TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2023;38(4):436–43
doi: 10.5505/tjo.2023.4108

ORIGINAL ARTICLE

Neutrophil-lymphocyte Ratio and Standardized Uptake Value of 18F-fluorodeoxyglucose Positron Emission Tomography for Prediction of Neoadjuvant Therapy Responses in Patients with Early-stage Breast Cancer

Gülin ALKAN ŞEN, Hande TURNA

Division of Medical Oncology, Department of Internal Medicine, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul-*Türkiye*

OBJECTIVE

The primary objective in operable breast cancer (BC) is to achieve a pathological complete response (pCR). Although some markers can predict pCR, there is still a need for additional factors.

METHODS

We retrospectively analyzed patients with early BC patients treated with neoadjuvant systemic treatment (NST) at the one academic center. Baseline neutrophile/lymphocyte ratio (NLR) and the maximum standardized uptake value (SUV_{max}) were analyzed before surgery and their relationship to pCR was determined.

RESULTS

Ninety-nine patients were included in our analysis. Overall, 36 patients (36.4% of the total) achieved pCR, while 63 patients (63.6% of the total) did not. High SUV_{max} at baseline was associated with worse prognostic factors, including larger tumor size, high grade, negative ER, and triple-negative breast cancer (TNBC). The median NLR was 1.85 for patients with pCR and 1.90 for those without pCR (p=0.392). Patients with pCR had a higher median baseline SUV_{max} than those with residual tumors (14.5 vs. 10, respectively, p=0.023).

CONCLUSION

Our findings demonstrated that baseline SUV_{max} is a predictor of pCR, patients with early BC who received NST. We found no association between baseline NLR and pCR.

Keywords: Breast cancer; FDG/PET SUV_{max}; neoadjuvant systemic therapy; neutrophil-lymphocyte ratio; pathological complete response.

INTRODUCTION

Neoadjuvant systemic treatment (NST) is a standard approach of the early breast cancer (BC). Pathological complete response (pCR) is a surrogate marker for the best prognosis in operable BC. Multiple markers predict NST responses, including tumor intrinsic subtype (Luminal A, Luminal B/Her2 positive, Her2 negative, Her2 enriched, and triple negative), Ki-67 score, tumor size, PD-L1 expression, and tumor-infiltrating

Received: July 19, 2023
Accepted: August 15, 2023
Online: September 01, 2023

Accessible online at:
www.onkder.org

Dr. Gülin ALKAN ŞEN
İstanbul Üniversitesi-Cerrahpaşa,
Cerrahpaşa Tıp Fakültesi,
İç Hastalıkları Anabilim Dalı,
Tıbbi Onkoloji Bilim Dalı,
İstanbul-Türkiye
E-mail: gulinalkan@msn.com

lymphocytes (TILs).[1] However, these factors are insufficient to predict pCR, and the need for additional predictive factors is a concerning issue.

The immune system of the host is crucial in BC.[2] A high neutrophile count has been linked to carcinogenesis and enhanced angiogenesis.[3] Although T lymphocytes play a crucial role in inhibiting tumor formation, neutrophils inhibit cytotoxic T lymphocytes carrying CD8 antigen and promote the development of metastasis.[4,5] In addition, a high neutrophile/lymphocyte ratio (NLR) was found to be associated with chemotherapy resistance.[6,7] This raised the question of whether the NLR could be used to predict pCR in clinical care. Numerous studies have investigated whether NLR is predictive or prognostic, with contradictory findings.[8–10]

In BC, the metabolic parameters of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) can provide indirect information about the biology of the tumor. One of the metabolic parameters of FDG-PET, the maximum standardized uptake value (SUV_{max}), was discovered to be associated with poor prognostic tumor characteristics, including large tumor size, axillary node involvement, high histological grade, and TNBC.[11,12] Recent evidence demonstrated that elevated SUV in early BC was indicative of the overexpression of specific genes.[13] Increased SUV_{max} at baseline was also found to be associated with pCR in the neoadjuvant setting.[14,15]

It is still unknown to what extent NLR reflects the host immune system and whether SUV_{max} reflects the aggressiveness of the tumor. Therefore, we conducted a retrospective study to evaluate the role of NLR and SUV_{max} as predictors of pCR.

