ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20220097

The effect of positron emission tomography/computed tomography in axillary surgery approach after neoadjuvant treatment in breast cancer

Ecem Memişoğlu[1], Ramazan Sarı[1]*

SUMMARY

OBJECTIVE: The aim of this study was to determine the role of positron emission tomography/computed tomography in the decision to perform axillary surgery by comparing positron emission tomography/computed tomography findings with pathology consistency after neoadjuvant chemotherapy.

METHODS: Patients who were diagnosed for T1-4, cN1/2 breast cancer receiving neoadjuvant chemotherapy in our clinic between January 2016 and February 2021 were evaluated. Clinical and radiological responses, axillary surgery, and histopathological results after neoadjuvant chemotherapy were evaluated.

RESULTS: Axillary involvement was not detected in positron emission tomography/computed tomography after neoadjuvant chemotherapy in 140 (60.6%) of 231 node-positive patients. In total, 88 (62.8%) of these patients underwent sentinel lymph node biopsy, and axillary lymph node dissection was performed in 29 (33%) of these patients upon detection of 1 or 2 positive lymph nodes. The other 52 (37.1%) patients underwent direct axillary lymph node dissection, and no metastatic lymph nodes were detected in 33 (63.4%) patients. No metastatic lymph node was found pathologically in a total of 92 patients without involvement in positron emission tomography/computed tomography, and the negative predictive value was calculated as 65.7%. Axillary lymph node dissection was performed in 91 (39.4%) patients with axillary involvement in positron emission tomography/computed tomography after neoadjuvant chemotherapy. Metastatic lymph nodes were found pathologically in 83 of these patients, and the positive predictive value was calculated as 91.2%.

CONCLUSION: Positron emission tomography/computed tomography was found to be useful in the evaluation of clinical response, but it was not sufficient enough to predict a complete pathological response. When planning axillary surgery, axillary lymph node dissection should not be decided only with a positive positron emission tomography/computed tomography. Other radiological images should also be evaluated, and a positive sentinel lymph node biopsy should be the determinant of axillary lymph node dissection.

KEYWORDS: Axilla. Breast. Neoadjuvant therapy.

INTRODUCTION

Neoadjuvant chemotherapy (NAC) can reduce the size of the primary tumor and eliminate axillary lymph node metastasis, preventing axillary lymph node dissection (ALND) and increasing the chance of breast-conserving surgery (BCS)[1]. NAC is a component of standard treatment for locally advanced breast cancers and breast cancers with negatively impacting tumor profiles such as triple-negative and human epidermal growth factor receptor 2 (HER-2) positive diseases. In recent years, using sentinel lymph node biopsy (SLNB) to evaluate axillary involvement has increased the importance of NAC. Prospective studies such as NSABP B27, ACOSOG-Z1071, SENTINA, SN-FNAC, and GANEA 2 performed in patients with clinically lymph node-positive (cN+) breast cancer before NAC showed that SLNB could be done in patients with no clinical lymph node involvement (cN0) after NAC[2-6]. In light of these studies, the St. Gallen consensus in 2019 recommended that SLNB is sufficient if three or more sentinel lymph nodes (SLN) are negative in patients with cN0 after NAC, and axillary lymph node dissection (ALND) should be performed in patients with cN+ after NAC and macrometastasis in SLNB[7].

One of the most important prognostic factors in breast cancer is axillary lymph node metastasis. Preoperative estimation of metastatic lymph nodes is helpful in identifying patients with few lymph node metastases, the need for SLNB, and the need to avoid unnecessary ALND. Clinical examination and radiological imaging methods are used to predict preoperative lymph node metastasis. After NAC, radiological imaging methods gain more importance in evaluating the response of these lymph nodes to treatment and in the surgical decision. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F FDG PET/CT) is a useful imaging

[1]Kartal Dr. Lütfi Kirdar Şehir Hastanesi, Department of General Surgery – Istanbul, Turkey.
*Corresponding author: sariramazan71@gmail.com
Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on March 21, 2022. Accepted on March 31, 2022.

method for staging, evaluating treatment response, and predicting the prognosis of breast cancer[8]. Almost all breast cancers show FDG uptake, but the intensity of FDG uptake is related to the breast cancer subtype. When compared to the ER-negative breast cancers, FDG uptake is higher in estrogen receptor-positive (ER+), triple-negative, and HER-2 expression-positive breast cancers[9].

