ORIGINAL ARTICLE
https://doi.org/10.29289/2594539420220018

Breast cancer and clinically negative status after neoadjuvant chemotherapy

Victor de Alencar Moura[1], Arthur Villarim Neto[1], Juliana Lopes de Aguiar Araújo[1], Kleyton Santos de Medeiros[1,2], Diana Taissa Sampaio Marinho Navarro[1]*

ABSTRACT

Introduction: Axillary dissection is increasingly less indicated for axillary evaluation of patients with breast cancer and clinically negative axilla. This study evaluated the application of sentinel lymph node in patients with clinical axillary remission after neoadjuvant chemotherapy. **Methods:** Prospective study carried out from December 2017 to July 2018, at the Liga Norte Riograndense Contra o Cancer. We considered 24 patients who had a positive axilla and after neoadjuvant chemotherapy had clinical axillary remission (ypN0). Only patients with a strongly positive status during physical examination were included, and biopsy and ultrasound examinations were not required to confirm axillary disease. The dual-tracer technique of sentinel lymph node biopsy followed by axillary dissection was used. **Results:** The accuracy of the sentinel lymph node in patients with clinical axillary remission was 91.7%, with a false negative rate of 13.3% (2/24). It was observed that 66.6% of patients were stage I after chemotherapy and 13 patients with negative sentinel lymph node biopsy no longer had axillary disease. During the sentinel lymph node biopsy procedure, 16 patients (79.1%) had only 1 sentinel lymph node removed. **Conclusions:** For patients with clinical axillary remission after neoadjuvant chemotherapy, sentinel lymph node biopsy has been included in clinical practice, reducing the indications for axillary dissection and, consequently, its morbidity. The dual-agent mapping technique of sentinel lymph node biopsy and a sample of 3 lymph nodes at surgery decrease false-negative rates and make the procedure safer.

KEYWORDS: breast cancer; sentinel lymph node biopsy; neoadjuvant therapy; lymphadenectomy.

INTRODUCTION

Breast cancer is the type of cancer that most affects women in the world[1,2]. According to Brazil's National Cancer Institute (Inca), it is estimated that 66,280 cases will be diagnosed in Brazil for each year of the 2020–2022 triennium, with an estimated risk of 61.61 cases per 100,000 women[2].

The evaluation of axillary involvement in patients with breast cancer is one of the essential prognostic factors for decision-making for additional adjuvant therapy[1]. Axillary dissection (AD) was the only one that safely identified patients with regional metastases, provided regional control and reduced the risk of axillary recurrence. According to Li et al.[3], the procedure is performed in approximately 36% of women diagnosed with breast cancer. It is noteworthy that this surgery leads to significant morbidity, including: postoperative pain, seroma, lymphedema, paresthesia, infection, decreased range of motion of the arm and pain due to injury to the intercostal and intercostobrachial nerves[3-6]. Giuliano et al.[4] report that AD used to control the disease has become, because of the various complications, an acceptable practice only when there is lymph node involvement[7-9].

Sentinel lymph node biopsy (SLNB) was introduced to diagnose breast cancer in the early 1990s as a method of assessing axillary status[3]. Veronesi et al.[7] started a randomized study at the European Institute of Oncology, which established the SLNB method in clinical practice[7,8]. In 2003, these researchers demonstrated, for the first time, that the results in terms of overall survival and being free of local and distant recurrences with SLNB are similar to those of AD in patients with tumors smaller than 2 cm and clinically negative axilla[9].

Currently, SLNB is considered the standard procedure for pathologically staging patients with clinically negative axilla[10]. According to Madison Collins et al.[11], this procedure involves

[1]Liga Contra o Câncer – Natal (RN), Brazil.
[2]Instituto de Ensino, Pesquisa e Inovação – Natal (RN), Brazil.
***Corresponding author:** dianataissa@msn.com
Conflict of interests: nothing to declare. Funding: none.
Received on: 06/02/2022. **Accepted on:** 10/18/2022.

locating the most likely lymph nodes to demonstrate axillary metastatic disease by injecting a radioactive colloid and/or blue dye into the breast. Such lymph nodes are detected and resected for intraoperative anatomopathological analysis.