MATERIALS AND METHODS

Patients

We retrospectively analyzed of 99 patients with invasive BC who were treated with NST at the Cerrahpaşa Medical Faculty between 2016 and 2020. Bilateral BCs, inflammatory BCs, and male BCs were all excluded. Patients' characteristics age, menopausal status, tumor characteristics (clinical T [cT] and clinical N [cN] stage, histopathological characteristics), and treatments all recorded.

All patients underwent FDG-PET/BT previous to NST. SUV_{max} was calculated in the primary tumor. The baseline NLR was calculated as the neutrophil count divided by the lymphocyte count obtained from the blood count performed within 2 weeks before starting NST. SUV_{max} and NLR were separated into low and high categories based on their median values. The median values for NLR and SUV_{max} were 1.9 and 12, respectively.

Surgical specimens' formalin-fixed, paraffin-embedded tissues were immunohistochemically stained for estrogen receptor (ER), progesterone receptor (PR), Her2, and ki-67. ER and PR positivity were defined as a cutoff value of ≥1%. Fluorescent or chromogenic in situ hybridization was performed for intermediate Her2 scores (2+). According to the definition of Goldhirsch et al.,[16] we used clinicopathological parameters to classify the breast cancer subtypes as follows: Luminal A (ER+, PR±, Her2-, Ki-67 <20%), luminal B/Her2-negative (ER+, PR±, Her2-, Ki-67 ≥ 20%), luminal B/Her2-positive (ER+, PR±, Her2+), Her2-enriched (ER-, PR-, Her2+), and TNBC (ER-, PR-, Her2-). pCR was defined as no evidence of invasive tumor both within the axilla and breast (ypT0/is, ypN0).

The study was approved by the Institutional Ethical Review Board and the need for informed consent was waived due to the retrospective nature of this study.

Statistical Analysis

Patients' characteristics, including pCR, baseline SUV_{max}, and baseline NLR, were compared using the Chi-square test for categorical data and the t-test for continuous data. For comparing ordinal variables, Mann–Whitney U-tests were conducted. Using a binary logistic regression model, univariable and multivariable analyses of clinicopathological factors associated with pCR were performed. Odds ratios (ORs) and 95% confidence intervals (CIs) with two-sided p values were given. The statistical analyses were conducted using SPSS version 23 and statistical significance was defined as $p<0.05$.

RESULTS

A total of 99 patients were evaluated. Median age was 46 (range 24–73). The majority of patients (n=54, 54.5%) were found to be premenopausal, while 11.5% were perimenopausal and 34.3% were postmenopausal. The majority of patients (n=50, 50.5%) had cT2 at initial clinical staging, while 13 patients (13.1%) had cT1, 15 patients (15.2%) had cT3, and 21 patients (21.2%) had cT4. Patients with cN2 were the most common (n=46, 46.5%), followed by those with cN1 (30.3%) and cN3 (23.25%). There were no cN0 tumors in our cohort. Twenty-seven patients (27.3%)

Turk J Oncol 2023;38(4):436–43
doi: 10.5505/tjo.2023.4108

Table 1 Baseline characteristics of patients according to NLR

	All patients (n=99) No. (%)		NLR<1.9 (n=49) No. (%)		NLR≥1.9 (n=50) No. (%)		p
	n	%	n	%	n	%	
Age							
Range	24–73		24–73		24–69		
Median	46		43		49.5		0.256
Menopausal status							
Premenopausal	54	54.5	29	59.2	25	50	
Perimenopausal	11	11.1	4	8.2	7	14	
Postmenopausal	34	34.3	16	32.7	18	36	0.468
cT							
1	13	13.1	7	14.3	6	12	
2	50	50.5	29	59.2	21	42	
3	15	15.2	6	12.2	9	18	
4	21	21.2	7	14.3	14	28	0.075
cN							
1	30	30.3	12	24.5	18	36	
2	46	46.5	24	49	22	44	
3	23	23.2	13	26.5	10	20	0.216
Grade							
1 or 2	57	57.6	29	59.2	28	56	
3	42	42.4	20	40.8	22	44	0.749
Ki67							
<14	18	18.2	7	14.3	11	22	
≥14	81	81.8	42	85.7	39	78	0.320
Subtype							
Luminal A	27	27.3	12	24.5	15	30	
Luminal B Her2 (–)	25	25.3	15	30.6	10	20	
Luminal B Her2 (+)	17	17.2	9	18.4	8	16	
Her2 enriched	14	14.1	7	14.3	7	14	
TNBC	16	16.2	6	12.2	10	20	0.728
SUV_{max}							
< 12	47	47.5	29	59.2	18	36	
≥ 12	57	52.5	20	40.8	32	64	**0.021**
pCR							
Yes	36	36.4	18	36.7	18	36	
No	63	63.6	31	63.3	32	64	0.939