In this study, it was aimed to evaluate the axillary involvement in PET/CT images before and after neoadjuvant treatment in breast cancer patients with axillary lymph node metastasis at the time of diagnosis, to compare the PET-CT findings and postoperative histopathology in order to evaluate its consistency as an imaging tool, and to assess the role of PET/CT in guiding the need for axillary dissection.

METHODS

Patient selection

The data of 867 patients who underwent surgery with the diagnosis of breast cancer in our clinic between January 2015 and December 2020 were analyzed retrospectively. A total of 231 cN+ patients who received NAC and underwent PET/CT imaging before and after NAC were included in the study. Patients who did not receive NAC or could not complete the treatment but had cN- disease before NAC and those diagnosed with stage 1 breast cancer were excluded from the study. All patients included in the study were evaluated and staged by clinical examination, mammography, ultrasonography, magnetic resonance imaging, and PET/CT before and after NAC. The metastatic axillary lymph nodes in the pre-NAC patient were confirmed by ultrasound-guided biopsy and/or PET/CT uptake.

Surgical technique

Surgical treatment was performed as per the standard guidelines. For the primary breast tumor, mastectomy or BCS was performed according to the patient's characteristics. Surgical management of the axilla has evolved over the years in light of studies and published guidelines. ALND was performed in 91 patients with (yc) N+ in the clinical staging performed after NAC.

In patients with 52 ycN- after NAC, in line with the prospective studies recommending SLNB before the 2019 St. Gallen consensus conference[10], SLNB was performed according to the surgeon's choice. However, ALND was performed on all of these patients. After the 2019 St. Gallen consensus conference, no additional intervention was performed in 59 ycN- patients with dual tracer mapping (radio-labeled colloid and patent blue) and removal of three or more negative lymph nodes. In some patients, in addition to the dual method, lymph nodes that were clip-marked at the time of needle biopsy were localized with wire and removed to reduce the false-negative rate. On the contrary, ALND was performed in 29 patients with one or more positive lymph nodes in the SLNB.

Clinical and pathological evaluation

Patient age, menopausal status, tumor size, lymph node involvement, the presence of metastasis, clinical tumor stage, histopathological type, histological and nuclear grade, tumor receptor (ER, the estrogen receptor; PR, progesterone receptor; and HER-2, human epidermal growth factor receptor) status, the molecular subtype of the tumor, Ki-67 level, PET/CT and radiological imaging findings before and after NAC, axillary clinical response status after NAC with ultrasonography, type of surgery, intraoperative frozen section findings, and final pathology findings were evaluated. Tumor staging was performed according to the 8th TNM staging system defined by the American Joint Committee on Cancer (AJCC). The pathological response after NAC was evaluated according to the CAP 2019 criteria determined by the College of American Pathologists (CAP).

Statistical data analysis

Data were analyzed using SPSS version 22. Frequency, percentage, mean, standard deviation, median, and interquartile range were used as descriptive statistical methods. Continuous variables were evaluated using the Kolmogorov-Smirnov and the Shapiro-Wilk tests. One-way ANOVA test was used for normally distributed continuous variables, and Mann-Whitney U and Kruskal-Wallis tests were used for abnormally distributed continuous variables. The Chi-square test was used to evaluate categorical data. To determine the positive predictive value (PPV) and negative predictive value (NPV) of PET/CT findings after NAC, the axillary lymph node status on PET/CT after NAC was compared with the final surgical pathology result. $p<0.05$ was considered significant for all comparisons.

RESULTS

The mean age of 231 patients who received NAC was 52.5±12.1 years. According to tumor molecular subtypes, 9.5% of patients were Luminal A (ER and/or PR+, HER-2-, ki-67 ≤14%), 59.7% of them were Luminal B (ER and/or PR+, HER-2- or +, ki-67 >14%), 19.5% of them were HER-2 positive (ER-, PR-, HER-2+), and 11.3% of them were triple-negative (ER-, PR-, HER-2-). In total, 197 of the 231 (85.3%)

patients had FNA-confirmed axillary metastases. A total of 34 (14.7%) patients with inconclusive FNA findings but uptake in the PET-CT were regarded as clinically positive for axillary metastases. The clinicopathological features of the patients before NAC are summarized in Table 1.

