The role of basal metabolic and volumetric ^{18}F-FDG PET/CT parameters and their changes in predicting pathological complete response in breast cancer patients receiving neoadjuvant chemotherapy

Ferat Kepenek[1] MD,
Hüseyin Karaoğlan[1] MD,
Canan Can[1] MD,
Halil Kömek[1] MD,
İhsan Kaplan[1] MD,
Hülya Etem[2] MD,
Senar Ebinç[3] MD,
Şeyhmus Kavak[4] MD,
Cihan Gündoğan[1] MD

1. Department of Nuclear Medicine, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkey
2.Department of Pathology, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkey
3.Department of Medical Oncology, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkey
4.Department of Radiology, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkey

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Corresponding author:
Ferat Kepenek MD
University of Health Sciences, Gazi Yaşargil Training and Research Hospital, Department of Nuclear Medicine, Talaytepe, Üçkuyular Mahallesi, Elazığ Yolu Üzeri 10.Km, 21070 Kayapınar/Diyarbakır, Turkey.
Phone: +90(412)2580060
Fax: +904122580101
feratkepenek@hotmail.com

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Abstract

Objective: The aim of this study is to investigate the roles of pre- and post treatment quantitative fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) parameters including maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) and their rate of change in predicting pathological complete response (pCR) in patients with local and locally advanced invasive breast cancer receiving neoadjuvant chemotherapy (NAC). **Subjects and Methods:** Ninety-eight patients who received NAC after being diagnosed with local and locally advanced invasive breast cancer between January 2017 and September 2021 were retrospectively included in our study. Molecular subtypes of all patients were determined. Maximum SUV, MTV, TLG, percent change in SUVmax (ΔSUVmax), ΔMTV, and ΔTLG obtained from PET/CT scans performed before and after NAC were calculated. The cut-off, area under curve (AUC), sensitivity, and specificity values of these parameters in predicting pCR were calculated using receiver operating characteristic (ROC) curves. **Results:** ΔTMTV (cut-off 94.01%, AUC: 0.846), ΔTTLG (cut-off 97.36%, AUC: 0.870), B2MTV (cut-off <1.75, AUC: 0.764), B2TLG (cut-off <2.11, AUC: 0.764), B2SUVmax (cut-off <1.58, AUC: 0.767), ΔBMTV (cut-off 93.67%, AUC: 0.851), ΔBTLG (cut-off 97.22%, AUC: 0.870), ΔBSUVmax (cut-off 84.99%, AUC: 0.846) calculated using ROC curves were found to significantly predict pCR with high sensitivity and specificity. **Conclusion:** We concluded that meta-bolic and volumetric PET/CT parameters, the rates of their change, and metabolic response during NAC may be important variables in predicting pCR in patients with breast cancer.

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Introduction

Neoadjuvant chemotherapy (NAC) is considered a standard treatment strategy that shrinks the tumor and increases the rate of pathological complete response (pCR), survival, and the success of breast conserving therapies in locally advanced breast cancer (BC) [1, 2]. The criterion for defining response to NAC is pCR. Achieving pCR after NAC is associated with higher progression-free survival (PFS) and overall survival (OS) rates [3]. Most patients are still resistant to NAC and possess a high risk of relapse and disease-related death. This increases the significance of predicting response to NAC in BC patients [4].

Imaging modalities that provide morphological information including mammography, computed tomography (CT), and magnetic resonance imaging (MRI) can be used to evaluate treatment response. However, these imaging modalities have been mostly replaced by positron emission tomography/computed tomography (PET/CT) that evaluates metabolic response because morphological changes appear later than metabolic changes [5, 6].

Recent literature on the use of fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT in predicting response to NAC has been promising. However, evaluation of metabolic and volumetric parameters is very limited in these studies [7, 8].

The aim of this study is to investigate the roles of pre- and post treatment quantitative ^{18}F-FDG PET/CT parameters including maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) and their rate of change in predicting pCR in patients with local and locally advanced invasive breast cancer receiving NAC.

