Original Article
Middle East Journal of Cancer; January 2023; 14(1): 153-161

Ultrasound Accuracy in Detection of Metastatic Axillary Lymph Nodes in Breast Cancer after Neoadjuvant Chemotherapy

Majid Akrami*, MD, Sepideh Sefidbakht, MD, Alireza Golchini***,****♦, MD, Masoumeh Ghoddusi Johari*, MD, Mehdi Shariat*, MD, Sedigheh Tahmasebi*, MD, Vahid Zangouri*, MD, Zahra Keumarsi*, BSc, Ashkan Omidi*****, MD, Mohadeseh Mashayekhi******, MD, Maral Mokhtari******, MD, Abdolrasoul Talei*, MD**

*Breast Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
**Department of Radiology, Shiraz University of Medical Sciences, Shiraz, Iran
***Department of Surgical Oncology Shiraz University of Medical Sciences, Shiraz, Iran
****General Medical Council, London, UK
*****School of Medicine, Islamic Azad University of Tehran, Faculty of Medicine, Tehran, Iran
******Department of Pathology, Shiraz University of Medical Sciences, Shiraz, Iran

Please cite this article as: Akrami M, Sefidbakht S, Golchini A, Ghoddusi Johari M, Shariat M, Tahmasebi S, et al. Ultrasound accuracy in detection of metastatic axillary lymph nodes in breast cancer after neoadjuvant chemotherapy. Middle East J Cancer. 2023;14(1):153-61. doi: 10.30476/mejc.2022.90917.1596.

Abstract

Background: In the present paper, the main diagnostic tool for re-evaluation of axillary lymph node involvement and planning of surgery after neoadjuvant chemotherapy (NAC) is ultrasound whose accuracy we aimed to determine herein. The high precision of ultrasound in diagnosis of metastatic axillary lymph nodes in untreated patients is well known; however, its worth in patients who received NAC is highly controversial.

Method: We enrolled 165 breast cancer patients receiving NAC in this retrospective cohort study. They all had undergone post-NAC ultrasound done before surgery. The ultrasound reports were reassessed and validated by a breast radiologist. Finally, the histopathology reports were compared to those of the ultrasound.

Results: Among 165 surveyed post-NAC ultrasounds, 53 women had positive results and 112 had negative results. Pathology and ultrasound reports were accordant in 93 women and adverse in 112 others. The false negative rate of post-NAC axillary ultrasound was calculated as 60.6%. The sensitivity and specificity of post-NAC AxUS were 39.4% and 79%, respectively. After NAC, there were certain changes in ultrasound reports from positive to negative in 50% and pathologic complete clearance was observed in just 28% of the women who were initially clinically lymph node positive.

Conclusion: Ultrasound was not found to be an accurate and appropriate tool for evaluation of axillary lymph node involvement in breast cancer patients who receive NAC. By changing the primarily established surgical plan from ALND to SLNB, based on the ultrasound findings, patients may remain undertreated. Furthermore, the axillary nodes pathologic clearance after NAC was observed in less than one third of the women who were initially clinically node positive; accordingly, surgeons should be cautious about the optimum response of axillary metastatic lymph nodes to NAC.

Keywords: Ultrasound precision, NAC, Axillary downstaging, Lymph node involvement, Breast chemotherapy

Received: April 25, 2021; Accepted: June 27, 2022

♦Corresponding Author:
Alireza Golchini, MD
Department of Surgical Oncology, Shiraz University of Medical Sciences, Shiraz, Iran
Email: sgolchini@yahoo.com

Middle East Journal of Cancer

Introduction

Axillary breast evaluation is an important part of breast cancer management. It has an impact on loco-regional and systemic treatment of the disease. Axillary lymph node status is also considered as one of the strongest prognostic factors for survival.[1] In locally advanced breast cancer, NAC is given in order to assess the tumor response to treatment and improve patients' survival.[2-4] It may also help surgeons to have less invasive surgery with the same oncologic result and a more favorable acute and chronic side-effect profile.[5] NAC has been increasingly used in the early stages of breast cancer for assessing patient response and prognosis.[6, 7] It may also provide a novel platform for investigating new drugs to improve survival in the future.