The highest clinical and pathological complete response after NAC was observed in the HER-2 positive group. When the axillary clinical response was evaluated, it was observed that the best response was in the HER-2 positive group. While the triple-negative group had the highest SLNB negativity, the

Table 1. Clinicopathological data and clinical and pathological response after neoadjuvant chemotherapy regarding molecular tumor subtype.

	Total (n=231)	Luminal A (n=22)	Luminal B (n=138)	HER 2+ (n=45)	Triple- (n=26)	p-value
Age (years)	52.51±12.10	56.72±13.45	52.63±12.14	52.37±11.55	48.70±11.03	0.147*
Mitosis index (ki-67)	35.00 [25.00]	10.00 [5.00]	30.00 [15.00]	40.00 [26.25]	60.00 [30.00]	<0.001†
Total LN	10.00 [9.00]	11.50 [4.75]	10.00 [9.00]	10.00 [10.25]	11.00 [13.50]	0.755†
Menopausal status						0.934‡
Premenopause	59 (25.5%)	5 (22.7%)	36 (26%)	12 (26.6%)	6 (23%)	
Perimenopause	27 (11.7%)	3 (13.6%)	14 (10.2%)	5 (11.1%)	5 (19.3%)	
Postmenopause	145 (62.8%)	14 (63.6%)	88 (63.8%)	28 (62.2%)	15 (57.7%)	
Histology						0.176‡
Ductal	222 (96.1%)	21 (95.5%)	132 (95.6%)	45 (100.0%)	24 (92.3%)	
Lobular	4 (1.7%)	–	4 (2.9%)	–	–	
Other	5 (2.2%)	1 (4.5%)	2 (1.5%)	–	2 (7.7%)	
cT						0.129‡
1	47 (20.4%)	7 (31.8%)	26 (18.8%)	11 (24.4%)	3 (11.5%)	
2	131 (56.7%)	11 (50.0%)	84 (60.9%)	26 (57.8%)	10 (38.6%)	
3	30 (13%)	3 (13.6%)	14 (10.15%)	6 (13.3%)	7 (26.9%)	
4	23 (9.9%)	1 (4.5%)	14 (10.15%)	2 (4.5%)	6 (23%)	
cN						0.291‡
0	1 (0.5%)	–	1 (0.7%)	0 (0%)	0 (0%)	
1	111 (48%)	11 (50.0%)	71 (51.4%)	20 (44.4%)	9 (34.6%)	
2	89 (38.5%)	8 (36.4%)	51 (37%)	21 (46.7%)	9 (34.6%)	
3	30 (13%)	3 (13.6%)	15 (10.9%)	4 (8.9%)	8 (30.8%)	
Metastasis						0.252‡
No	220 (95.2%)	22 (100.0%)	131 (94.9%)	41 (91.1%)	26 (100.0%)	
Yes	11 (4.8%)	–	7 (5.1%)	4 (8.9%)	–	
Staging						0.130‡
2A	31 (13.4%)	5 (22.7%)	19 (13.7%)	6 (13.4%)	1 (3.8%)	
2B	61 (26.4%)	6 (27.3%)	40 (29%)	10 (22.2%)	5 (19.2%)	
3A	82 (35.5%)	7 (31.8%)	48 (34.8%)	19 (42.2%)	8 (30.8%)	
3B	18 (7.8%)	1 (4.5%)	11 (8%)	2 (4.4%)	4 (15.4%)	
3C	27 (11.7%)	3 (13.6%)	13 (9.4%)	3 (6.7%)	8(30.8%)	
4	12 (5.2%)	–	7 (5.1%)	5 (11.1%)	–	
PET breast involvement						0.007‡
Positive involvement	78 (33.8%)	4 (18.2%)	40 (29%)	23 (51.1%)	11 (42.3%)	
Negative involvement	153 (66.2%)	18 (81.8%)	98 (71%)	22 (48.9%)	15 (57.7%)	
PET axillary involvement						0.001‡
Positive involvement	143 (61.9%)	11 (50.0%)	82 (59.4%)	39 (86.6%)	11 (42.3%)	
Negative involvement	88 (38.1%)	11 (50.0%)	56 (40.6%)	6 (13.4%)	15 (57.7%)	

Continue...