Subjects and Methods

Patient selection and study design

Ninety-eight patients who received NAC after being diagnosed with locally advanced invasive BC between January 2017 and September 2021 were retrospectively included in our study. Patients who were diagnosis with invasive but non-inflammatory breast cancer via core needle biopsy, underwent ^{18}F-FDG PET/CT imaging, have stage II or III disease, and later received NAC were included. Patients who have missing data, have distant metastasis at the time of definite diagnosis, have a tumor in both breasts, have additional malignancies, refuse surgical treatment or NAC, have a prior history of breast operation, or could not complete chemotherapy were excluded. Patients' age, menopause status, clinical stage, status of hormone receptors, and molecular subtypes were recorded. This study was conducted in concordance with the Good Clinical Practice guidelines and the current law. Approval from the local ethics committee was obtained (approval no: 901/2021).

Histopathological evaluation

All patients were diagnosed with BC using tru-cut biopsy. Estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor(HER2), E-cadherin and Ki-67 expression statuses were analyzed from the biopsyspecimens [9]. Immunohistochemistry scores of 3+ were considered HER2-positive, and gene amplification was confirmed using fluorescentin situ hybridization (FISH) method for scores of 2+ equivocal [10]. Ki-67 index 15% and above were considered high [11]. Molecular subtypes of breast cancer were determined according to ER, PR, and HER2 positivity, and Ki67 levels. ER/PR (+), HER2 (-), and low Ki-67 index was considered as luminal A; ER/PR (+) and high Ki-67 index or HER2 positivity as luminal B; ER/PR (-) and HER2 (-) as triple negative or basal-like; and ER/PR (-), HER 2 (+) was considered as HER2 enriched group. Specimens obtained during the surgical resection after the NAC was completed were evaluated by an experienced pathologist. Miller-Payne grade 5 was considered as complete response [12].

Neoadjuvant treatment

The majority of patients received 6 to 8 cycles of anthracycline and taxane-based NAC. HER2-positive patients also received trastuzumab. Breast conserving surgery or modified radical mastectomy was performed approximately 30 days after the last cycle of NAC.

^{18}F-FDG PET/CT imaging protocol

All patients were asked to fast and stop intravenous (IV) glucose intake for at least 6 hours before undergoing scans. Patients' blood glucose levels were confirmed to be ≤140 mg/dL finger-stick method and 3.5-5.5MBq/kg of ^{18}F-FDG was intravenously administered. One hour after the injection, CT images (120kV, 80mAs/slice, 700mm transaxial FOV, no gap, 64x0.625mm collimation, pitch 1.4, 0.5s rotation time, 3.3mm slice thickness, 512x512 matrix) from the vertex to the middle of the thigh in the supine position were obtained using the Discovery IQ 4 ring 20cm axial FOV PET/CT device (GE Healthcare, Milwaukee, WI, USA). Then, PET images were obtained at 2.5 minutes per bed position (3D FOV 20cm, ordered subset expectation-maximization algorithm [OSEM] 5 iterations/12 subset, full width at half maximum [FWHM] 3mm). Intravenous non-ionic contrast material was administered to all patients without any contraindications at 1.5mL/kg dose.

Evaluation of ^{18}F-FDG-PET/CT images

Pre- and post-treatment all ^{18}F-FDG PET/CT images were evaluated by 2 nuclear medicine physicians with at least 10 years of experience using PET volume computerized assisted reporting (PET-VCAR, GE, USA) (GE Advantage Workstation software version AW 4.7) software. Volumetric regions of interest (VOI) were drawn manually in three planes to include the lesion on the primary breast lesion and axillary lymph nodes. Metabolic tumor volume, TLG (MTV x SUVmean) and SUVmax parameters were calculated automatically by using a 40% SUV threshold. Total MTV (TMTV1) and total TLG (TTLG1) were found by adding the parameters obtained from the primary tumor (B1MTV and B1TLG) and the axilla (A1MTV and A1TLG) from the pre-treatment scans. Also, post-treatment total MTV (TMTV2) and total TLG (TTLG2) were calculated by adding the parameters obtained from the primary breast tumor (B2MTV and B2TLG) and the axilla (A2MTV and A2TLG) from the post-treatment scans. B1Suvmax, A1Suvmax, B2Suvmax, A2 SUvmax measurements from the primary breast tumor and the axilla before and after NAC were recorded. Lastly, percent change in breast SUVmax ΔBSUVmax), percent change in axilla SUVmax (ΔASUVmax), percent change in TMTV (ΔTMTV), percent change in breast MTV (ΔBMTV), percent change in axilla MTV (ΔAMTV), percent change in TTLG (ΔTTLG), percent change in breast TLG (ΔBTLG), and percent change in axilla TLG (ΔATLG) were calculated using the following formula:

ΔSUVmax = (post-treatment SUVmax – pre-treatment SUVmax)/pre-treatment SUVmax × 100

Statistical Analysis

SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program was used for statistical analyses. Normality of univariate data was evaluated using Kolmogorov-Smirnov test. Mann-Whitney U test was used to compare two independent groups in terms of quantitative data. Categorical variables were compared with Pearson's chi-squared test using the findings of Fisher's exact test. Sensitivity and specificity for the association between the actual classification and the classification according to the cut-off values calculated according to the variables were tested and expressed using receiver operating curve (ROC) analysis. Univariate and multivariate logistic regression analyses were used to analyze the association between pCR after NAC and predictive variables. Quantitative variables were expressed as mean±standard deviation (SD) and median (minimum-maximum), while categorical variables were expressed as n (%). All variables were assessed within 95% confidence interval and $P<0.05$ was considered statistically significant.

Results

The mean age of the 98 patients, who were all female, was

49.14 (26-91) years. Eighty-nine patients (90.8%) had invasive ductal carcinoma (IDC), 5 patients (5.1%) had invasive lobular carcinoma (ILC), and 4 patients (4.08%) had mucinous carcinoma. The primary tumor of 52 patients (53%) was in the right breast. Eighteen patients (20.2%) had luminal A, 46 patients (51.7%) had luminal B, 13 (14.6%) had triple negative, and 12 patients (13.5%) had HER2-enriched molecular subtype. Seventy-one patients (72.5%) could not achieve pCR (non-pCR) while only 27 (27.5%) achieved pCR. Scans of a patient who achieved pCR with neoadjuvant treatment is shown in Figure 1. Histopathological characteristics and pre- and post-treatment PET/CT parameters are summarized in Table 1.

Median age, B2MTV, B2TLG, B2SUVmax, ΔBMTV, ΔBTLG, ΔBSUVmax, TMTV2, TTLG2, ΔTMTV, and ΔTTLG values were significantly higher in non-pCR patients than pCR patients (P: 0.014, 0.025, 0.011, 0.01, 0.003, 0.001, 0.001, 0.022, 0.011, 0.003, and 0.001, respectively). Estrogen and progesterone receptor positivity was higher in non-pCR patients, while HER2 positivity was significantly higher in the pCR group (Table 2).

ΔTMTV (cut-off 94.01%, AUC: 0.846), ΔTTLG (cut-off 97.36%, AUC: 0.870), B2MTV (cut-off <1.75, AUC: 0.764), B2TLG (cut-off <2.11, AUC: 0.764), B2SUVmax (cut-off <1.58, AUC: 0.767), ΔBMTV (cut-off 93.67%, AUC: 0.851), ΔBTLG (cut-off 97.22%, AUC: 0.870), ΔBSUVmax (cut-off 84.99%, AUC: 0.846) calculated using ROC curves were found to significantly predict pCR with high sensitivity and specificity (Figure 2) (Table 3).

Univariate logistic regression analyses revealed that estrogen receptor status, progesterone receptor status, HER2, ΔTMTV, ΔTTLG, B2MTV, B2SUVmax, B2TLG, ΔBMTV, ΔBTLG and ΔBSUVmax were statistically significant in predicting pCR (P: 0.029, 0.049, 0.017, 0.011, 0.008, 0.024, 0.008, 0.008, 0.004, 0.004, and 0.004, respectively) (Table 4). However, multivariate analyses failed to show a significant parameter predicting pCR (Table 5).

Discussion

In this retrospective study investigating the roles of metabolic and volumetric ^{18}F-FDG PET/CT in predicting pCR in patients with breast cancer receiving NAC, we found that ΔTMTV, ΔTTLG, B2MTV, B2SUVmax, B2TLG, ΔBMTV, ΔBTLG and ΔBSUVmax measurements were factors predicting pCR.

The pathological response of the tumor to treatment is evaluated as the criterion for determining response to NAC. Pathological complete response is achieved in 10% to 40% of patients and is defined as the absence of invasive carcinoma in the breast and axilla. The studies have shown that patients who achieve pCR after NAC have better long-term outcomes [13, 14]. A recent prospective study reported a 12.2% pCR rate [3]. In their study with 169 BC patients, Groheux et al. (2015) found the rate of pCR to be 23.7% [15]. Consistently with the literature, the rate of pCR in the current study was 27.5%.