Residual tumor could be found in 50%-60% of axillary lymph node post-NAC treatments.[8] Determining axillary status prior to the surgery can help surgeons have a more comprehensive insight into their extent of axillary involvement. This insight may reduce invasiveness of surgical manipulation, as a result of which the rate of acute and chronic morbidities declines.

Different methods have been tested to assess pre-operative axillary condition after NAC.[9, 10] However, none of them has been proved as the standard of care due to their shortcomings and paucity of strong data. Ultrasound is easily

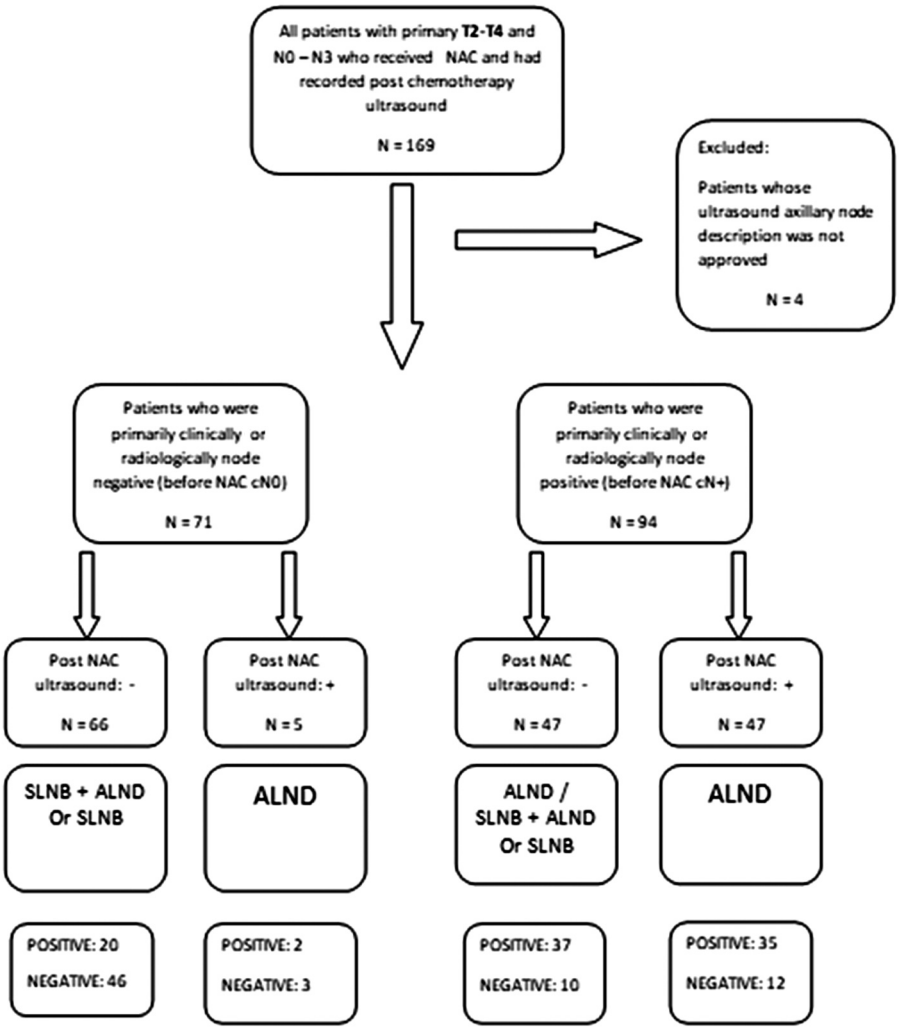

Figure 1. Partitioned performed axillary surgery plan for the initially and post-neoadjuvant ultrasound positive and negative groups and lymph nodes involvement results.
NAC: Neoadjuant chemotherapy

Table 1. Baseline and clinical characteristics of the patients (continued)

