagnostic test after neoadjuvant chemotherapy, analyzing its accuracy in a group of patients with breast cancer at the Solca Guayaquil Oncology Institute. The sentinel node identification index in these patients and the percentage of false negatives were evaluated to present additional evidence of this technique's usefulness in QTN cases.

Materials and methods

Study design

This is a retrospective, observational, analytical, and longitudinal study.

Scenery

The study was carried out in the mastology service of the National Oncology Institute "Dr. Juan Tanca Marengo" - Solca Guayaquil. The study period covers January 2015 to December 2020.

Participants

Eighty-one female patients diagnosed with a malignant breast tumor who received neoadjuvant chemotherapy with clinically negative axilla were included. Group A comprised 52 patients who underwent surgery with selective sentinel node biopsy with lymph node sampling. In comparison, group B comprised 29 patients who received axillary lymphadenectomy. Patients with surgically unresectable breast cancer, cT4, distant metastases, cancer in another organ, inflammatory breast cancer, and incomplete neoadjuvant chemotherapy treatment were excluded.

Variables
The variables are sentinel node biopsy, neoadjuvant chemotherapy, diagnostic accuracy, and axillary staging.

Data sources/measurement
The source was indirect, and the Intranet system clinical record was used for each variable. The data of each patient were compiled, and the instrument used for this purpose was a form filled out by the authors with the information from the medical records. Data collection and provision had the prior approval of the Department of Teaching and Research of the National Oncological Institute Dr. Juan Tanca Marengo - ION Solca Guayaquil.

Avoidance of bias
Patients with inconsistent or incomplete medical records were excluded.

Study size
The present study has a nonprobabilistic sample; all potential cases were used according to the inclusion criteria.

Statistical methods
The tabulation of data obtained, analysis, and preparation of tables and graphs were carried out with the help of the Microsoft Excel 2020 (v16.42) program and SPSS Statistics v28.0.1.0 (142). Descriptive statistical analysis was performed using frequencies and percentages for qualitative variables, measures of central tendency with minimum and maximum ranges for quantitative variables, and the standard deviation and the interquartile range depending on the distribution of the variables studied. The chi-square or Fisher's exact test was used to compare categorical variables. The preparation of contingency tables allowed the calculation of the sentinel node's identification rate and false negatives, global precision, sensitivity, and specificity. The survival analysis used the Kaplan–Meier method and the log rank test to determine the curve difference. The 95% confidence interval, with P <0.05, was considered to determine statistical significance.

Results
Eighty-one patients with clinically negative axillary breast cancer after neoadjuvant chemotherapy were analyzed (Figure 1).

Clinical characterization
Initially, 28 patients had clinically positive axilla, which became clinically negative after QTN. The remaining 53 patients had clinically negative axilla throughout the process. The sample was divided into two groups. Group A, comprising 52 patients, received SLNB with lymph node sampling, and group B, comprising 29 patients, underwent axillary lymphadenectomy. The mean age was 58 years ± 11.2 (95% CI 55.4-60.4), with an age range between 30 and 88 years, representing 98.8% of women older than 35. The median preoperative tumor size was 4 cm ± 1.3 (95% CI 3.8-4.4). The most frequent histopathological diagnosis was invasive ductal carcinoma (65.3%), followed by lobular (19.8%), mixed (2.5%), and mucinous (2.5%) carcinoma. Regarding the molecular subtypes of breast cancer, 16% of the tumors were of the luminal A subtype, 38.3% were light B, 32.1% were Her2 positive, and 13.6% were triple negative (Table 1).

In group A, the histopathological study of lymph nodes after surgery showed that at least one sentinel node could be dissected in 48 of the 52 cases, obtaining an identification percentage of 92.3%. The radioisotope did not migrate from the breast to the node in the four unidentified cases. Twelve of 52 patients were sentinel and nodal sampling positive (true positive 23.1%), while 29 of 52 were sentinel and nodal sampling negative (true negative 55.8%);

5 of 52 patients were sentinel-negative, and at least one lymph node was positive in the sampling (9.6% false negatives), while 6 of 52 (11.5%) positive sentinel cases were negative in the sample (false positives).