Neoadjuvant chemotherapy is offered to patients with locally advanced disease to reduce tumor staging or its size, aiming to reduce the extent of surgery, which is necessary, especially in patients who obtained complete clinical and radiological responses[12,13].

According to Frasson et al.[14], the use of neoadjuvant chemotherapy in the last decade made it possible to expand the indication for conservative surgery, in addition to raising questions about the ideal local therapy for the axilla. With the current neoadjuvant chemotherapy regimens, an increase in the rates of pathological complete response in breast and axillary remission (yN0) was observed, which led to the study of SLNB in patients who had a clinically positive axilla. When axillary lymph nodes are negative before neoadjuvant chemotherapy, SLNB is recommended, in line with all international guidelines[15-17].

Prospective multi-institutional studies, such as SENTINA[15], ACOSOG Z1071[16] and SN FNAC[17], evaluated the accuracy of SLNB in patients with clinically positive axilla who received neoadjuvant chemotherapy. SENTINA[15] had a false-negative (FN) rate of 14.2%, while ACOSOG Z1071[16] had a 12.6% rate.

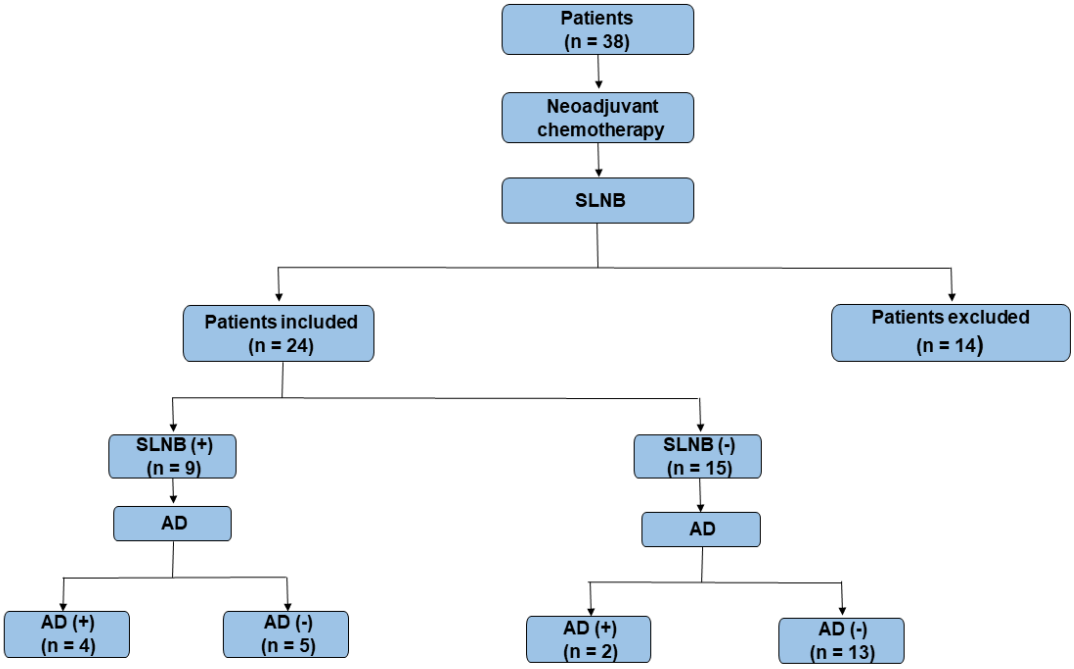
In Brazil, at the time of study recruitment, some services recommended AD for women with a clinically positive axilla prior to neoadjuvant chemotherapy, regardless of axillary response. Knowing that clinical examination of the axilla has a high margin of false-positive results and is insufficient to justify axillary lymphadenectomy, we evaluated the change in axillary status of patients with clinically positive axilla undergoing neoadjuvant chemotherapy (cN1-2) to negative (ycN0), through SLNB followed by AD.

Thus, the study aimed to evaluate the accuracy of SLNB and FN rate in patients undergoing neoadjuvant chemotherapy and axillary clinical remission.

METHODS

A prospective observational study was carried out at the Mastology Service of Liga Norte Riograndense contra o Câncer (Natal, Brazil) from December 2017 to July 2018.