Table 1. Continuation.

	Total (n=231)	Luminal A (n=22)	Luminal B (n=138)	HER 2+ (n=45)	Triple- (n=26)	p-value
Clinical response						0.033‡
No response	47 (20.3%)	6 (27.3%)	32 (23.2%)	3 (6.7%)	7 (26.9%)	
Partial response	129 (55.8%)	13 (59.1%)	77 (55.8%)	24 (53.3%)	15 (57.7%)	
Complete response	53 (22.9%)	3 (13.6%)	29 (21%)	18 (40%)	4 (15.4%)	
Pathological response (CAP)						<0.001‡
No residual tumor	63 (27.3%)	0 (0.0%)	29 (21%)	23 (51.1%)	11 (42.3%)	
Full response	29 (12.5%)	2 (9.1%)	16 (11.6%)	9 (20%)	2 (7.8%)	
Moderate response	38 (16.5%)	3 (13.6%)	25 (18.1%)	4 (0.9%)	6 (23%)	
Minimal / no response	101 (43.7%)	17 (77.3%)	68 (49.2%)	9 (20%)	7 (26.9%)	
SLNB groups						0.071‡
Negative	119 (78.8%)	10 (66.7%)	65 (73%)	32 (71.1%)	12 (92.3%)	
1–2 lymph node	19 (12.6%)	2 (13.3%)	14 (15.8%)	2 (4.4%)	1 (7.7%)	
3 lymph node	13 (8.6%)	3 (20.0%)	10 (11.2%)	–	–	
pN						<0.001‡
0	101 (43.7%)	1 (4.5%)	51 (37%)	35 (77.7%)	14 (53.9%)	
1	83 (36%)	13 (59.1%)	59 (42.7%)	6 (13.4%)	5 (19.2%)	
2	29 (12.5%)	6 (27.3%)	16 (11.6%)	3 (6.7%)	4 (15.4%)	
3	18 (7.8%)	2 (9.1%)	12 (8.7%)	1 (2.2%)	3 (11.5%)	

Data are denoted as mean±standard deviation, median [IQR], and n (%). *One-way ANOVA test. †Kruskal-Wallis test. ‡Chi-square test.

HER-2 positive group had the lowest lymph node metastases in the final pathology (Table 1).

HER-2 positivity, triple-negative subtype, and the absence of axillary lymph node involvement in PET/CT were the most critical factors in reducing pN after NAC (p<0.005). Although lymph node metastasis was higher in postmenopausal patients, this difference was not statistically significant (p=0.534) (Table 2).

SLNB was performed in 88 (62.8%) of 140 (60.6%) patients without axillary lymph node involvement in PET/CT after NAC, and ALND was performed in 29 (33%) patients who underwent SLNB after detecting one or more lymph node metastases. A total of 52 (37.1%) patients who underwent ALND without SLNB had negative PET-CT findings, and 33 (63.4%) of these 52 patients had no lymph node metastasis in the final histopathology. No metastatic lymph node was observed in 92 of the 140 patients, and the negative predictive value (NPV) was calculated as 65.7%. Direct ALND was performed in 91 (39.4%) patients with axillary involvement in PET/CT after NAC. Metastatic lymph nodes were detected in 83 of 91 patients, and the positive predictive value (PPV) was calculated as 91.2%. The sensitivity of PET/CT in detecting metastatic lymph nodes was 63.3%, and the specificity was 92%. A receiver operating characteristic analysis was performed to evaluate the overall predictive ability of PET/CT in

Table 2. Factors affecting pathological lymph node involvement after neoadjuvant chemotherapy.