Figure 1. Classification flowchart of participating cases.

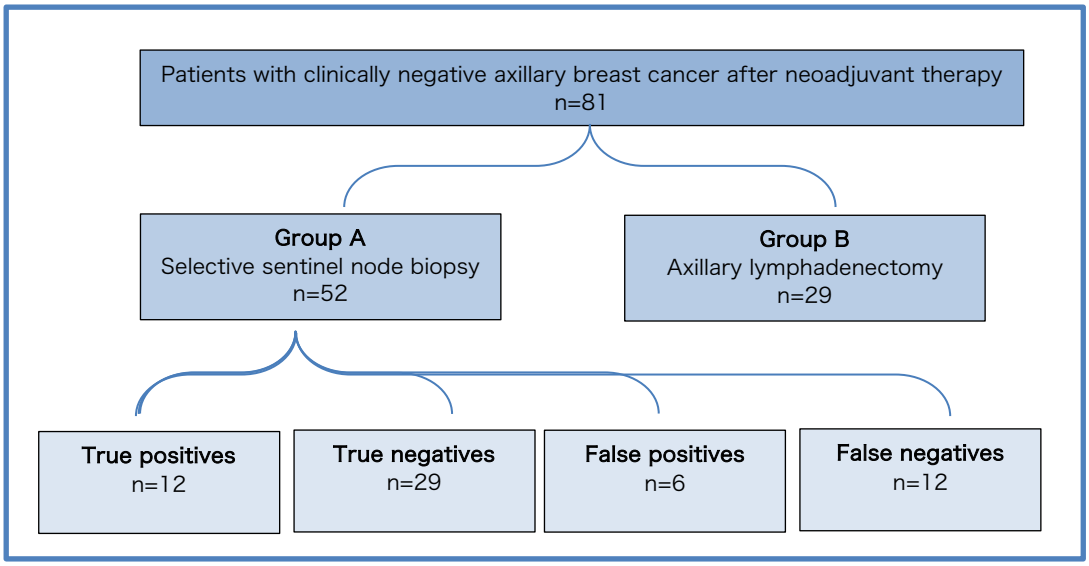

Table 1. Clinical characterization of the patients.

Characteristic	no	%	*P*
Clinical stage of previous QTN axilla			
Positive armpit	28	34.6%	
Negative armpit	53	65.4%	
Procedure applied in armpit			
BSGC	52	64.2%	
Axillary lymphadenectomy	29	35.8%	
Age			
<35 years	1	1.2%	
>35 years	80	98.8%	
Tumor size			
Less than 5 cm	54	66.7%	0.2
Greater than 5 cm	27	33.3%	
Histopathological diagnosis			
Ductal	61	75.3%	<0.001
Lobular	16	19.8%	
Mixed	2	2.5%	
Mucinous	2	2.5%	
Molecular Subtype			
Light A	13	16%	0.003
Light B	31	38.3%	
HER2 positive	26	32.1%	
Triple negative	11	13.6%	

Table 2. Pathologic status of sentinel nodes and nodal sampling (axillary staging).

Selective Sentinel Lymph Node Biopsy	Lymph node sampling		Total n=52
	Positive n=17	Negative n=35	
Positive	12 (VP)	6 (FP)	18
Negative	5 (FN)	29 (VN)	3. 4

*VP: True Positive, FP: False Positive; FN: False Negative, VN: True Negative. Percentage of false negatives: FN/(VP+FN) = 5/(18+5) = 21.7%.

The percentage of false negatives was 21.7% (95% CI 5.5 – 31.8), *P* = 0.001. The overall accuracy rate of the sentinel node was 90%, the sensitivity was 70.6% (95% CI 44 – 88.6), and the specificity was 82.9% (95% CI 65.7 – 92.8) (Table 2).

Discussion

In the present study of a total of 52 patients who received SLNB after neoadjuvant chemotherapy, a sentinel node identification percentage of 92.3% was found, similar to that reported in other studies, such as that of Damin et al. [7] and the SENTINA clinical trial [8], with detection rates of 93.2% and 90%, respectively. Several traditional techniques can be unique or combined depending on the surgeon's decision and the resources available in the institution.