Twenty-four women, all newly diagnosed with clinically positive breast and axillary cancer undergoing neoadjuvant chemotherapy, who showed clinical axillary remission (ypN0), were included in the study by our research group and followed up. Patients with inflammatory breast cancer (T4d) and those in whom there was no sentinel lymph node migration and labeling by 99m technetium (99mTc) and patent blue (n=14) were excluded because of the risk of lymphatic obstruction due to neoplastic involvement. Double-labeling of SLNB was used with the periareolar injection of 2 mL of patent blue and the injection of 0.4 mL of the radioactive drug combined with a colloid (phytate-99mTc) with an activity of 300 microcurie in each injection. Figure 1 schematically shows the distribution of patients according to the study criteria.



SLNB: Sentinel lymph node biopsy; AD: Axillary dissection.

Figure 1. Distribution of patients according to Sentinel lymph node biopsy and Axillary dissection results.

All participants provided written informed consent and completed questionnaires prior to the procedure. The study was approved by the LNRCC Human Research Ethics Committee (CAAE: 80296917.4.000.5293; Approval No.: 2.416.417) and conducted following ethical principles, considering the guidelines of the National Research Council of Brazil, which regulate studies in humans.

Data were obtained through interviews with patients and review of their medical history. Sociodemographic characteristics, in addition to age, personal history, previous breast surgery, location and size of the tumor, clinical staging, immunohistochemistry, molecular subtype, type of surgery after neoadjuvant chemotherapy and data from the anatomopathological examination were studied.

Categorical variables were represented as absolute and relative frequencies and the accuracy, sensitivity, specificity, positive predictive value and negative predictive value of the SLNB for axillary content were calculated. Fisher's exact test was used to assess the association of SLNB results with sociodemographic and clinical variables. SPSS 24 for Windows (Statistical Package for Social Sciences; IBM, USA) was used for data analysis.

RESULTS

The axillary content of 38 patients was evaluated and, meeting the inclusion criteria, 24 of them with breast cancer and clinically positive axilla underwent neoadjuvant chemotherapy with axillary clinical remission (ypN0). Table 1 shows the distribution of patients in terms of SLNB and AD results.

Figure 1 considers three age distribution ranges, where there were 16 patients between 30 and 60 years old (66.7% of

Table 1. Distribution of cases and association test according to Sentinel lymph node biopsy results.

	n	%	SLNB (-)		SLNB (+)		Significance (p-value)
			n	%	n	%	
Age (years)							
<30	1	4.2	1	100.0	0	0.0	0.71
≥30 and ≤60	16	66.7	10	62.5	6	37.5	
>60	7	29.2	4	57.1	3	42.9	
Prior breast							
Yes	2	8.3	0	0.0	2	100.0	0.13
No	22	91.7	15	68.2	7	31.8	
Breast							
Right	12	50.0	7	58.3	5	41.7	0.67
Left	12	50.0	8	66.7	4	33.3	
Surgery							
Mastectomy	11	45.8	5	45.5	6	54.5	0.13
Quadrantectomy	13	54.2	10	76.9	3	23.1	
Tumor size (cm)							
≤2.0	17	70.8	13	76.5	4	23.5	**0.05**
>2.0 and ≤5.0	5	20.8	2	40.0	3	60.0	
>5.0	2	8.3	0	0.0	2	100.0	
Histological grade							
HG I	1	4.2		0.0	1	100.0	0.41
HG II	12	50.0	8	66.7	4	33.3	
HG III	11	45.8	7	63.6	4	36.4	
Nuclear grade							
NG 1	0	0.0	0	0.0	0	0.0	0.53
NG 2	3	12.5	1	33.3	2	66.7	
NG 3	21	87.5	14	66.7	7	33.3	
ALI							
Yes	5	20.8	1	20.0	4	80.0	**0.04**
No	19	79.2	14	73.7	5	26.3	

Source: Liga Norte Riograndense Contra o Câncer.
SLB: Sentinel lymph node biopsy; HG: histological grade; NG: nuclear grade; ALI: Angiolymphatic invasion

the cases), with only one patient under 30 (4.2%). The second largest contribution was from the group over 60 years old, with seven cases (29.2%). It was observed that all patients did not have previous breast cancer and 67% of them had no family history of the disease.