	pN		p-value
	Negative	Positive	
Menopausal status			0.534†
Premenopause	27 (45.8%)	32 (54.2%)	
Perimenopause	14 (51.8%)	13 (48.2%)	
Postmenopause	60 (41.4%)	85 (58.6%)	
Grade			0.001†
Grade 1	2 (11.8%)	15 (88.2%)	
Grade 2	63 (40.9%)	91 (59.1%)	
Grade 3	36 (60.0%)	24 (40.0%)	
HER 2			<0.001*
Negative	32 (24.6%)	98 (75.4%)	
Positive	69 (68.3%)	32 (31.7%)	
Molecular subtype			<0.001*
Luminal A	1 (4.6%)	21 (95.4%)	
Luminal B	51 (36.9%)	87 (63.1%)	
HER 2+	35 (77.7%)	10 (22.3%)	
Triple-	14 (53.8%)	12 (46.2%)	
PET axillary involvement			<0.001*
Negative involvement	92 (65.7%)	48 (34.3%)	
Positive involvement	8 (8.7%)	83 (91.3%)	

*Chi-square test. †Mann-Whitney U test.

determining axillary status. The AUC (area under the curve) was 0.774 (95%CI 0.713–0.835, p<0.001) (Figure 1).

In the PET/CT evaluation of 172 patients who underwent axillary lymph node dissection after NAC, 81 (47.1%) had no involvement of the axilla. However, in the final pathology, no metastatic lymph node was detected in 40.7% of these patients. The metastatic lymph node was detected in 82.2% of 91 (52.9%) patients who had axillary involvement in PET/CT after NAC and underwent ALND.

DISCUSSION

The surgical management of the axilla after neoadjuvant therapy is still a controversial issue. Today, axillary lymph node dissection is the standard treatment for patients with an N2 pre-NAC axillary stage or an N1 with no clinical response in axillary involvement after NAC10. On the contrary, in patients who do not have clinical axillary involvement after NAC and underwent SLNB, ALND is still performed if the SLNB is positive. However, studies on the adequacy of radiotherapy instead of ALND in these patients are still ongoing[11,12].

Identifying patients who do not require ALND is difficult but essential. By meticulously evaluating the axillary clinical response after NAC, we can avoid ALND and its morbidities and improve the patient's quality of life. Lymphedema is seen in one of five patients who undergo ALND, and the incidence of lymphedema increases to one in four patients with the addition of radiotherapy to the treatment. Lymphedema significantly affects the quality of life of the patient[13]. While searching for a solution to improve the quality of life, the best treatment should be determined without ignoring the risk of recurrence and its effect on survival. NAC is recommended to avoid ALND in breast cancer patients with biopsy-proven axillary lymph node metastases.

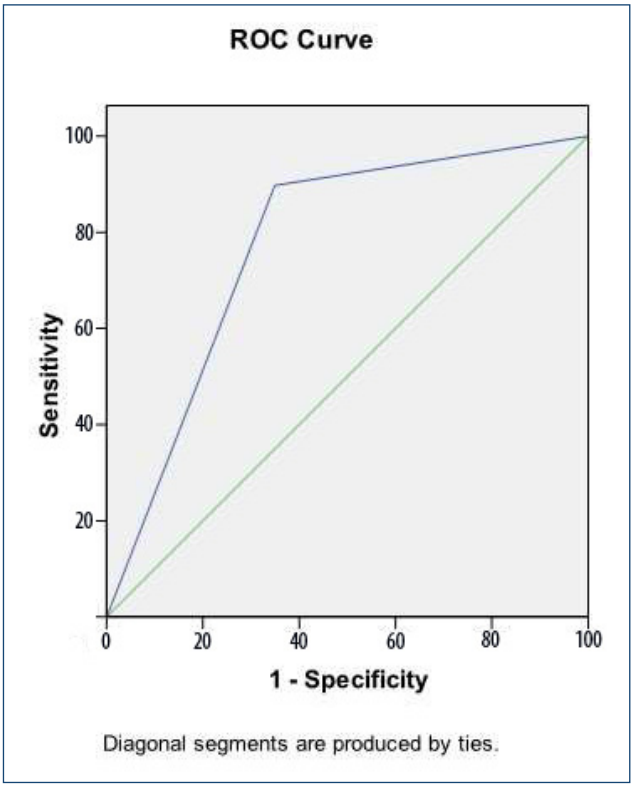

Figure 1. Receiver operating characteristic analysis for positron emission tomography/computed tomography in determining axillary status.