NLR: Neutrophile/lymphocyte ratio; TNBC: Triple-negative breast cancer; SUV_{max}: Standardized uptake value

were diagnosed with luminal A tumors, 25 patients (25.3%) with luminal B/Her2-negative tumors, 17 patients (17.2%) with luminal B/Her2-positive tumors, 14 patients (14.1%) with Her2-enriched tumors, and 16 patients (16.2%) with TNBC. Neoadjuvant chemotherapy was administered to all patients, typically including taxane+anthracycline and/or cyclophosphamide, and trastuzumab and pertuzumab were administered additionally to all Her2-positive patients. The baseline characteristics of all patients are shown in Table 1. Overall, 36 patients (36.4% of the total) achieved pCR, while 63 patients (63.6% of the total) did not. 2 (5.6%) luminal A patients, 11 (30.6%) luminal B/Her2-negative patients, 10 (27.8%) luminal B/Her2-positive patients, 8 (22.2%) Her2 enriched patients, and 5 (13.9%) TNBC patients achieved pCR.

When we compared patients with low and high NLR (with a cutoff of 1.9), we found that high NLR was associated with higher SUV_{max} (p=0.021). There were no another significant differences between

groups according to NLR (Table 1). NLR was also not related to pCR in our study (p=0.939). The median NLR was 1.85 for patients with pCR and 1.90 for those without pCR (p=0.392) (Fig. 1a).

Our study's coprimary endpoint was to examine whether or not there is a correlation between SUV_{max} at baseline and pCR. High SUV_{max} at baseline (cutoff of 12) was associated with worse prognostic factors, including larger tumor size, high grade, negative ER and TNBC, and high NLR (Table 2). High SUV_{max} was also significantly associated with pCR (p=0.003). Patients with PCR had a higher median baseline SUV_{max} than those with residual tumors (14.5 vs. 10, p=0.023) (Fig. 1b).

We performed univariable and multivariable analyses for clinicopathological factors that were associated with pCR. Baseline SUV_{max}, histologic grade, Ki-67, and tumor subtype were the factors that were significantly associated with pCR in univariable analysis (Table 3). High baseline SUV_{max} was significantly associated with high pCR in univariable analysis (OR 3.70; 95% CIs 1.52–8.96; p=0.004) and it remained a significant factor in a multivariable analysis adjusted for other clinicopathological factors (OR 3.48; 95% CIs 1.20–10.08; p=0.021). High histologic grade was also associated with pCR in both univariable and multivariable analyses; for univariable analysis (OR 2.80; 95% CIs 1.20–6.51; p=0.017) and multivariable analysis (OR 3.05; 95% CIs 1.20–9.15; p=0.046). Among the tumor subtypes, only the luminal B/Her2 (+) subtype remained significant in multivariable analysis (OR = 9.89; 95% CI=1.21–80.70; p=0.032).