As for previous breast surgery (Table 1), 22 patients (91.7%) had not undergone the procedure. The tumor was equally located between the right and left breast, with a predominant location (54.2% of cases) in the upper lateral quadrant.

With regard to initial clinical staging, tumor size results were divided into four categories: ≤2.0 cm, >2.0 cm and ≤5.0 cm, >5.0 cm, and tumors with skin invasion. Nodules >2.0 cm and ≤5.0 cm were observed in 16 patients (67%), tumors larger than 5.0 cm in another five (21%) and skin invasion in three (12%). With regard to clinical axillary involvement, 19 (79.1%) had a positive axilla (N1), and axillary lymph node cluster (N2) was recorded in five. Based on this information, these patients were initially evaluated for stage II (58.0%) and stage III (42.0%).

As for molecular subtype, the following distribution of patients was observed: two luminal A (8.3%), 10 luminal B (41.6%), two luminal hybrid (8.3%), six triple-negative (25.0%) and four HER2 (16.6%).

At the end of neoadjuvant chemotherapy, of the 24 patients, 11 (45.8%) underwent mastectomy and 13 underwent conservative surgery (54.2%).

In 70.8% of patients, the tumors were ≤2.0 cm and in 20.8%, they were >2.0 cm and ≤5.0 cm, while and only 8.3% had tumors >5.0 cm. With regard to anatomical staging, the following distribution of patients was obtained: 16 in stage I (66.6%), five in stage II (20.8%) and three in stage III (12.5%), showing a decrease in anatomical staging in most patients.

As observed in the anatomopathological examination, one patient had histological grade (HG) I (4.2%), 12 HG II (50%) and 11 HG III (45.8%). Considering nuclear grade (NG), three patients showed NG 2 (12.5%) and 21, NG 3 (87.5%).

Angiolymphatic invasion (ALI), in turn, was detected in five patients (20.8%), of which four had SLNB with a positive result, while in 19 there was a negative ALI (79.2%), and in 14 of them, SLNB resulted negative.

Table 1 presents the exploratory data analysis and Fisher exact test, which was used to profile the patients and determine the association of the SLNB result (positive or negative) with some variables. Regarding the 95% confidence level, there was evidence of an association between the SLNB result and the ALI variables and tumor size (cm) ($p \leq 0.05$).

During the surgical procedure of women treated with neoadjuvant chemotherapy, from 16 of them (79.1%), a sentinel lymph node was removed; out of five, two (20.8%) were extracted and from only three (12.5%), three or more lymph nodes were extracted. With SLNB, it was found that nine patients (37.5%) had positive SLNB, and after AD, four (44.4%) still had lymph node involvement. Of those who had a negative SLNB (62.5%), 13 (86.6%) did not really have lymph node involvement after AD. On the other hand, considering non-sentinel lymph nodes, two patients had negative SLNB and lymph node involvement in AD.

Table 2 shows the results of the accuracy test, in which the SLNB test showed 91.7% accuracy, 81.8% sensitivity and 100.0% specificity. These results are graphically presented in Figure 2. It can be seen in Table 2 that the SLNB showed 91.7% accuracy, indicating the percentage of patients classified correctly in both examinations, that is, it represents those who had a positive diagnosis in the SLNB and in the AD, and negative in both examinations. Sensitivity indicates that 81.8% (9/11) of patients were SLNB positive, and the final diagnosis confirmed this finding.

Considering the necessary AD for all patients with the first positive diagnosis, the positive predictive value was 100%, and consequently, the false-positive rate was equal to zero. On the other hand, a negative predictive value and FN rate of 86.7 and 13.3%, respectively, were observed. Therefore, it appears that, out of every 100 negative tests, this result is confirmed in 86.7, as shown in Figure 3.

Table 2. Accuracy test.

Test	%
Accuracy	91.7
Sensitivity	81.8
Specificity	100.0
Positive predictive value	100.0
Negative predictive value	86.7
False-negative	13.3

Source: Liga Norte Riograndense Contra o Câncer.