With their advantages of being non-invasive and early detection of chemotherapy response, imaging modalities achieved a solid place in predicting pCR in the daily clinical practice along with clinical and pathological factors. However, it has been shown that conventional imaging techniques (including mammography and ultrasound) are not effective in predicting pCR [16]. Even though some studies indicate that MRI can predict pCR, their specificities are not adequately high [17].

Fluorine-18-FDG PET/CT is superior to conventional imaging modalities in terms of visualizing the functional beha-

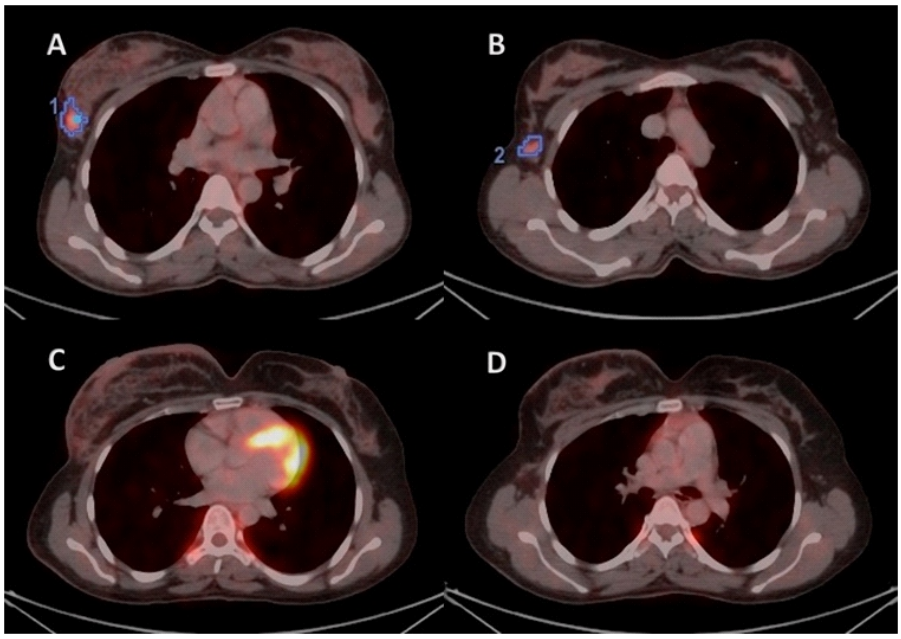

Figure 1. A 33-years-old invasive ductal carcinoma (Luminal B) patient. TMTV was 15.02, TTLG was 32.70, ΔTMTV was 100%, and ΔTTLG was 100%. The primary tumor in the upper outer quadrant of the right breast (A) and right axillary lymph node invasion (B) before treatment are seen. Pathological complete response was achieved with treatment both at the primary breast lesion (C) and the axilla (D).

Table 1. *Descriptive parameters.*

	N	Mean	Std. Deviation	Median	Minimum	Maximum
B1MTV	98	22.9	33.29	10.8	0.8	183.0
B1TLG	98	121.8	222.18	49.5	1.4	1500.0
B1SUV	98	9.9	6.31	8.2	1.3	29.4
A1MTV	98	17.1	62.36	3.9	0.1	604.0
A1TLG	98	45.0	84.97	8.3	0.3	541.5
A1SUV	98	5.9	6.73	3.5	1.2	31.3
B2MTV	35	7.0	17.33	3.2	0.0	102.0
B2TLG	35	16.4	55.00	5.9	0.0	328.7
B2SUV	35	2.5	2.59	1.8	0.0	9.9
A2MTV	35	1.6	7.78	0.0	0.0	46.2
A2TLG	35	5.2	28.51	0.0	0.0	169.0
A2SUV	35	0.5	1.32	0.0	0.0	7.2
ΔBMTV	35	-63.5	44.32	-77.8	-100.0	71.2
ΔBTLG	35	-74.4	66.61	-94.6	-100.0	279.6
ΔBSUV	35	-62.9	70.66	-81.1	-100.0	320.3
ΔAMTV	28	-73.4	102.90	-100.0	-100.0	438.3
ΔATLG	28	-68.7	149.15	-100.0	-100.0	691.0
ΔASUV	28	-88.8	26.53	-100.0	-100.0	26.5
HSUVmax1	98	10.5	6.56	9.3	2.2	31.3
TMTV1	98	39.9	72.69	18.3	0.8	631.3
TTLG1	98	166.9	248.94	83.6	1.4	1556.8
TMTV2	35	8.7	25.07	3.5	0.0	148.2
TTLG2	35	21.5	83.30	5.9	0.0	497.6
ΔTMTV	35	-67.8	45.02	-82.1	-100.0	117.4
ΔTTLG	35	-74.2	69.16	-95.7	-100.0	279.6