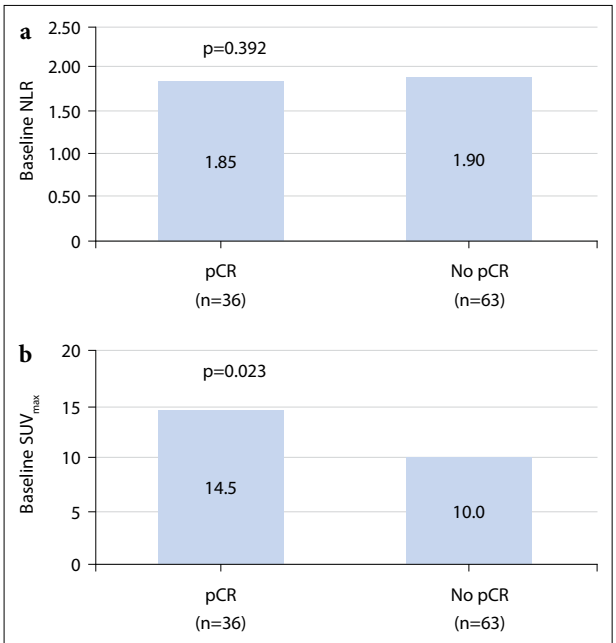

Fig. 1. Comparison of patients as pCR and non-pCR. (a) According to baseline median NLR and (b) according to baseline median SUV_{max}.
NLR: Neutrophile/lymphocyte ratio.

DISCUSSION

The results of our study showed that baseline high SUV_{max} was associated with poor prognostic features. Patients with a high SUV_{max} at baseline had larger tumors, more ER negativity, a higher tumor grade, and more TNBC and Her2 enriched type. Similarly, these findings corroborated with previous studies that increased uptake show aggressive tumor features.[17,18] Despite these unfavorable prognostic characteristics, our results showed that tumors with a high SUV_{max} at baseline had significantly more pCR both univariable and multivariable analyses. In support of our findings, baseline tumor metabolism as assessed by FDG PET/CT has also been shown to be associated with the final histopathologic status after neoadjuvant chemotherapy, with higher SUV_{max} values for pCR.[15]

Another study demonstrated a correlation between baseline FDG uptake and TILs levels in patients with TNBC and Her2 positive BC.[19] Although TNBC (30%) and Her2+ (~20%) BC patients have significantly higher proportions of primary tumors with high TILs than luminal-like carcinoma (13%), increased TILs in the tumor have been found to predict NST responses for all BC subtypes.[20] In a systemic review of 15 studies, it has also been found that TNBC is filtrated by the highest incidence of TILs, with a 20% prevalence of lymphocyte-predominant breast cancer (LPBC), followed by Her2+ (either hormone receptor positive or negative) BC (LPBC: 16%), with the luminal-like BC subgroup (HR+/Her2-) showing the lowest degree of TIL infiltration as well as the lowest incidence of LPBC (6%).[21] Given that tumors with a high SUV_{max} are more frequently Her2 positive and TNBC, it is possible that a high SUV_{max} is associated with an inflammatory response and that this is indicative of a pCR.

We found no correlation between baseline NLR and pCR in this study. Although several previous reports have suggested that high NLR associated with low pCR,[7,22] some studies did not detect association between NLR and pCR.[23,24] In contrast, a number of studies have linked a high NLR to pCR.[25] Some studies found that NLR was only significantly associ-

Turk J Oncol 2023;38(4):436–43
doi: 10.5505/tjo.2023.4108

Table 2 Baseline characteristics of patients according to SUV_{max}

	SUV_{max}<12 (n=47) No. (%)		SUV_{max}≥12 (n=52) No. (%)		p
	n	%	n	%	
Age					
Range	27–70		24–73		
Median	46		47.5		0.779
Menopausal status					
Premenopausal	26	55.3	28	53.8	
Perimenopausal	3	6.4	8	15.4	
Postmenopausal	18	38.3	16	30.8	0.814
cT					
1	11	23.4	2	3.8	
2	25	53.2	25	48.1	
3	5	10.6	10	19.2	
4	6	12.8	15	28.8	0.001
cN					
1	14	29.8	16	30.8	
2	19	40.4	27	51.9	
3	14	29.8	9	17.3	0.383
Grade					
1 or 2	33	70.2	24	46.2	
3	14	29.8	28	53.8	0.016
Ki67					
<14	10	21.3	8	15.4	
≥14	37	78.7	44	84.6	0.448
Subtype					
Luminal A	18	38.3	9	17.3	
Luminal B Her2 (–)	13	27.7	12	23.1	
Luminal B Her2 (+)	9	19.1	8	15.4	
Her2 enriched	2	14.3	12	23.1	
TNBC	5	10.6	11	21.2	0.003
NLR					
< 1.9	29	61.7	20	38.5	
≥ 1.9	18	38.3	32	61.5	0.021
pCR					
Yes	10	21.3	26	50	
No	37	78.7	26	50	0.003