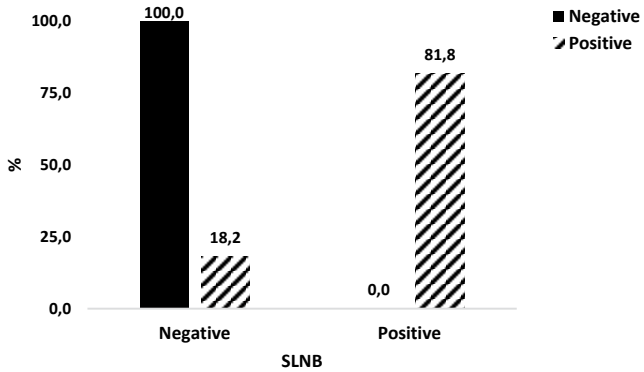


Figure 2. Distribution of patients according to Sentinel lymph node biopsy results.

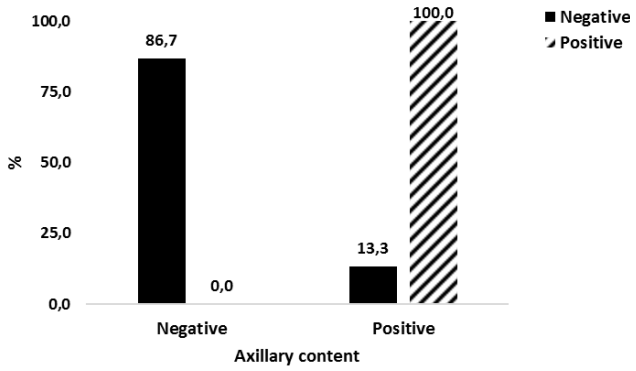


Figure 3. Distribution according to axillary dissection results.

DISCUSSION

In the treatment of local and systemic breast cancer, accurate staging and proper management of the axilla are important for successful treatment. Sentinel lymph node biopsy is the standard procedure for axillary evaluation in patients with clinically negative axilla. According to Boughey et al.[16], axillary ultrasonography with percutaneous biopsy was initially used to determine staging and guide the surgical procedure, leading patients to lymphadenectomy in cases with biopsy-proven nodal metastasis. Lymph node biopsy has curbed AD as a means of staging cases of clinically and radiologically negative breast cancer[18].

Neoadjuvant chemotherapy is being increasingly recommended in patients with breast cancer. Although there is so far no proof of survival gain compared to adjuvant chemotherapy, its benefit is demonstrated in the reduction of staging, aiming at the indication of conservative surgery in the breast and less morbidity in the axilla. In addition, pathological complete response to neoadjuvant chemotherapy can serve as a good indicator of disease-free survival.

In this work, a regimen with anthracyclines and taxanes was used in most patients (91.6%), and it was observed that after neoadjuvant chemotherapy, 66.6% were in stage I and 54.2% underwent quadrantectomy, demonstrating the effectiveness of the treatment.

In this study, the assessment of axillary involvement was performed by means of a physical examination, where axilla ultrasonography, fine needle aspiration or core biopsy was not mandatory to define case management because of the costs of the procedures. Knowing that there is a risk of false-positive evaluation of around 17% in the clinical examination of the axilla, as described by Navarro et al.[19], confirmation of lymph node involvement by ultrasound and biopsy is suggested, as recommended in the ACOSOG trials Z1071[16], SENTINA[15] and SN FNAC[17].

The originally reported SLNB FN rate was 5% to 10%, with sensitivity ranging from 90% to 95%. The safety of the procedure was confirmed by the NSABP B-32 study, which showed recurrence of 0.4% compared to 0.7% of AD. It is known that, with neoadjuvant chemotherapy, the lymphatic drainage of the axilla is altered due to fibrosis or blockage of the lymphatic vessels, which can make it difficult to identify the sentinel lymph node and, consequently, result in an increase in the FN rate[20-24]. It is expected that this index will be less than 10%, which was not observed initially in ACOSOG Z1071 (12.6%), SENTINA (14.2%) or SN FNAC (13.4%).

Considering the 24 patients evaluated in the present study, an FN rate of 13.3% was found, which was also higher than expected but similar to that of large studies. To correlate the two patients with FN results, it was observed that both had only one metastatic lymph node in the axillary content without extracapsular extension. As a poor prognostic factor, one showed in the initial clinical examination axilla involvement with a cluster of lymph nodes (N2), three lymph nodes were removed from one and only one from the other.