	Frequency	Percentage
Breast		
Left	79	47.8
Right	86	52.2
Operation		
Mastectomies	83	50.3
BCS	76	46.0
Mastectomies and BCS	6	3.7
Axillary		
ALND	111	67.3
SLNB	40	24.2
Both (first SLNB then ALND)	14	8.5
Permanent pathology		
In situ (Tumor regression after neoadjuvant chemotherapy)	4	2.4
Invasive ductal carcinoma	144	87.3
Invasive lobular carcinoma	4	2.4
Other cases	13	7.9
Tumor size		
I	64	38.6
II	46	27.7
III	5	3.0
Unknown	50	30.7
Tumor grade		
I	14	8.4
II	77	46.4
III	20	12.0
Unknown	55	33.1
Insitu component		
No	57	34.5
Yes	53	32.12
Unknown	55	33.4
Nuclear grade		
I	16	9.6
II	32	19.3
III	14	8.4
Unknown	102	62.7
Multifocal		
No	79	47.6
Yes	14	8.4
Unknown	72	44.0
Tumor necrosis		
No	64	38.6
Yes	47	28.3
Unknown	54	33.1
Type of lymph node involvement		
Vascular	49	29.7
Pre-neural	4	2.4
None	43	26.0
All over	19	11.5
Unknown	50	30.3
Margin		
Free	120	71.7
Positive	10	6.0
Missing	35	21.7
ER		
No	42	25.3
Yes	108	65.1
Unknown	15	9.6
PR		
No	57	34.3
Yes	93	56.0

Table 1. Baseline and clinical characteristics of the patients(continued)

	Frequency	Percentage
Unknown	15	9.6
HER2		
No	83	50.0
Yes	65	39.2
Unknown	17	10.8
Luminal		
A	63	38.0
B	44	26.5
Enriched	21	12.7
Triple negative	21	12.7
Unknown	16	10.2
Post-chemotherapy		
No	73	44.0
Yes	46	38.6
Unknown	27	17.4
Radiotherapy		
No	35	21.1
Yes	130	78.9
Hormone therapy		
No	65	39.76
Yes	100	60.24
Recurrence		
No	155	93.4
Yes	10	6.6

BCS: Breast conserving surgery; ALND: Aaxillary lymph node dissection; SLNB: Sentinel lymph node dissection; ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth factor receptor 2

accessible and the least invasive method which can be applied under this condition.

Lymph node round or irregular shape, decreased echogenicity, deformation, increased cortical thickness, and loss of mobility among other features are considered as radiological positive criteria for lymph node involvement.[11] However, ultrasonic value of these criteria in post-NAC setting have not been accepted globally.

Hence, in this study, we compared lymph node status in post-NAC ultrasound with permanent pathology in order to determine its sensitivity, specificity, as well as positive and negative predictive values.

Furthermore, we investigated ultrasound capability in predicting ypN0 and ypN+ patient in post-NAC setting.

Patients and Methods

Study setting

This survey was conducted in Shiraz Breast Clinic, which is the main referral center for breast cancers in south of Iran. Patients are referred to this breast clinic from multiple medical health centers within the city and from other provinces (mostly those from southern Iran). This paper is part of breast cancer registry, entitled as Shiraz Breast Cancer Registry (SBCR) Protocol, whose design has been described before.[12]

It should be noted that all the patients had written and signed a consent form at the beginning of the registry. Additionally, all the data and patients' details used from the registry were anonymous. The registry is affiliated to Shiraz University of Medical Sciences and contains data on more than 9000 breast cancer patients. The present research was approved by the Institutional Review and Ethics Board of Shiraz University of Medical Sciences (ethics code: IR.SUMS.REC.1400.044).

Study protocol

In this retrospective study, the medical records of 710 women with breast cancer who received NAC were assessed from March 2016 to October 2020.

The inclusion criteria were considered as follow: all the women above the age of 18, with histologically proven T1- 4, N0-2, and M0

Table 2. Mean, Sd, and 95% confidence interval for the quantitative parameters

	Mean	SD	95% Confidence interval for mean
Primary tumor size	3.43	1.387	(3.22-3.65)
Secondary tumor size	1.77	1.357	(1.50-2.04)
Number of lymph involved	3.40	6.445	(2.14-4.66)
Lymph number removed	12.42	8.728	(10.71-14.13)

invasive breast carcinoma, who had undergone 3 to 10 courses of NAC, with at least one primary axillary ultrasonography (AxUS) before NAC, one AxUS after chemotherapy, before surgery (post-NAC AxUS), and complete clinicopathological and surgical report data.