In the patients who received SLNB, double labeling with a Technetium-99 m detector gamma probe and echo-guided labeling in the skin of the lymph node using charcoal were used in this study. It should be noted that in the present study, only cases after CTN were evaluated, unlike SENTINA. This prospective multicenter study assigned 1,737 patients into four arms, where two groups of patients with clinically negative axillae who underwent SLNB were analyzed. [8], the first group before the QTN and the second after the QTN. It is meritorious to indicate that this is not a habitual practice of our institution.

The meta-analysis by Cui et al. indicated that using double labeling, identification percentages between 70% and 100% were obtained, and in the specific case of radioisotope use, 89% was obtained [9]. The data revealed by these studies are similar to those obtained at our institution, Hospital Solca Guayaquil.

Regarding false negatives, the present investigation obtained a false negative rate of 21.7% after neoadjuvant chemotherapy (QTN) (sensitivity 70.6% and specificity 82.9%). These data differ from what was reported in SENTINA [8]; after QTN, the percentage of false negatives was 14.2% in the axillary regression group.

In other clinical trials (ACOSOG-Z1071, SN-FNAC) [10, 11], they evaluated the efficacy of the sentinel node in a group of patients with initially positive axillae with complete response to QTN, where the overall percentages of false negatives were 12.6% to 14.2% [12], which was higher than the percentage of 10% considered safe [2]. These results are explained by the presence of patients who had clinically positive axilla before CTN. Among the measures that can be chosen to reduce the percentage of false negatives is double marking [6] and lymph node sampling of at least three lymph nodes. The rate of false negatives will vary according to the response of the disease to CTN, and the challenge lies in accurately selecting patients with negative SLNB after CTN whose disease has a lower risk of progressing to nonsentinel node metastasis [13].

Limitations of this research paper include the retrospective design and the inherent restrictions accompanying such studies. Inconsistencies in medical records reduced the total study population, which could affect the final data set. The similarity of results in the number of patients with negative axilla before QTN compared with the number of patients who received SLNB is a mere coincidence, in the same way as the number of cases of positive axilla with the number of patients who underwent lymphadenectomy. For the present study, only the diagnostic accuracy of sentinel node biopsy in patients with clinically negative axilla after neoadjuvant chemotherapy was evaluated in a general way. The relationship between false

positives and patients who initially had a clinically positive axilla before QTN was not analyzed. This will be the subject of study in a future investigation.

Conclusions

The status of the axillary nodes is an important prognostic factor to guide the locoregional and systemic treatment of breast cancer. Sentinel node detection after CTN remains controversial for predicting axillary status. The study found that SLNB is an effective method for detecting sentinel nodes in patients with clinically negative breast and axillary cancer, even after neoadjuvant chemotherapy. However, there is a significant risk of false negatives after CTN, which may lead to the need to perform additional axillary lymphadenectomy for a more accurate assessment of axillary staging. Selective sentinel node biopsy after neoadjuvant chemotherapy can be adequate if methods that increase the percentage of sentinel node identification and reduce the probability of false negatives are used for its detection, such as the identification and marking of positive pre-CTN nodes, the double tracer technique, and dissection of at least three axillary nodes.

Abbreviations

SLNB: selective sentinel lymph node biopsy
QTN: neoadjuvant chemotherapy

Administrative information

Additional Files

None declared by the authors.

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Does not apply.

Author contributions

Carlos Humberto Malatay González: Conceptualization, formal analysis, supervision, project administration.
Cinthya Abigail Apolo Carrión: Conceptualization, research, methodology, writing of the original draft.
Felix Josué Carofilis Gallo: Conceptualization, research, visualization, writing, revision, and final edition.
María Elena Zamora Villavicencio: Visualization, supervision, validation.
All the authors have read and approved the final version of the manuscript.

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Availability of data and materials

Data are available upon request to the corresponding author.

Statements

Ethics committee approval

No studies of databases or medical records are needed.

Consent for publication

It is not required when images, resonances, or tomographic studies of specific patients are not published.

Conflicts of interest

None.

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