With the aim of reducing the FN rate, some trials evaluated the use of double-labeling of the sentinel lymph node, samples with more than three lymph nodes and clipping the involved lymph node (targeted axillary dissection, TAD), reaching FN rates as low as 2.4%[25-27]. These studies did not establish a minimum number of lymph nodes to be removed and used double-labeling, since these techniques are complementary and reduce the FN rate in most studies, especially in patients undergoing neoadjuvant chemotherapy[28]. With this, an accuracy of 91.7% was achieved, which indicates the percentage of patients correctly classified by SLNB and AD, simultaneously.

In the study conducted by Boughey et al.[16] in a subgroup of patients from ACOSOG Z1071, metastatic lymph node clipping during pre-neoadjuvant chemotherapy was found to decrease FN rates with resection of the clipped lymph node during surgery. It was observed that the FN rate was 6.8% (95%CI 1.9–16.5) in cases where the clip was identified in the sentinel lymph node sample compared to 19.0% of the records where it was in the axillary content, and not in one of the lymph nodes. In cases where the clip was not identified during surgery, the FN rate was 14.3%, similar to 13.4% in patients who did not have a clip.

In this study, because of operating costs, it was not possible to clip the metastatic lymph node at the time of diagnosis. Galimberti et al.[29] and Nguyen et al.[30] state that this low FN rate achieved through TAD does not change the outcome (local recurrence), and therefore, lymph node clipping is not an essential procedure.

The negative predictive value of 86.7% shows that a large number of patients with negative SLNB who received neoadjuvant chemotherapy no longer had axillary disease and could have benefited from not having AD. This value is above that found in the literature, which ranges from 40% to 70%[31]. This is related to an excellent response to neoadjuvant chemotherapy but could also be a reflection of false-positive evaluations of the axilla that were not confirmed by cytology and the small sample size.

Evidence of the association of the SLNB result with the IAL and tumor size variables was observed in this study and that of Hubie et al.[31] In a meta-analysis, Degnim et al.[32] showed that metastases in non-sentinel lymph nodes are mainly associated with tumor size, ALI, more than one positive sentinel lymph node, sentinel lymph node with metastasis greater than 2 mm and extracapsular extension.

Currently, the National Comprehensive Cancer Network[33], in its guidelines, and the major centers involved in cancer research recommend SLNB after neoadjuvant chemotherapy (level of evidence 2B), which demonstrates and validates less aggressive surgical procedures, which are already a reality in the management of the axilla.

CONCLUSION

In this study, we obtained a high SLNB identification rate and good prediction of axillary status in patients with axillary clinical remission after receiving neoadjuvant chemotherapy. Despite the small sample size and the short period of data collection, the FN rate was compatible with that reported in the literature. As a limitation, the use of physical examination alone and the removal of only the sentinel lymph node from most patients should be highlighted. The results of this study are of clinical significance, and SLNB in patients with axillary clinical remission after neoadjuvant chemotherapy has proven to be safe, making it possible to discuss changes in the protocol in some centers in Brazil.

ACKNOWLEDGMENTS

We thank the statistician Ythalo Hugo da Silva Santos, from the Instituto de Ensino, Pesquisa e Inovação da Liga contra o Câncer, for his contribution to the statistical analysis in this study.

AUTHORS' CONTRIBUTION

VAM: Conceptualization, Data Curation, Formal Analysis, Investigation. Methodology, Visualization, Writing – Original Draft. AVN: Conceptualization, Data Curation, Investigation, Methodology, Validation, Visualization, Writing – Original Draft. JLAA: Conceptualization, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Original Draft, Writing – Review & Editing. KSM: Investigation, Methodology, Validation, Visualization, Writing – Original Draft, Writing – Review & Editing. DTSMN: Conceptualization, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Original Draft, Writing – Review & Editing.