As it is known, the NAC response varies according to the molecular subtype of breast cancer, and the primary tumor response is not always similar to the axillary response. According to studies, the rate of no metastasis in axillary lymph nodes in the final pathology after NAC was found to be 0–29% in luminal tumors, 45–82% in HER-2 positive tumors, and 47–67% in triple-negative tumors[14-18]. In our study, these rates were 4.5% in luminal A, 37% in luminal B, 77.7% in HER-2 positive, and 53.9% in triple-negative tumors. With a detailed clinical and radiological evaluation of the axilla before surgery, surgeons can identify patients suitable for SLNB or avoid unnecessary SLNB by identifying patients who require upfront axillary lymph node dissection. Thus, the patients are properly evaluated preoperatively to avoid unnecessary procedures that lengthen the duration of the surgery. The sensitivity of ultrasonography in predicting residual axillary lymph node metastasis is higher than clinical examination and magnetic resonance imaging or PET/CT. However, PET-CT, even though not recommended in the standard guidelines, has been widely used by medical oncologists in our facility and the country in general to assess the NAC response. There are studies in the literature reporting that PET/CT imaging can change preoperative clinical staging and that the surgical procedure can be changed by avoiding unnecessary SLNB[19,20]. Orsaria et al.[21] reported the sensitivity of PET/CT for axillary lymph node staging as 87%, specificity as 90%, PPV as 93%, and NPV as 82%. The authors stated that PET/CT could guide clinical practice by predicting tumor behavior for axillary staging. In our study, the sensitivity, specificity, PPV, and NPV of PET/CT for axillary lymph node staging were 63.3, 92, 91.2, and 65.7%, respectively. PET/CT was false-negative in 34.3% and false-positive in 8.8% of patients, so ALND could have been avoided in 8.8% of these patients. Therefore, ALND should not be decided with only a positive PET/CT. Other radiological images should also be evaluated, and a positive SLNB should be the determinant of ALND.

The most important limitations of our study are its retrospective nature and the small number of patients. Another critical point is that since the data of the study were extracted from

medical records, imaging methods such as ultrasonography and magnetic resonance imaging, which were used to evaluate the clinical response, could not be compared with PET/CT data due to missing data. In addition, our clinical axillary response was low after NAC. We think most patients may not have benefited from the NAC due to the luminal nature of their disease.

CONCLUSION

As a result of the study, PET/CT was found to be useful in the evaluation of clinical response, but it was not sufficient alone to predict a complete pathological response. When planning axillary surgery according to PET/CT findings after NAC, even if there is no axillary involvement, it should be confirmed with ultrasound, and then SLNB should be performed.

AUTHORS' CONTRIBUTIONS

EM: Conceptualization, Data curation, Methodology, Project administration, Visualization, Writing – review & editing. **RS:** Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft.