All the patients with missing pre- and post-NAC AxUS report and other clinicopathological data were excluded from this study.

After file reviewing, 169 eligible women aged 28 to 71 years old were enrolled in this study.

Primary nodal assessment and the reason of receiving NAC

In the present study, we did not focus on ultrasound accuracy in patients' axilla at the time of diagnosis and before receiving the NAC or so called the "primary AxUS", although some surgeons decided to perform axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB) based on the primary clinical findings or primary AxUS report. The biopsy proving of node involvement did not have to be included in this study. All the patients were candidate for receiving NAC according to the following criteria: locally advanced breast cancer, early stage breast cancer with high tumor to breast ratio, as well as triple-negative, hormone-negative and HER2-positive status breast cancer. A number of patients underwent NAC according to the cancer surgeons and oncologists board decision in order to postpone the surgery for different reasons (Figure 1).

Secondary nodal assessment after receiving NAC and before surgery

This was a retrograde study in which we included all the digital and hard copy ultrasound reports that had been prepared by different radiologists in various private run and public clinics through March 2016 to October 2020. A radiologist in radiology department reviewed all the reports and confirmed their validity. Post-NAC AxUSs were performed at the local sites on diagnosis of oncologists or oncology surgeons with the use of commercially available standard equipment for all the patients. The reports in which at least one of the following features was mentioned for lymph node description would be considered as malignant or positive:

1 – Round shape or irregular
2 – Heterogenic structure or lumpy tissue contour
3 – Prominent anechoic component in lymph node
4 – Dislocation or deformation of hilum
5 – Conglomeration of lymph node
6 – Cortical thickness (more than a third of node or more than 3 mm)
7 – Immobility or limited mobility
8 – Irregular margins or blurred contours
9 – Attached or matted lymph node

Accordingly, the absence of suspicious features and frank expressions of "Normal", "No lymph node", or "Reactive" were considered as "Negative" ultrasound report.

Among the 169 reports centrally reviewed, four patients were excluded by central and observer radiologist from the study due to lack of adequate information and the fact that their ultrasound report was below our standard levels.

The NAC, axillary surgery details, and nodal evaluation

All the ultrasounds were requested by an oncologist or a surgeon mainly in order to plan the most proper surgery and adjuvant treatments.

All the patients received the combination of Anthracyclies- and Taxane-based regimes between three to eight cycles and were then referred to the surgical oncologist. The surgical intervention was performed following the secondary ultrasound (or post-NAC AxUS) within 1 to 3 weeks after the NAC last session.

Table3. The agreement between the ultrasound diagnosis and pathology report

	Frequency	Percentage
Ultrasound description of axilla lymph node (Post-chemotherapy)		
Positive US report	52	31.5
Negative US report	113	68.5
Pathologic involving		
Positive	94	57.0
Negative	71	43.0
Type of diagnosis		
True	93	56.4
False	72	43.6

SD: Standard deviation; US: Ultrasound

Axillary surgical intervention was performed independently from the breast involvement and primary and post-NAC T stages. The surgical oncologists' decisions on performing ALND or SLNB were mainly based on the primary ultrasound report and clinical examination or axillary lymph node biopsy results. SLNB was performed by radiolabelled colloid or in combination with methylene blue. There were 90 subjects with the initial involvement of axilla in the "primary" ultrasound report, who underwent ALND; the others underwent SLNB alone or ALND following positive SLNB results.

Adequacy of axillary surgery in four patients who underwent merely SLNB based on clearance report in second ultrasound (while their primary ultrasound was positive) were proven by monthly follow-up visits until January 2021 – the time of this article authorship.

All the surgeries and node samplings were conducted or directly supervised by surgical oncologists who attended the operation rooms in the hospitals affiliated with Shiraz University of Medical Sciences. Moreover, frozen section and permanent histopathology evaluations were done and checked at least twice and confirmed by pathologists of Shiraz University.

Statistical analysis

Sensitivity and specificity were determined for the overall evaluations of AUS and histopathological results. They were reported as receiver-operating characteristic (ROC) curve and the area under curve (AUC). All the analyses were performed using SPSS software for windows, version 23.0 and a *P*-value of less than or equal to 0.05 was considered to be statistically significant.

