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Original Article

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Are Changes in PET/CT SUV_{max} Associated with Pathologic Complete Response in Breast Cancer Patients Receiving Neoadjuvant Therapy?

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ABSTRACT

Aim: Non-invasive predictors of pathologic complete response (pCR) after neoadjuvant chemotherapy (NAC) are needed in breast cancer (BC). We evaluated whether serial fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) maximum standardized uptake value (SUV_{max}) metrics [baseline, preoperative, and the percentage change of SUV_{max} (ΔSUV_{max} %)] and complete metabolic response (CMR) are associated with pCR.

Methods: This retrospective single-center cohort included patients treated with NAC followed by surgery who underwent paired baseline and preoperative ^{18}F-FDG PET/CT. Primary tumor SUV_{max} was recorded on both scans, ΔSUV_{max} % was calculated, and CMR was defined as complete resolution of pathologic FDG uptake on the preoperative scan. pCR was defined as ypT0/is ypN0.

Results: Fifty-six patients were included (median age, 51.5 years). Subtypes were HR^+/HER2- (50%), $HER2^+$ (30.3%), and triple-negative BC (TNBC) (19.7%). Overall, pCR occurred in 25% (14/56) and CMR occurred in 35.7% (20/56). Baseline SUV_{max} differed by subtype (highest in TNBC), and pCR rates varied significantly (lowest in luminal, highest in HER2+). Compared with the non-pCR group, the pCR group had lower preoperative SUV_{max} (0.68 vs 4.33; p=0.001) and higher ΔSUV_{max}% (95.89% vs 54.10%; p=0.001). In univariate logistic regression, lower preoperative SUV_{max} [odds ratio (OR): 0.64; p=0.04]., higher ΔSUV_{max}% (OR: 1.06 per 1% increase; p=0.01), and CMR (OR: 6.75; p=0.01) were associated with pCR.

Conclusion: In this retrospective cohort, end-of-NAC ^{18}F-FDG PET/CT findings—especially a low preoperative SUV_{max} and CMR—were associated with a higher likelihood of pCR while ΔSUV_{max}% contributed incremental predictive signal.

Keywords: Breast cancer, complete metabolic response, neoadjuvant therapy, pathologic complete response, PET-CT

Introduction

Neoadjuvant chemotherapy (NAC) has become a key component of modern breast cancer (BC) treatment, offering tumor downstaging and providing an *in vivo* assessment of treatment sensitivity [1]. In this setting, achieving a pathologic complete response (pCR) is strongly associated with improved outcomes, especially in triple-negative BC (TNBC) and human epidermal growth factor receptor 2 (HER2)-positive BC [2]. Thus, regulatory authorities (drug agencies) have accepted pCR as an endpoint that can support accelerated approval of new therapies in high-risk early-stage BC, underscoring the clinical and translational (bench-to-bedside) importance of pCR.

However, pCR can only be confirmed postoperatively, and there remains a practical need for non-invasive biomarkers that can predict the pathologic response during neoadjuvant treatment. Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) provides a quantitative measure of tumor metabolism, while PERCIST defines response based on uptake changes from baseline to follow-up imaging [3]. Prior studies suggest that declines in FDG uptake—often summarized by pre- to post-treatment

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changes in standardized uptake value (SUV) metrics [e.g., absolute or percent maximum SUV (SUV_{max}) reduction]—may help predict pCR [4,5]. Moreover, pooled evidence indicates that PET-defined metabolic response provides prognostic information beyond pCR, with interim and end-of-treatment PET response correlating with survival outcomes [6].

Although metabolic changes on PET/CT may help predict response to NAC, reported performance varies across studies, likely reflecting differences in patient populations, subtype distribution, treatment regimens, scan timing, and response definitions. To address the gap in real-world evidence with paired baseline and preoperative imaging, we conducted an exploratory single-center study to evaluate whether PET-derived SUV_{max} metrics are associated with pCR after NAC.