(continued)

		N	%
Estrogen receptor			
	Yes	60	65.9
	No	31	34.1
Progesterone receptor			
	Yes	53	58.9
	No	37	41.1
HER2			
	Yes	37	41.6
	No	52	58.4
E-cadherin			
	Yes	51	91.1
	No	5	8.9
Tumor location			
	Left	46	47
	Right	52	53
Molecular subtype			
	Luminal a	18	20.2
	Luminal b	46	51.7
	Triple negative	13	14.6
	HER2 enriched	12	13.5
pCR			
	Yes	27	27.5
	No	71	72.5

vior of the tumor by measuring the SUVmax before and after NAC [18]. Initial studies with PET/CT were performed using SUVmax. Baseline SUVmax failed to predict pCR and could not reach a cut-off value [19, 20]. Another study with luminal B patients reported that median BSUVmaxl value did not exhibit a significant difference between the patients who achieved and did not achieve pCR (P: 0.13) [21]. Our study findings support the current literature; there was no statistically significant association between pCR and metabolic parameters in baseline PET/CT.

Humber et al. (2015) observed a strong correlation between the SUVmax of the residual tumor in PET2 and pathological response; mean PET2 SUVmax was 3.2±1.6 in the non-pCR group and 2.3±1.1 in the pCR group (P: 0.003). The cut-off value of SUV2 was found to be 2.1 using ROC analysis (AUC: 0.73, P: 0.003) [22] .Groheux et al. (2013) reported a weak correlation between the SUV of PET2 and pCR[19]. In our study, the median SUVmax in PET2 was 1.03 in the pCR group while it was 3.03 in the non-pCR group, and the difference was statistically significant. The cut-off for BSUVmax in PET2 was 1.58, with an AUC of 0.767.

In a recent study performed on 54 triple-negative patients using ΔSUVmax, ΔSUVmax, ΔSUVmean, and ΔSUVpeak parameters were found to have high AUC in predicting pCR (0.86, 0.85, and 0.80, respectively) [15]. Another study with locally advanced patients showed the sensitivity and specificity of ΔBSUVmax in predicting pCR to be 70% and 88%, respectively, when the cut-off was 84% (AUC: 0.856, P<0.0001) [23]. In the study with luminal B patients, the sensitivity and specificity of ΔBSUVmax in predicting pCR to be 85.7% and 100%, respectively, when the cut-off was 69% (AUC: 0.900, P<0.0001) [21]. In another study, where the cut-off for ΔSUVmax was found to be 38%, the researchers reported the AUC to be 0.73, the sensitivity 62.2%, and

Table 2. *Comparison of ^{18}F-FDG PET/CT and immunohistochemistry parameters in patients with and without pCR.*