NLR: Neutrophile/lymphocyte ratio; TNBC: Triple-negative breast cancer; SUV_{max}: Standardized uptake value

ated with pCR in patients with TNBC, but not in those who were HR+/Her2.[26] We were unable to perform subgroup analyses due to an insufficient number of patients. However, although NLR is a reliable prognostic factor in patients with localized BC receiving adjuvant chemotherapy, the results are less conclusive for patients with localized disease receiving NST.[8]

When we compared patients based on their baseline NLR, baseline characteristics were comparable with the exception of baseline SUV_{max}. We found that patients with a greater SUV_{max} had a greater NLR. This may be due to differences in inflammatory response. Although there was a correlation between high SUV_{max} and high NLR, there was no correlation between NLR ratio and pCR. We attributed this to the fact that NLR is not a reliable biomarker for pCR. Adjuvant and neoadjuvant cohorts have investigated the prognostic value of various T-cell subpopulations. Multiple retrospective series of unselected BC patients receiving neoadjuvant chemotherapy revealed an association between pCR rates

Table 3 ORs and 95% CIs for pCR

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.00 (0.96–1.04)	0.795		
Menopausal status				
Premenopausal	Ref			
Perimenopausal	1.81 (0.48–6.77)	0.376		
Postmenopausal	1.52 (0.62–3.71)	0.355		
SUV_{max}				
<12	Ref		Ref	
≥12	3.70 (1.52–8.96)	**0.004**	3.48 (1.20–10.08)	**0.021**
cT				
1	Ref			
2	0.90 (0.25–3.16)	0.870		
3	1.40 (0.31–6.33)	0.662		
4	0.64 (0.14–2.76)	0.550		
cN				
1	Ref			
2	1.32 (0.51–3.41)	0.555		
3	0.48 (0.13–1.65)	0.245		
Grade				
1 or 2	Ref		Ref	
3	2.80 (1.20–6.51)	**0.017**	3.05 (1.02–9.15)	**0.046**
Ki-67				
<14	Ref		Ref	
≥14	12.9 (1.64–101.9)	**0.015**	4.14 (0.31–54.28)	0.279
Subtype				
Luminal A	Ref		Ref	
Luminal B Her2 (–)	9.82 (1.90–50.76)	**0.006**	4.94 (0.66–36.54)	0.117
Luminal B Her2 (+)	17.85 (3.15–101.1)	**0.001**	9.89 (1.21–80.70)	**0.032**
Her2 enriched	16.66 (2.79–99.56)	**0.002**	4.66 (0.59–36.44)	0.142
TNBC	5.68 (0.95–33.91)	0.057	1.09 (0.12–9.53)	0.932

ORs: Odds ratio; CI: Confidence interval; SUV_{max}: Standardized uptake value; TNBC: Triple-negative breast cancer

and high levels of total T-cells (CD3+) as well as high infiltration of T helper (CD4+) and cytotoxic (CD8+) subsets.[27] It led us to suppose that NLR in patients receiving NST was unreliable and non-specific, as it was unable to reflect the increasing subpopulation of T-cells in the tumor. Obviously, all of these speculations need to be clarified by further and comprehensive research.

Our study has several limitations: First, its retrospective nature; and second, its small sample size. We were unable to conduct subgroup analyses. Moreover, we were unable to analyze the TILs. Although most patients received anthracycline and taxane-based NST, Her2-positive patients received Her2-targeted therapy. This may have influenced the pCR rate. There is a need for prospective studies with larger patient populations receiving the same NST and pathological analysis of TILs. At present, the NLR and baseline SUV_{max} cutoff values have not been established. Since there is no validated value, the median value was used as the threshold for both. However, these values should be supported by additional research.