Methods

Study Design and Patients

This retrospective, single-center cohort study evaluated the association between serial ^{18}F-FDG PET/CT parameters and pCR in patients with BC treated with NAC. The analysis focused on patients who had paired baseline and preoperative ^{18}F-FDG PET/CT scan performed in routine practice to quantify treatment-related changes in tumor metabolic activity. Eligible patients were those who (i) were diagnosed with BC, (ii) were treated with NAC followed by definitive surgery, and (iii) underwent both a baseline PET/CT (prior to NAC) and a preoperative PET/CT (after completion of NAC and before surgery), with available clinicopathologic data. Patients with missing key imaging or pathology data, non-interpretable PET/CT studies or evidence of metastatic disease at baseline were excluded. Demographic and baseline clinicopathologic variables were abstracted from medical records and pathology reports. Tumors were categorized into subtypes consistent with the study tables: luminal (HR^+/HER2-), HER2 positive, and TNBC; (ER-/PR-/HER2-).

^{18}F-FDG PET/CT Acquisition and Image Analysis

All patients underwent whole-body ^{18}F-FDG PET/CT according to institutional clinical protocols. Patients fasted prior to tracer injection; serum glucose was assessed before imaging; PET acquisition was performed after an uptake period. PET images were reconstructed using standard corrections (attenuation, scatter, and decay) and reviewed on a dedicated workstation by experienced nuclear medicine physicians. For each scan, the primary tumor SUV_{max} was recorded. Percent change of SUV_{max} (ΔSUV_{max}) between baseline and preoperative scans was calculated as follows:

$$\Delta SUVmax\ (\%) = \frac{SUVmax_{baseline} - SUVmax_{preop}}{SUVmax_{baseline}} 100$$

A binary metabolic response variable was also defined as a complete metabolic response (CMR), indicating complete resolution of pathologic FDG uptake at the primary tumor site on the preoperative scan.

Pathologic Assessment and Study Endpoint

After completion of NAC, surgical specimens were evaluated by breast pathologists according to routine institutional standards. The primary endpoint was pCR, defined as no residual invasive carcinoma in the breast and in sampled axillary lymph nodes, while allowing residual *in situ* disease (ypT0/is ypN0), consistent with common definitions used in NAC trials.

This study was conducted in accordance with institutional and national ethical standards and the Declaration of Helsinki. Ethical approval was obtained from the Ankara University Faculty of Medicine Human Research Ethics Committee (approval no: İ09-644-23, date: 02.11.2023). Given the retrospective nature of the study, the ethics committee waived the requirement for written informed consent.

Statistical Analysis

Continuous variables were summarized using appropriate descriptive statistics. Comparisons of metabolic parameters across BC subtypes were performed using parametric or non-parametric tests, depending on the distributional assumptions; categorical variables were compared using the χ^2 test or Fisher's exact test. Associations between PET-derived variables (baseline SUV_{max}, preoperative SUV_{max}, ΔSUV_{max}%, and CMR) and pCR were explored using univariate logistic regression, reporting odds ratios (ORs) with 95% confidence intervals (CIs). Because of the limited sample size and relatively low number of pCR events, multivariable modeling was not emphasized, as any adjusted model would likely be underpowered and prone to overfitting. Two-sided p values <0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Fifty-six patients were included. The median age was 51.5 years (interquartile range 43.5-57.7). Most patients were postmenopausal (57.2%), had invasive ductal carcinoma, no special type (invasive ductal carcinoma/no special type) histology (92.8%), and presented with clinically node-positive disease (91.1%). Clinical stage was II in 60.7% of patients and III in 39.3%. The cohort comprised 50.0% luminal, 30.3% HER2-positive and 19.7% TNBC tumors (Table 1).

Baseline tumor metabolic activity differed significantly across tumor subtypes (p=0.001), with the highest SUV_{max} in TNBC and the lowest in luminal tumors (Table 2). In contrast, preoperative SUV_{max} and ΔSUV_{max} % did not differ significantly by subtype (p=0.71 and p=0.39, respectively). Overall, pCR was achieved in 25.0% of patients, and CMR was observed in 35.7% of patients. Response rates varied by subtype: pCR was lowest in luminal tumors (7.7%) and highest in HER2-positive disease (52.0%) (p=0.03). CMR rates were numerically higher in the luminal and HER2-positive subgroups than in TNBC, although the difference was not statistically significant (p=0.46) (Table 2). Notably, although CMR was relatively frequent in luminal tumors, the pCR rate remained low.