	No pCR					pCR					
	N	**Mean**	**Med**	**Min**	**Max**	**N**	**Mean**	**Med**	**Min**	**Max**	**P**
Age	71	52.46	49.00	26	91	27	45.82	42.5	29	74	.014*
Kİ67	42	27.02	20.00	0	80	18	26.11	20.0	0	95	.708**
B1MTV	71	24.47	11.92	1.300	163.000	27	18.65	7.0	.823	183.00	.084**
B1TLG	71	119.68	53.49	1.97	1249.92	27	127.39	32.9	1.44	1500.0	.311**
B1SUV	71	9.63	8.47	.10	29.35	27	10.57	7.9	2.08	26.68	.682*
A1MTV	71	19.86	4.38	0.1	604.000	27	9.65	2.9	0.1	87.140	.238**
A1TLG	71	47.26	9.20	0.2	541.51	27	39.22	7.5	0.2	310.93	.702**
A1SUV	71	5.44	3.62	1.2	27.52	27	6.99	3.4	1.3	31.25	.864**
B2MTV	26	8.51	3.82	0.00	102.00	9	2.16	0.0	0.00	8.93	.025**
B2TLG	26	20.57	6.71	0.00	328.68	9	4.21	0.0	0.00	20.54	.011**
B2SUV	26	3.03	2.10	0.00	9.85	9	1.03	0.0	0.00	5.16	.010**
A2MTV	26	2.14	0.00	0.000	46.190	9	.130	0.0	0.000	1.170	.281**
A2TLG	26	6.89	0.00	0.00	168.96	9	.15	0.0	0.00	1.43	.330**
A2SUV	26	.58	0.00	0.00	7.17	9	.18	0.0	0.00	1.64	.38**3
ΔBMTV	26	-54.44	-75.02	-100.00	71.20	9	-92.91	-100.0	-100.00	-54.63	.003**
ΔBTLG	26	-66.23	-89.59	-100.00	279.62	9	-98.12	-100.0	-100.00	-87.56	.001**
ΔBSUV	26	-52.82	-67.50	-100.00	320.26	9	-92.10	-100.0	-100.00	-68.95	.001**

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ΔAMTV	21	-65.19	-100.0	-100.00	438.34	7	-98.01	-100.0	-100.00	-86.09	.335**
ΔATLG	21	-58.34	-100.0	-100.00	691.01	7	-99.64	-100.0	-100.00	-97.48	.302**
ΔASUV	21	-85.43	-100.0	-100.00	26.46	7	-99.00	-100.0	-100.00	-93.07	.244**
HSUVmax1	71	10.48	9.80	2.32	29.35	27	10.66	8.0	2.2	31.25	.777**
TMTV1	71	44.34	21.04	1.56	631.30	27	28.30	13.6	.82	191.41	.049**
TTLG1	71	166.94	101.21	2.11	1425.44	27	166.62	47.3	1.44	1556.77	.194**
TMTV2	26	10.66	3.94	0.00	148.19	9	2.30	0.0	0.00	10.10	.022**
TTLG2	26	27.46	6.71	0.00	497.64	9	4.37	0.0	0.00	20.54	.011**
ΔTMTV	26	-60.01	-78.84	-100.00	117.41	9	-93.02	-100.0	-100.00	-54.63	.003**
ΔTTLG	26	-65.92	-92.97	-100.00	279.62	9	-98.17	-100.0	-100.00	-87.56	.001**
Estrogen receptor	n		%		n		%				
	Negative	18		27.2		13		52			0.25[c]
	Positive	48		72.7		12		48			
Progesterone receptor											
	Negative	23		34.8		14		58.3			0.40 [c]
	Positive	43		65.2		10		41.7			

(continued)

HER2						
	Negative	43	66.1	9	37.5	0.14 [c]
	Positive	22	33.9	15	62.5	
E-cadherin						
	Negative	5	12.5	0	0	0.172 [c]
	Positive	35	87.5	16	100	
Molecular subtype						
	Luminal a	16	24.6	2	5.8	0.290 [c]
	Luminal b	33	50.7	13	38.2	
	Triple negative	9	13.8	14	41.1	
	HER2 enriched	7	10.7	5	14.7	
Tumor location						
	Left	38	53.5	14	51.8	0.587 [c]
	Right	33	46.5	13	48.2	

**: independent t test, **: mann-whitney u test c:pearson chi square test, HSuvmax: Highest SUVmax, med: median, min: minimum, max: maximum*