CONCLUSION

Our study results that baseline SUV_{max} is a predictor of pCR, patients with early BC who received NST. Our study also showed that baseline SUV_{max} is corelated with poor tumor characteristics. Although tumor aggressiveness is associated with a poor prognosis, the high pCR rate in tumors with increased SUV_{max} suggests that this is associated with an increased inflammatory response

Turk J Oncol 2023;38(4):436–43
doi: 10.5505/tjo.2023.4108

rather than poor prognostic characteristics. To confirm our findings, it is necessary to conduct additional research with larger patient populations and to investigate mechanisms that may have caused this condition, such as TILs. Finally, our data showed that NLR is not a predictor of pCR in patients treated with NST; however, due to the population heterogeneity and/or small sample size of our study, additional clinical trials are necessary.

Peer-review: Externally peer-reviewed.

Conflict of Interest: All authors declared no conflict of interest.

Ethics Committee Approval: The study was approved by the İstanbul University-Cerrahpaşa Clinical Research Ethics Committee (no: 691992, date: 22/05/2023).

Financial Support: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Authorship contributions: Concept – G.A.Ş., H.T.; Design – G.A.Ş., H.T.; Supervision – G.A.Ş., H.T.; Funding – G.A.Ş., H.T.; Materials – G.A.Ş., H.T.; Data collection and/or processing – G.A.Ş., H.T.; Data analysis and/or interpretation – G.A.Ş., H.T.; Literature search – G.A.Ş., H.T.; Writing – G.A.Ş., H.T.; Critical review – G.A.Ş., H.T.

REFERENCES

1. Derouane F, van Marcke C, Berlière M, Gerday A, Fellah L, Leconte I, et al. Predictive biomarkers of response to neoadjuvant chemotherapy in breast cancer: current and future perspectives for precision medicine. Cancers (Basel) 2022;14(16):3876.
2. Savas P, Salgado R, Denkert C, Sotiriou C, Darcy PK, Smyth MJ, et al. Clinical relevance of host immunity in breast cancer: from TILs to the clinic. Nat Rev Clin Oncol 2016;13(4):228–41.
3. Wculek SK, Malanchi I. Neutrophils support lung colonization of metastasis-initiating breast cancer cells. Nature 2015;528(7582):413–7.
4. Niederhuber JE. Cancer vaccines: the molecular basis for t cell killing of tumor cells. Oncologist 1997;2(5):280–3.
5. Coffelt SB, Kersten K, Doornebal CW, Weiden J, Vrijland K, Hau CS, et al. IL-17-producing γδ T cells and neutrophils conspire to promote breast cancer metastasis. Nature 2015;522(7556):345–8.
6. Asano Y, Kashiwagi S, Onoda N, Noda S, Kawajiri H, Takashima T, et al. Predictive value of neutrophil/lymphocyte ratio for efficacy of preoperative chemotherapy in triple-negative breast cancer. Ann Surg Oncol 2016;23(4):1104–10.
7. Chen Y, Chen K, Xiao X, Nie Y, Qu S, Gong C, et al. Pretreatment neutrophil-to-lymphocyte ratio is correlated with response to neoadjuvant chemotherapy as an independent prognostic indicator in breast cancer patients: a retrospective study. BMC Cancer 2016;16:320.
8. Corbeau I, Jacot W, Guiu S. Neutrophil to lymphocyte ratio as prognostic and predictive factor in breast cancer patients: a systematic review. Cancers (Basel). 2020;12(4):958.
9. Graziano V, Grassadonia A, Iezzi L, Vici P, Pizzuti L, Barba M, et al. Combination of peripheral neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio is predictive of pathological complete response after neoadjuvant chemotherapy in breast cancer patients. Breast 2019;44:33–8.
10. Bae SJ, Cha YJ, Yoon C, Kim D, Lee J, Park S, et al. Prognostic value of neutrophil-to-lymphocyte ratio in human epidermal growth factor receptor 2-negative breast cancer patients who received neoadjuvant chemotherapy. Sci Rep 2020;10(1):13078.
11. Kim BS, Sung SH. Usefulness of 18F-FDG uptake with clinicopathologic and immunohistochemical prognostic factors in breast cancer. Ann Nucl Med 2012;26(2):175–83.
12. Qu YH, Long N, Ran C, Sun J. The correlation of (18) F-FDG PET/CT metabolic parameters, clinicopathological factors, and prognosis in breast cancer. Clin Transl Oncol 2021;23(3):620–7.
13. Ueda S, Kondoh N, Tsuda H, Yamamoto S, Asakawa H, Fukatsu K, et al. Expression of centromere protein F (CENP-F) associated with higher FDG uptake on PET/CT, detected by cDNA microarray, predicts high-risk patients with primary breast cancer. BMC Cancer 2008;8:384.
14. Schwarz-Dose J, Untch M, Tiling R, Sassen S, Mahner S, Kahlert S, et al. Monitoring primary systemic therapy of large and locally advanced breast cancer by using sequential positron emission tomography imaging with [18F]fluorodeoxyglucose. J Clin Oncol 2009;27(4):535–41.
15. García Vicente AM, Cruz Mora M, León Martín AA, Muñoz Sánchez Mdel M, Relea Calatayud F, Van Gómez López O, et al. Glycolytic activity with 18F-FDG PET/CT predicts final neoadjuvant chemotherapy response in breast cancer. Tumour Biol 2014;35(11):11613–20.
16. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thürlimann B, Senn H-J. Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol 2011;22(8):1736–47.
17. Basu S, Chen W, Tchou J, Mavi A, Cermik T, Czerniecki B, et al. Comparison of triple-negative and