Table 1. Baseline clinicopathological characteristics of the study cohort (n=56)

Variables	n, %
Age, years (IQR)	51.5 (43.5-57.7)
Menopausal status	
Premenopausal	24 (42.8)
Postmenopausal	32 (57.2)
Histology	
IDC, NST	52 (92.8)
Other	4 (7.2)
cT	
T1-T2	37 (71.1)
T3-T4	15 (28.9)
cN	
Positive	51 (91.1)
Negative	5 (8.9)
Subtype	
Luminal	28 (50)
HER2- positive	17 (30.3)
TNBC	11 (19.7)
Grade	
2	35 (62.5)
3	21 (37.5)
Ki-67, %	
≤20	6 (12.2)
>20	43 (87.8)

IQR: Interquartile range, cT: Clinical tumor stage, cN: Clinical nodal stage, HER2: Human epidermal growth factor receptor 2, IDC, Invasive ductal carcinoma, NST: No special type, Ki-67, Proliferation index, TNBC: Triple-negative breast cancer

Overall, CMR was significantly associated with pCR; patients who achieved CMR had higher pCR rates than patients without CMR (Figure 1; p=0.004). Using pCR as the reference standard among patients with complete paired CMR and pCR data (n=51), CMR demonstrated 71.4% sensitivity, 73.0% specificity, 50.0% PPV, and 87.1% NPV for predicting pCR; performance varied by subtype, with particularly low PPV in luminal disease (Table 3).

Compared with patients without pCR, those with pCR showed a markedly greater metabolic decline (ΔSUV_{max} %, 95.89% vs 54.10%; p=0.001). In univariate logistic regression, lower preoperative SUV_{max} (OR: 0.64, 95% CI: 0.42-0.98; p=0.04), higher ΔSUV_{max} % (OR: 1.06, 95% CI: 1.01-1.11; p=0.01), and CMR (OR: 6.75, 95% CI: 1.71-26.50; p=0.01) were associated with higher odds of pCR, while baseline SUV_{max} showed a borderline association (OR: 1.09, 95% CI: 1.00-1.20; p=0.05) (Table 4).

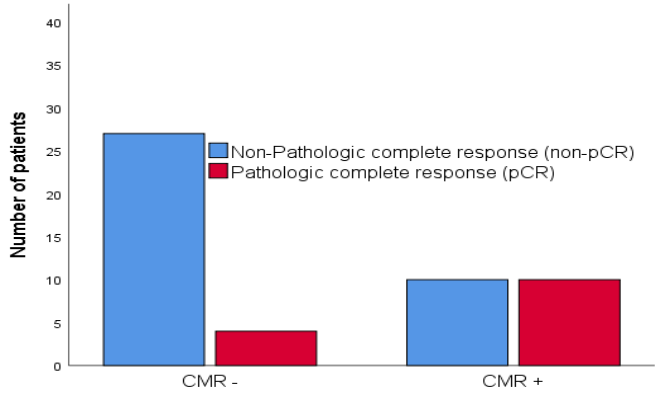

Figure 1. Relationship between CMR and pCR
CMR: complete metabolic response, pCR: Pathologic complete response

Table 2. Metabolic PET parameters and treatment response outcomes by breast cancer subtype

Variables	Luminal type (n=28)	HER2⁺ (n=17)	TNBC (n=11)	p value
Baseline SUV_{max}, (median)	7.99 (3-17.6)	13.53 (3.1-24)	17.84 (9.7-40.1)	0.001
Preoperative SUV_{max}, (median)	2.2 (0-8)	0 (0-13)	2.8 (0-25.6)	0.71
ΔSUV_{max}, %	63.9	77.4	47.6	0.39
pCR, %	2 (7.7)	9 (52)	3 (33)	0.03
CMR, %	10 (35)	8 (47)	2 (18)	0.46