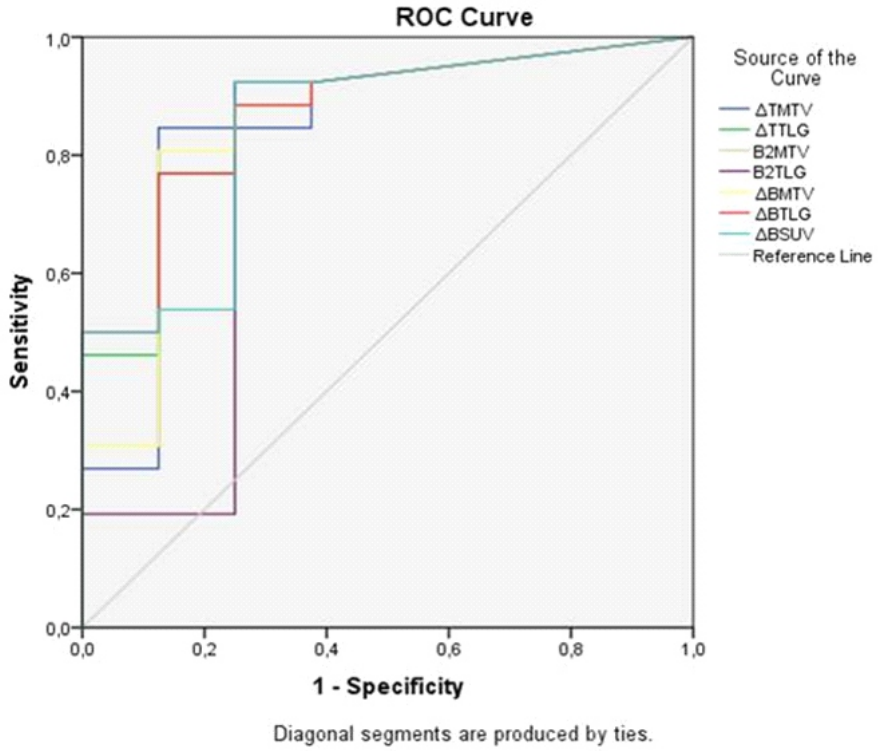

Figure 2. ROC curves for detecting pCR.

Table 3. *Cut-off, sensitivity, and specificity values of variables in predicting pCR.*

Test Result Variable(s)	Area	Std. Errora	P	Sensitivity	Specificity
ΔTMTV<-94.01	.846	.089	.003	84.6	87.5
ΔTTLG<-97.36	.870	.072	.002	76.9	75
B2MTV<1.75	.764	.123	.026	73.1	75
B2TLG<2.11	.764	.123	.026	76.9	75
B2SUV<1.58	.767	.121	.024	76.9	75
ΔBMTV<-93.67	.851	.085	.003	80.8	75
ΔBTLG<-97.22	.870	.069	.002	80.8	75
ΔBSUV<-84.99	.846	.079	.003	76.9	75

Table 4. *pCR univariate logistic regression analysis.*

	B	p	OR	95% CI for EXP(B)	
				Lower	Upper
Tumor location (1)	-.002	.996	.998	.415	2.399
Estrogen receptor	-1.061	.029	.346	.133	.898
Progesterone receptor	-.962	.049	.382	.147	.994
HER2	1.181	.017	3.258	1.231	8.620
E-cadherin	20.420	.999	738.502.817.090	.000	.
Molecular subtype	.455	.079	1.576	.949	2.616
Kİ67	-.002	.880	.998	.973	1.024
ΔTMTVc	-2.944	.011	.053	.005	.508
ΔTTLGc	-2.457	.008	.086	.014	.527
B2MTVc	-2.097	.024	.123	.020	.758
B2SUVc	-2.457	.008	.086	.014	.527
B2TLGc	-2.457	.008	.086	.014	.527
ΔBMTVc	-3.381	.004	.034	.003	.343
ΔBTLGc	-2.688	.004	.068	.011	.432
ΔBSUVc	-2.688	.004	.068	.011	.432

Table 5. *Multivariate logistic regression analysis.*

	B	P	OR	95% CI for EXP(B)	
				Lower	Upper
ΔTMTVc	-49.277	.999	.000	.000	
ΔTTLGc	18.083	1.000	71.352.960.519	.000	.
B2MTVc	-9.402	1.000	.000	.000	.
B2SUVc	33.097	1.000	236.506.238.861.399.000	.000	.
B2TLGc	-39.386	1.000	.000	.000	.
ΔBTLGc	9.240	1.000	10.305.424	.000	.
ΔBSUVc	-49.937	.999	.000	.000	.
Estrogen receptor	-52.839	.996	.000	.000	.
Progesterone receptor	34.756	.997	1.242.504.119.121.890.000	.000	.
HER2	17.102	.997	26.751.950.657	.000	.

the specificity 77.8% [19]. In a study that included triple negative BC patients, the median ΔBSUVmax was significantly higher in patients who achieved pCR than patients who did not (87.7% vs. 75.2%, respectively, P: 0.02) [24]. On the other hand, another study failed to exhibit a significant correlation between ΔSUVmax and pCR [25]. The cut-off value for ΔBSUVmax was 84.99% in our study (AUC: 0.846, sensitivity: 76.9%, specificity: 75%).