estrogen receptor-positive/progesterone receptor-positive/HER2-negative breast carcinoma using quantitative fluorine-18 fluorodeoxyglucose/positron emission tomography imaging parameters: a potentially useful method for disease characterization. Cancer 2008;112(5):995–1000.
18. Mavi A, Cermik TF, Urhan M, Puskulcu H, Basu S, Yu JQ, et al. The effects of estrogen, progesterone, and C-erbB-2 receptor states on 18F-FDG uptake of primary breast cancer lesions. J Nucl Med 2007;48(8):1266–72.
19. Murakami W, Tozaki M, Sasaki M, Hida AI, Ohi Y, Kubota K, et al. Correlation between (18)F-FDG uptake on PET/MRI and the level of tumor-infiltrating lymphocytes (TILs) in triple-negative and HER2-positive breast cancer. Eur J Radiol 2020;123:108773.
20. Denkert C, von Minckwitz G, Darb-Esfahani S, Lederer B, Heppner BI, Weber KE, et al. Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: a pooled analysis of 3771 patients treated with neoadjuvant therapy. Lancet Oncol 2018;19(1):40–50.
21. Stanton SE, Adams S, Disis ML. Variation in the incidence and magnitude of tumor-infiltrating lymphocytes in breast cancer subtypes: a systematic review. JAMA Oncol. 2016;2(10):1354–60.
22. Bae SJ, Ahn SG, Ji JH, Chu CH, Kim D, Lee J, et al. Prognostic value of neutrophil-to-lymphocyte ratio and early standardized uptake value reduction in patients with breast cancer receiving neoadjuvant chemotherapy. J Breast Cancer 2022;25(6):485–99.
23. Eryilmaz MK, Mutlu H, Salim DK, Musri FY, Tural D, Coskun HS. The neutrophil to lymphocyte ratio has a high negative predictive value for pathologic complete response in locally advanced breast cancer patients receiving neoadjuvant chemotherapy. Asian Pac J Cancer Prev 2014;15(18):7737–40.
24. Suppan C, Bjelic-Radisic V, La Garde M, Groselj-Strele A, Eberhard K, Samonigg H, et al. Neutrophil/Lymphocyte ratio has no predictive or prognostic value in breast cancer patients undergoing preoperative systemic therapy. BMC Cancer 2015;15:1027.
25. von Au A, Shencoru S, Uhlmann L, Mayer L, Michel L, Wallwiener M, et al. Predictive value of neutrophil-to-lymphocyte-ratio in neoadjuvant-treated patients with breast cancer. Arch Gynecol Obstet 2023;307(4):1105–13.
26. Zhou Q, Dong J, Sun Q, Lu N, Pan Y, Han X. Role of neutrophil-to-lymphocyte ratio as a prognostic biomarker in patients with breast cancer receiving neoadjuvant chemotherapy: a meta-analysis. BMJ Open 2021;11(9):e047957.
27. Dieci MV, Miglietta F, Guarneri V. Immune infiltrates in breast cancer: recent updates and clinical implications. Cells 2021;10(2):223.