P values were calculated using the Kruskal-Wallis test for continuous variables and the chi-square test or Fisher's exact test for categorical variables: as appropriate
HER2: Human epidermal growth factor receptor 2, TNBC: Triple-negative breast cancer, SUV_{max}: Maximum standardized uptake value, ΔSUV_{max}: Percent change of SUV_{max} (baseline to preoperative), pCR: Pathologic complete response, CMR: Complete metabolic response

Table 3. Diagnostic performance of CMR for predicting pCR

Group	n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Overall	51	71.4	73.0	50.0	87.1
Luminal	25	100.0	65.2	20.0	100.0
HER2-positive	17	66.7	75.0	75.0	66.7
TNBC	9	66.7	100.0	100.0	85.7

Overall analysis includes patients with complete paired CMR and pCR data (n=51)
PPV: Positive predictive value, NPV: Negative predictive value, TNBC: Triple-negative breast cancer, HER2: Human epidermal growth factor receptor 2, pCR: Pathologic complete response, CMR: Complete metabolic response, TNBC, Triple-negative breast cancer

Table 4. Univariate logistic regression analysis of FDG PET/CT metabolic parameters associated with pathologic complete response (pCR)

Variables		pCR	
	OR	95% CI	p
Baseline FDG/PET SUV_{max}	1.09	1.00-1.20	0.05
Preoperative FDG/PET SUV_{max}	0.64	0.42-0.98	0.04
ΔSUV_{max} %	1.06	1.01-1.11	0.01
CMR	6.75	1.71-26.50	0.01

ORs are expressed per 1-unit increase. For ΔSUV_{max} %: the OR reflects the change in odds of pCR per 1% increase in $\Delta SUVm_{ax}$ %. For clinical interpretability: ΔSUV_{max} % can also be modeled per 10% increase (ΔSUV_{max} %/10), %: Percentage
pCR: Pathologic complete response, OR: Odds ratio, CI: Confidence interval, FDG: Fluorodeoxyglucose, PET: Positron emission tomography, SUV_{max}: Maximum standardized uptake value, ΔSUV_{max}: Percent change of SUV_{max} (baseline to preoperative), CMR: Complete metabolic response

Discussion

In this retrospective single-center cohort with paired baseline and preoperative ^{18}F-FDG PET/CT, metabolic response measures were significantly associated with pCR. Compared with the non-pCR group, patients achieving pCR had a markedly lower preoperative SUV_{max} and a substantially greater metabolic decline (ΔSUV_{max}: 95.89% vs 54.10%; p=0.001). Achieving CMR was associated with higher odds of pCR, suggesting that marked suppression of FDG uptake after NAC may increase the likelihood of a pathologic response at surgery. This is consistent with prior studies showing that residual FDG uptake and the degree of metabolic decline can indicate chemosensitivity in BC, especially in aggressive subtypes [7,8].

Our data underscore the importance of end-of-NAC PET, consistent with Akimoto et al. [9], who reported that post-NAC SUV_{max} predicted pCR (and recurrence-free survival) in HER2-positive and TNBC, whereas baseline SUV_{max} and ΔSUV_{max} did not. In our cohort, however, metabolic change also carried a signal: compared with the non-pCR group, patients achieving pCR exhibited a greater metabolic decline, reflected by a significantly higher ΔSUV_{max} % (95.89% vs 54.10%; p=0.001). Conceptually, post-treatment uptake is closest to a "metabolic residual disease" readout and may therefore map more directly to residual viable tumor than baseline avidity or relative change alone-especially when cohorts include luminal disease where pCR is intrinsically uncommon [10]. Notably, we observed a subtype-dependent discordance between metabolic and pathologic responses, most evident in luminal tumors, where CMR occurred relatively frequently despite a low pCR rate. This likely reflects lower, heterogeneous FDG avidity and the possibility that microscopic residual invasive disease remains below PET detectability, underscoring that PET-defined CMR should be interpreted cautiously as a surrogate for pCR in luminal disease. Although absolute post-treatment SUV may be more informative in heterogeneous populations, several studies have shown that marked metabolic declines can also help identify responders [11]. In TNBC, Kiyoto et al. [12] reported that a ΔSUV_{max} cut-off of 81.3% provided meaningful discrimination for pCR (area under the curve ~0.79)-poor metabolic response consistently indicated non-pCR. Similarly, the multicenter Japanese study identified an optimal peak SUV normalized to lean body mass (SUL_{peak}) decrease of 84.3% for predicting pCR and showed that CMR and pCR were associated with longer PFS [13]. Overall, ΔSUV-based thresholds may be particularly informative in selected aggressive phenotypes and when implemented as pre-specified decision rules.