Results

The mean age of the subjects was 43.64 ± 11.22 (in the range of 28-71). Table 1 represents an overview of the patients' clinicopathological features. In addition, table 2 depicts the mean size and number of lymph node involvement before and after NAC.

Amongst the 165 eligible women, secondary (post-NAC) ultrasound was reported as "malignant" (or positive) in 52 (31.5%), consisting of 37 true positive and 15 false positive (according to the permanent pathology), and as "negative" in 113 (68.5%) patients, comprising 56 true and 57 false negatives (Table 4).

The ultrasound and nodal pathology reports were concordant in 93 (56.4 %) women, while contrary in 72 (43.6 %) (Table 3).

The sensitivity and specificity of post-NAC ultrasound were estimated to be 39.4 % and 79%, respectively, with AUC of 59.1% (CI: 0.5-.0.67, $P = 0.045$).

ALND was performed in 111 cases, SLNB in 40, and both SLNB and ALND in 14 patients. Finally, permanent pathology evaluation reported nodal metastasis in 94 (57% were pN+) women and 71 (43% were pN-) were free of metastasis.

Since 57 out of 113 women whose ultrasound had reported no residual disease in axilla, eventually had metastasis in their lymph nodes (57 ultrasound reports were falsely negative), the false negative rate (FNR) was 60.6 %.

Pathologic nodal clearance

We are fully aware that we cannot calculate the nodal pathological complete response to NAC since axillary nodal involvements were not proven by needle biopsy in all the patients.

Table 4. Comparison of frequency of the ultrasound diagnosis and pathology

		Pathology		Total
		Negative	Positive	
Ultrasound report				
Negative	Count	56	57	113
	%	49.5%	50.5%	68.5%
Positive	Count	15	37	52
	%	28.9%	71.2%	31.5%
Total	Count	71	94	165
	%	43.0%	57.0%	100.0%

Among 94 women with primary positive ultrasound report or clinical exam (primary cN+), 26 were pathological nodal free (27.66% of the involved nodes were responsive to NAC), that all of them had received six to eight courses of NAC.

Regardless of the ultimate pathologic results, according to the post-NAC AxUS, down-staging was observed in 50% of the patients (47 of 94 women) and in the rest of them, the nodes remained unchanged (50%).

Among those who had down staged according to the post-NAC, 33 cases (70.2%) were pathologically involved. It should be noted that among those patients with no change in nodal involvement, 74.4 % were still pathologically involved.

Discussion

Axillary ultrasound accuracy in our study and in comparison with previous studies

The sensitivity and specificity of post-NAC ultrasound were respectively estimated as 39.4% and 79% in this study, which are almost the same as those in three prominent studies about the post-NAC ultrasound accuracy. Although the Z1071(Alliance) trial mainly focused on post-NAC SLNB accuracy performed with 611 cases, the false negative rate, sensitivity, and specificity of post-NAC ultrasound (AxUS) were 65.38%, 34.61%, and 77.54%, respectively.[8] NAC is given to reduce the primary tumor burden and to curtail the extend of the surgery. The most available and easiest diagnostic tool for re-evaluation of tumor extension is believed to be ultrasound. Its excellent accuracy in detection of untreated metastatic lymph nodes has been proven in other trials. Ultrasound has been accepted as a precise and beneficial tool for planning axilla surgery in patients who have not already received any surgical or medical treatments. Sensitivity of ultrasound in axillary lymph node detection has been reported to be as high as 70%-99% and its specificity as 83%-97% in patients initially diagnosed with breast cancer.[13, 14] Meanwhile, the reliability of ultrasound in patients with previous surgical or chemical intervention (especially NAC) has been controversial so far and still remains a challenging part in their diagnosis and treatment process.

Murency et al., in 2019, published their trial during which the false negative rate, sensitivity, and specificity of 135 women examined by AxUS were reported as 47.2%, 52.8%, and 78.3%, respectively.[15] The multicenter SENTINA trial results of 1240 patients was published in 2017, 16 with a sensitivity of 23.9% and specificity of 91.7% (Table 5).