REFERENCES

1. Zhong J, Sun DS, Wei W, Liu X, Liu J, Wu X, et al. Contrast-enhanced ultrasound-guided fine-needle aspiration for sentinel lymph node biopsy in early-stage breast cancer. Ultrasound Med Biol. 2018;44(7):1371-8. https://doi.org/10.1016/j.ultrasmedbio.2018.03.005
2. Brasil. Instituto Nacional do Câncer (INCA). Incidência de câncer no Brasil: síntese de resultados e comentários. Rio de Janeiro: INCA; 2021 [cited on Apr15 2021]. Available from: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//estimativa -2020-incidencia-de-cancer-no-brasil.pdf
3. Li CZ, Zhang P, Li RW, Wu CT, Zhang XP, Zhu HC. Axillary lymph node dissection versus sentinel lymph node biopsy alone for early breast cancer with sentinel node metastasis: a meta-analysis. Eur J Surg Oncol. 2015;41(8):958-66. https://doi.org/10.1016/j.ejso.2015.05.007
4. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial. JAMA. 2011; 305(6): 569-75. https://doi.org/10.1001/jama.2011.90
5. Ozcan LC, Giuliano AE. Is axillary lymph node dissection necessary after a positive sentinel lymph node biopsy? Adv Surg. 2017;51(1):165-78. https://doi.org/10.1016/j.yasu.2017.03.013
6. Ersoy YE, Kadioglu H. Review of novel sentinel lymph node biopsy techniques in breast cancer patients treated with neoadjuvant chemotherapy. Clin Breast Cancer. 2018;18(4):e555-9. https://doi.org/10.1016/j.clbc.2018.01.004
7. Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. Lancet. 1997;349(9069):1864-7. https://doi.org/10.1016/S0140-6736(97)01004-0
8. Veronesi U, Paganelli G, Viale G, Galimberti V, Luini A, Zurrida S, et al. Sentinel lymph node biopsy and axillary dissection in breast cancer: results in a large series. J Natl Cancer Inst. 1999;91(4):368-73. https://doi.org/10.1093/jnci/91.4.368
9. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med. 2003;349(6):546-53. https://doi.org/10.1056/NEJMoa012782
11. Biglia N, Bounous VE, Gallo M, Fuso L, Sgro LG, Maggiorotto F, et al. Feasibility and oncological safety of sentinel node biopsy in breast cancer patients with a local recurrence. Breast. 2018;41:8-13. https://doi.org/10.1016/j.breast.2018.06.004
12. Madison Collins BA, O'Donoghue C, Sun W, Zhou J-M, Ma Z, Laronga C, et al. Use of axillary lymph node dissection

(ALND) in patients with micrometastatic breast cancer. J Surg Res. 2017;215:55-9. https://doi.org/10.1016/j.jss.2017.03.039

13. Qiu S-Q, Zhang G-J, Jansen L, de Vries J, Schroder CP, de Vries EGE, et al. Evolution in sentinel lymph node biopsy in breast cancer. Crit Rev Oncol Hematol. 2018;123:83-94. https://doi.org/10.1016/j.critrevonc.2017.09.010

14. Boughey JC, Alvarado MD, Lancaster RB, Fraser Symmans W, Mukhtar R, Wong JM, et al. Surgical standards for management of the axilla in breast cancer clinical trials with pathological complete response endpoint. NPJ Breast Cancer. 2018;4:26. https://doi.org/10.1038/s41523-018-0074-6

15. Frasson A, Novita G, Millen E, Zerwes F, Brenelli F, Urban C, et al. Doenças da mama: guia de bolso baseado em evidências. 1st ed. Rio de Janeiro: Editora Atheneu; 2013.

16. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol. 2013;14(7):609-18. https://doi.org/10.1016/S1470-2045(13)70166-9

17. Boughey JC, Ballman KV, Le-Petross HT, McCall LM, Mittendorf EA, Ahrendt GM, et al. Identification and resection of the clipped node decreases the false-negative rate of sentinel lymph node surgery in patients presenting with node positive breast cancer (T0-T4, N1-2) who receive neoadjuvant chemotherapy – results from ACOSOG Z1071 (Alliance). Ann Surg. 2016;263(4):802-7. https://doi.org/10.1097/SLA.0000000000001375

18. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. J Clin Oncol. 2015;33(3):258-64. https://doi.org/10.1200/JCO.2014.55.7827

19. Navarro DTSM, Aguiar MG, Galvão MFO, Germano TCO, Lajus TBP, Oliveira TCA et al. Clinical and histopathological axillary assessment. Mastology. 2018;(1):7-10. http://doi.org/10.29289/z2594539420180000255