REFERENCES

1. Vaidya JS, Massarut S, Vaidya HJ, Alexander EC, Richards T, Caris JA, et al. Rethinking neoadjuvant chemotherapy for breast cancer. BMJ. 2018;360:j5913. https://doi.org/10.1136/bmj.j5913
2. Mamounas EP, Brown A, Anderson S, Smith R, Julian T, Miller B, et al. Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer: results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. J Clin Oncol. 2005;23(12):2694-702. https://doi.org/10.1200/JCO.2005.05.188
3. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Alliance for Clinical Trials in Oncology. 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. https://doi.org/10.1001/jama.2013.278932
4. 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
5. Boileau JF, Poirier B, Basik M, Holloway CM, Gaboury L, Sideris L, et al. 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
6. Classe JM, Loaec C, Gimbergues P, Alran S, de Lara CT, Dupre PF, et al. Sentinel lymph node biopsy without axillary lymphadenectomy after neoadjuvant chemotherapy is accurate and safe for selected patients: the GANEA 2 study. Breast Cancer Res Treat. 2019;173(2):343-52. https://doi.org/10.1007/s10549-018-5004-7
7. Balic M, Thomssen C, Würstlein R, Gnant M, Harbeck N. St. Gallen/Vienna 2019: a brief summary of the consensus discussion on the optimal primary breast cancer treatment. Breast Care. 2019;14(2):103-10. https://doi.org/10.1159/000499931
8. Langer A. A systematic review of PET and PET/CT in oncology: a way to personalize cancer treatment in a cost-effective manner? BMC Health Serv Res. 2010;10:283. https://doi.org/10.1186/1472-6963-10-283
9. Groheux D, Giacchetti S, Moretti JL, Porcher R, Espié M, Lehmann-Che J, et al. Correlation of high 18F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. Eur J Nucl Med Mol Imaging. 2011;38(3):426-35. https://doi.org/10.1007/s00259-010-1640-9
10. Burstein HJ, Curigliano G, Loibl S, Dubsky P, Gnant M, Poortmans P, et al. Estimating the benefits of therapy for early-stage breast cancer: the St. Gallen International Consensus Guidelines for the primary therapy of early breast cancer. Ann Oncol. 2019;30(10):1541-57. https://doi.org/10.1093/annonc/mdz235
11. ClinicalTrials.gov. Comparison of axillary lymph node dissection with axillary radiation for patients with node-positive breast cancer treated with chemotherapy (ALLIANCE A011202) ClinicalTrials.gov [Internet] Available from: https://clinicaltrials.gov/ct2/show/NCT01901094
12. National Comprehensive Cancer Network (NCCN). Breast cancer (version 1.2020). Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
13. Gillespie TC, Sayegh HE, Brunelle CL, Daniell KM, Taghian AG. Breast cancer-related lymphedema: risk factors, precautionary measures, and treatments. Gland Surg. 2018;7(4):379-403. https://doi.org/10.21037/gs.2017.11.04
14. Rouzier R, Perou CM, Symmans WF, Ibrahim N, Cristofanilli M, Anderson K, et al. Breast cancer molecular subtypes respond differently to preoperative chemotherapy. Clin Cancer Biol 2005;11(16):5678-85. https://doi.org/10.1158/1078-0432.CCR-04-2421
15. Boughey JC, McCall LM, Ballman KV, Mittendorf EA, Ahrendt GM, Wilke LG, et al. Tumor biology correlates with rates of breast-conserving surgery and pathologic complete response after neoadjuvant chemotherapy for breast cancer: findings from the ACOSOG Z1071 (Alliance) Prospective Multicenter Clinical Trial. Ann Surg 2014;260(4):608-14. https://doi.org/10.1097/SLA.0000000000000924
16. Kim JY, Park HS, Kim S, Ryu J, Park S, Kim SI. Prognostic nomogram for prediction of axillary pathologic complete response after neoadjuvant chemotherapy in cytologically proven node-positive breast cancer. Medicine. 2015;94(43):e1720. https://doi.org/10.1097/MD.0000000000001720
17. Mamtani A, Barrio AV, King TA, Van Zee KJ, Plitas G, Pilewskie M, et al. How often does neoadjuvant chemotherapy avoid axillary dissection in patients with histologically confirmed nodal metastases? Results of a prospective study. Ann Surg Oncol. 2016;23(11):3467-74. https://doi.org/10.1245/s10434-016-5246-8
18. Diego EJ, McAuliffe PF, Soran A, McGuire KP, Johnson RR, Bonaventura M, et al. Axillary staging after neoadjuvant chemotherapy for breast cancer: a pilot study combining sentinel lymph node biopsy with radioactive seed localization of pre-treatment positive axillary lymph nodes. Ann Surg Oncol 2016;23(5):1549-53. https://doi.org/10.1245/s10434-015-5052-8

19. Groheux D, Giacchetti S, Espié M, Vercellino L, Hamy AS, Delord M, et al. The yield of 18F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. J Nucl Med. 2011;52(10):1526-34. https://doi.org/10.2967/jnumed.111.093864

20. Pritchard KI, Julian JA, Holloway CM, McCready D, Gulenchyn KY, George R, et al. Prospective study of 2-[^{18}F]fluorodeoxyglucose positron emission tomography in the assessment of regional nodal spread of disease in patients with breast cancer: an Ontario clinical oncology group study. J Clin Oncol. 2012;30(12):1274-9. https://doi.org/10.1200/JCO.2011.38.1103

21. Orsaria P, Chiaravalloti A, Caredda E, Marchese PV, Titka B, Anemona L, et al. Evaluation of the usefulness of FDG-PET/CT for nodal staging of breast cancer. Anticancer Res. 2018;38(12):6639-52. https://doi.org/10.21873/anticanres.13031