Recently, volumetric PET/CT parameters have quickly come into routine practice. Two different studies have reported that TLG, which is volumetric PET/CT parameter, is superior to SUVmax in evaluating treatment response [19, 26].

In their study with 47 patients, El-Gaid et al. (2022) calculated the AUC to be 0.846 and P value to be 0.003 for ΔBSUVmax in predicting pCR and found its sensitivity and specificity to be 92.7% and 83.3%, respectively. For ΔBTLG, AUC was 0.801 and P value was 0.018 with a sensitivity of 82.9% and specificity of 83.3%. However, the researcher could not demonstrate a cut-off value for ΔBMTV [27]. In the current study, we found both the ΔBTLG (AUC: 0.87, P: 0.002, 80.8% sensitivity, and 75% specificity) and the ΔBMTV (AUC: 0.851, P: 0.003, 76.9% sensitivity, and 75% specificity) [27]. Im et al. (2013) found that ΔMTV (cut-off <93.2%, AUC: 0.886) and ΔTLG (cut-off <95.8%, AUC: 0.886) parameters predict pCR with a higher AUC than ΔSUVmax (cut-off <63.6%, AUC: 0.743) [28]. In a study by Lee et al. (2014), the sensitivity, specificity, and accuracy of ΔSUVmax were 80.0%, 96.8%, and 94.4%, respectively, when the cut-off was 75.4%. With a 95.9% cut-off, the sensitivity, specificity, and accuracy of ΔMTV were 100%, 80.6%, and 83.3%, respectively. When the cut-off for ΔTLG was taken as 97.9%, its sensitivity, specificity, and accuracy were also 100%, 80.6%, and 83.3%, respectively [29]. In their study comparing EORTC and PERCIST criteria, Lian et al. (2020) observed a higher sensitivity and specificity with PERCIST than EORTC. SUVpeak, SUVmax, TLG, and MTV predicted pCR with 70.7%, 60.0%, 75.0%, and 71.4% accuracy rates, respectively, with the highest accuracy rates being of TLG and MTV [7]. In contrast to the studies mentioned above, Humbert et al. (2015) could not demonstrate a significant correlation between various tumor volume parameters (MTV1, MTV2, ΔMTV, TLG1, TLG2 and ΔTLG) and pCR[22]. In our study the cut-off for ΔTMTV was 94.01% with AUC: 0.844 and the cut-off for ΔTTLG was 97.36% with AUC: 0.870. The parameter with the highest sensitivity and specificity in predicting pCR was ΔTMTV, 84.6% and 87.5%, respectively.

A recent study by Abd El-Gaid et al. (2022) could not demonstrate a cut-off value for ΔMTV in predicting pCR in patients with locally advanced breast cancer using ROC analysis. However, the researchers could determine the area under the curve with high sensitivity and specificity using breast ΔSUVmax, lymph node ΔTLG (cut-off: 86.6%), and lymph node ΔMTV (cut-off: 55%) parameters [27]. On the contrary, we observed no correlation between pCR and lymph node PET parameters.

In a study evaluating 435 patients receiving NAC, Ki-67 index, along with PET/CT parameters was shown to be higher in patients who achieved pCR than patients who did not (59.53% vs 47.62%, P<0.001) [30]. Humbert et al. (2015) found that pCR was correlated with the status of hormone receptors (P: 0.04) [22]. In our study, estrogen and progesterone receptor positivity was observed to be higher in the non-pCR group, while HER2 positivity was significantly higher in the pCR group. Also, univariate analyses showed that estrogen receptor positivity, progesterone receptor positivity, and HER2 positivity were significant in predicting pCR (OR: 0.346, 0.382, 3.248, respectively).

The major limitations of our study are its retrospective nature, the limited number patients with post-treatment PET/CT imaging, and being unable to include lymphovascular invasion, perineural invasion, and grade data, which could be predictive for pCR, in the statistical analyses, because they could not be reached in the pathology reports of the patients.

In conclusion, we determined that metabolic and volumetric PET/CT parameters, the rates of their change, and metabolic response during NAC may be important variables in predicting pCR in patients with breast cancer.

The authors declare that they have no conflicts of interest.

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