20. Boughey JC, Ballman KV, Le-Petross HT, McCall LM, Mittendorf EA, Ahrendt GM, et al. Identification and resection of the clipped node decreases the false-negative rate of sentinel lymph node surgery in patients presenting with node positive breast cancer (T0-T4, N1-2) who receive neoadjuvant chemotherapy – results from ACOSOG Z1071 (Alliance). Ann Surg. 2016;263(4):802-7. https://doi.org/10.1097/SLA.0000000000001375

21. Charalampoudis P, Markopoulos C, Kovacs T. Controversies and recommendations regarding sentinel lymph node biopsy in primary breast cancer: A comprehensive review of current data. Eur J Surg Oncol. 2018;44(1):5-14. https://doi.org/10.1016/j.ejso.2017.10.215

22. Krag DN, Anderson SJ, Julian TB. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: Overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010;11(10):927-33. https://doi.org/10.1016/S1470-2045(10)70207-2

23. King TA, Morrow M. Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy. Nat Rev Clin Oncol. 2015;12(6):335-43. https://doi.org/10.1038/nrclinonc.2015.63

25. Park KU, Caudle A. Management of the axilla in the patient with breast cancer. Surg Clin North Am. 2018;98(4):747-60. https://doi.org/10.1016/j.suc.2018.04.001

26. Caudle AS, Bedrosian I, Milton DR, DeSnyder SM, Kuerer HM, Hunt KK, et al. Use of sentinel lymph node dissection after neoadjuvant chemotherapy in patients with node-positive breast cancer at diagnosis: Practice patterns of American Society of Breast Surgeons members. Ann Surg Oncol. 2017;24(10):2925-34. https://doi.org/10.1245/s10434-017-5958-4

27. Caudle AS. Intraoperative Pathologic Evaluation with Targeted Axillary Dissection: Editorial for "Intraoperative touch imprint cytology in targeted axillary dissection after neoadjuvant chemotherapy among breast cancer patients with initial axillary metastasis". Ann Surg Oncol. 2018;25(11):3112-4. https://doi.org/10.1245/s10434-018-6666-4

28. Teshome M, Hunt KK. Sentinel node biopsy after neoadjuvant chemotherapy in initial node-positive patients: why or why not? Curr Surg Rep. 2015;3(12):1-7. https://doi.org/10.1007/s40137-015-0089-y

29. Harlow S, Weaver D. Sentinel lymph node biopsy in breast cancer: Techniques Up to Date [Internet]. 2014. [cited on Jan 5 2018]. Available from: http://www.uptodate.com/contents/sentinel-lymph-node-biopsy-in-breast

30. Galimberti V, Ribeiro Fontana SK, Maisonneuve P, Steccanella F, Vento AR, Intra M, et al. Sentinel node biopsy after neoadjuvant treatment in breast cancer: five-year follow-up of patients with clinically node-negative or node-positive disease before treatment. Eur J Surg Oncol. 2016;42(3):361-8. https://doi.org/10.1016/j.ejso.2015.11.019

31. Nguyen TT, Hoskin TL, Day CN, Degnim AC, Jakub JW, Hieken TJ, et al. Decreasing use of axillary dissection in node-positive breast cancer patients treated with neoadjuvant chemotherapy. Ann Surg Oncol. 2018;25(9):2596-602. https://doi.org/10.1245/s10434-018-6637-9

32. Hubie DP, Minari CL, Guerreiro JA, Linhares JC, Ribeiro R, Hatschbach SBB. Linfonodo sentinela positivo e dissecção axilar: são os nomogramas úteis na decisão? (Positive sentinel lymph node and axillary dissection: are nomograms useful in the decision?). Rev Bras Mastologia. 2011;21(3):111-7. Degnim AC, Griffith KA, Sabel MS, Hayes DF, Cimmino VM, Diehl KM, et al. Clinicopathologic features of metastasis in nonsentinel lymph nodes of breast carcinoma patients. Cancer. 2003;98(11):2307-15. https://doi.org/10.1002/cncr.11803

33. NCCN. Clinical Practice Guidelines in Oncology: Breast Cancer, Version 4.2020. National Comprehensive Cancer Network [Internet]. 2020 [cited on Feb 8, 2021]. Available from: www.nccn.org

This is an open access article distributed under the terms of the Creative Commons license.