The low accuracy of axillary ultrasound after chemotherapy despite its high diagnostic values in the initial stages of diagnosis, in which patients do not receive any chemotherapy agents, could be attributed to certain reasons:

1 – Tissue-induced edema, inflammation, and fibrosis in axillary lymph nodes due to chemotherapy agents will definitely lower the ultrasound accuracy.

2 – The partial response of metastatic lymph nodes to the chemotherapy agents in which the majority of malignant cells disappear macroscopically to an extent, is not detectable via ultrasound, but microscopically are still present.

3 – NAC-receiving patients are in a more

Table 5. Calculated values of post-chemotherapy axillary ultrasound false negative rate, sensitivity, and specificity in our study and two other prospective studies

Study	False negative rate	Sensitivity	Specificity
Z1071 (Alliance)	65.38%	34.61%	77.54%
Murency et al. (2019)	47.2%	52.8%	78.3%
SENTINA trial	--	23.9 %	91.7%
Our study	60.6%	39.4%	79.0%

advanced level of disease than those who initially undergo surgery; therefore, the involvement of deeper parts of axilla where the Rotter's lymph node is located and nodes in levels 2 and 3 may be more probable; naturally, these nodes are more likely to hide from the ultrasound.[17, 18]

4 – There are micrometastases in some positive reported lymph nodes that are not normally detectable through ultrasound, but are clinically important.

Metastatic axillary lymph node down-staging after chemotherapy

We cannot claim to have calculated the complete pathologic response rate of metastatic lymph nodes to neoadjuvant chemotherapy because some of our patients did not undergo biopsy of suspicious lymph nodes at the time of diagnosis and at the beginning of their treatment. Nonetheless, we gained the axillary lymph node involvement based on ultrasound examination, which changed from positive to negative in about just half of the patients (47 of 94 women who had initially positive ultrasound report were AxUS negative after NAC).

These data may challenge the benefits of NAC in the down-staging of metastatic lymph nodes.

Our measures, being 39.4% for sensitivity and 60.6% for false negative rate for post-NAC axillary ultrasound, were rather disappointing.

Oncologists and surgeons should be prudent when changing the primarily established treatment plan. If surgeons firstly decide to perform standard axillary node dissection, the clearance of involved lymph nodes in AxUS should not allure them to curtail the axilla surgery just based on ultrasound report.

Regarding the 12% false negative rate of SLNB alone and 10% false negative rate of the combination of SLNB and ultrasound in NAC-receiving women in Z1071 trail,[19] trusting post-NAC ultrasound, particularly in patients who are primarily node positive, can jeopardize their life. Thus, surgeons need further accurate diagnostic tools, if they decide to change ALND to SLNB.

Moreover, despite the apparent breast tumor sizes response to NAC, the axillary complete clearance following NAC happened just in a third of those who were initially clinically node positive. This finding should also keep us cautious about the results of NAC on the down-staging of the affected axilla.

Conclusion

Despite the proven excellent accuracy of ultrasound for the detection of metastatic axillary lymph nodes, it is not a trustable diagnostic tool in patients who received NAC.

The present devices and measures of ultrasound lack enough accuracy for confirming the presence or absence of metastatic lymph nodes in axilla after NAC.

Funding

This work was funded by Shiraz Breast Cancer Registry, Breast Diseases Research Center.

Acknowledgement

Authors would like to thank all the staff members who assisted us in data collection at the breast clinic.

Conflict of Interest

None declared.

References

1. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. *Cancer*. 1989;63(1):181-7. doi: 10.1002/1097-0142(19890101)63:1<181::aid-

cncr2820630129>3.0.co;2-h.
2. Liu SV, Melstrom L, Yao K, Russell CA, Sener SF. Neoadjuvant therapy for breast cancer. *J Surg Oncol*. 2010;101(4):283-91. doi: 10.1002/jso.21446.
3. Specht J, Gralow JR. Neoadjuvant chemotherapy for locally advanced breast cancer. *Semin Radiat Oncol.* 2009;19(4):222-8. doi: 10.1016/j.semradonc.2009.05.001.
4. Mathew J, Asgeirsson KS, Cheung KL, Chan S, Dahda A, Robertson JF. Neoadjuvant chemotherapy for locally advanced breast cancer: a review of the literature and future directions. *Eur J Surg Oncol.* 2009;35(2):113-22. doi: 10.1016/j.ejso.2008.03.015.
5. Wang M, Hou L, Chen M, Zhou Y, Liang Y, Wang S, et al. Neoadjuvant chemotherapy creates surgery opportunities for inoperable locally advanced breast cancer. *Sci Rep.* 2017;7:44673. doi: 10.1038/srep44673.
6. Killelea BK, Yang VQ, Mougalian S, Horowitz NR, Pusztai L, Chagpar AB, et al. Neoadjuvant chemotherapy for breast cancer increases the rate of breast conservation: results from the National Cancer Database. *J Am Coll Surg*. 2015;220(6):1063-9. doi: 10.1016/j.jamcollsurg.2015.02.011.
7. Liedtke C, Mazouni C, Hess KR, André F, Tordai A, Mejia JA, et al. Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. *J Clin Oncol.* 2008;26(8):1275-81. doi: 10.1200/JCO.2007.14.4147.
8. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA.* 2013;310(14):1455-61.
9. Chen JH, Feig BA, Hsiang DJ, Butler JA, Mehta RS, Bahri S, et al. Impact of MRI-evaluated neoadjuvant chemotherapy response on change of surgical recommendation in breast cancer. *Ann Surg*. 2009;249(3):448-54. doi: 10.1097/SLA.0b013e31819a6e01.
10. Fowler AM, Mankoff DA, Joe BN. Imaging neoadjuvant therapy response in breast cancer. *Radiology.* 2017;285(2):358-75.
11. Pinheiro DJ, Elias S, Nazário AC. Axillary lymph nodes in breast cancer patients: sonographic evaluation. *Radiol Bras.* 2014;47(4):240-4. doi: 10.1590/0100-3984.2013.1689.
12. Talei A, Tahmasebi S, Akrami M, Zangouri V, Rezaianzadeh A, Arasteh P, et al. The Shiraz Breast Cancer Registry (SBCR): study design and primary reports. *Per Med.* 2018;15(6):471-9. doi: 10.2217/pme-2018-0047.
13. Jackson RS, Mylander C, Rosman M, Andrade R, Sawyer K, Sanders T, et al. Normal axillary ultrasound excludes heavy nodal disease burden in patients with breast cancer. *Ann Surg Oncol.* 2015;22(10):3289-95. doi: 10.1245/s10434-015-4717-7.
14. Sencha AN, Evseeva EV, Mogutov MS, Patrunov YN. Breast ultrasound: Springer Science & Business Media. 1st edition: Springer-Verlag: Berlin Heidelberg; 2014.p. 202-222.
15. Morency D, Dumitra S, Parvez E, Martel K, Basik M, Robidoux A, et al. Axillary lymph node ultrasound following neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: Results from the SN FNAC study. *Ann Surg Oncol.* 2019;26(13):4337-45. doi: 10.1245/s10434-019-07809-7.
16. Laws A, Hughes ME, Hu J, Barry WT, Dominici L, Nakhlis F, et al. Impact of residual nodal disease burden on technical outcomes of sentinel lymph node biopsy for node-positive (cN1) breast cancer patients treated with neoadjuvant chemotherapy. *Ann Surg Oncol.* 2019;26(12):3846-55. doi: 10.1245/s10434-019-07515-4.
17. Osorio-Silla I, Gómez Valdazo A, Sánchez Méndez JI, York E, Díaz-Almirón M, Gómez Ramírez J, et al. Is it always necessary to perform an axillary lymph node dissection after neoadjuvant chemotherapy for breast cancer? *Ann R Coll Surg Engl.* 2019;101(3):186-92. doi: 10.1308/rcsann.2018.0196.
18. Schwentner L, Helms G, Nekljudova V, Ataseven B, Bauerfeind I, Ditsch N, et al. Using ultrasound and palpation for predicting axillary lymph node status following neoadjuvant chemotherapy - Results from the multi-center SENTINA trial. *Breast.* 2017;31:202-7. doi: 10.1016/j.breast.2016.11.012.
19. Boughey JC. Identifying residual nodal disease in sentinel lymph node surgery after neoadjuvant chemotherapy for breast cancer. *Ann Surg Oncol*. 2019;26(12):3794-7. doi: 10.1245/s10434-019-07733-w.