Our study focuses on pCR, but the broader evidence base supports the prognostic significance of end-of-NAC PET [14]. Emmering et al. [15] demonstrated that residual FDG uptake on preoperative PET was inversely associated with disease-free survival (DFS) (HR 4.09) and appeared superior to histopathology-based response grading in their dataset. More contemporary analyses reinforce this theme using quantitative cut-offs and node-focused assessment. García Vicente et al. [16] (n=132) found that end-of-treatment PET predicted nodal histopathologic response and that binary nodal assessment was associated with both overall survival (OS) and DFS; they also reported cut-offs for ΔSUV change at early and end timepoints and noted an end-of-treatment ΔSUV threshold linked to DFS. Taken together, these data support the biological plausibility of our finding that lower post-treatment SUV is associated with pCR, while also underscoring the heterogeneity in PET metrics across studies. Indeed, the "best" PET metric likely depends on subtype (luminal vs. $HER2^+$/TNBC), scan timing (interim vs end-of-NAC), and endpoint (pCR vs DFS/OS); accordingly, post-treatment SUV_{max} may perform best in $HER2^+$/TNBC cohorts, whereas ΔSUV-based cut-offs and PERCIST-defined CMR may be particularly informative in selected settings, such as TNBC. One possible explanation is that $HER2^+$ and triple-negative tumors are often more FDG-avid at baseline and may undergo more pronounced metabolic changes during neoadjuvant treatment, making post-treatment SUV_{max} and response-based metrics such as ΔSUV and PERCIST-defined CMR more informative in these settings. However, these observations should be interpreted cautiously, given the limited sample size and the exploratory nature of the subgroup analyses.

Study Limitations

This study has limitations typical of retrospective single-center analyses, including a modest sample size, potential selection bias (inclusion of only patients with paired PET/CT), and heterogeneity in systemic therapy regimens and in the timing of imaging relative to treatment and surgery. While

our study does not report long-term survival outcomes, pCR is widely regarded as a robust surrogate endpoint for prognosis in high-risk BC, particularly in the $HER2^+$ and TNBC subtypes. In addition, we used SUV_{max}-based metrics (rather than the PERCIST-preferred SUL_{peak}), which may increase susceptibility to noise. Nonetheless, SUV_{max} remains widely reported and clinically intuitive. The absence of statistically significant differences in CMR rates across subtypes should be interpreted cautiously because of the small number of cases in the TNBC subgroup. The study may have been underpowered to detect moderate subtype-specific differences in metabolic response. Finally, multivariable modeling may have been underpowered, and the observed associations—especially for categorical CMR—should be interpreted with appropriate caution.

Conclusion

Overall, our results support a practical and clinically intuitive message: very low residual uptake on preoperative PET/CT (and/or achievement of CMR) is associated with a higher likelihood of pCR, whereas substantial residual uptake suggests persistent viable disease. Taken together, these findings support end-of-NAC PET/CT as a pragmatic adjunct for response assessment, but not a substitute for surgical pathology-particularly in luminal disease.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ankara University Faculty of Medicine Human Research Ethics Committee (approval no: İ09-644-23, date: 02.11.2023).

Informed Consent: Given the retrospective nature of the study, the ethics committee waived the requirement for written informed consent.

Footnotes

Authorship Contributions

Concept: B.D., H.A.Y., Design: B.D., H.A.Y., A.D., Data Collection or Processing: B.D., Ç.S., Analysis or Interpretation: B.D., H.A.Y., Ç.S., A.D., Literature Search: B.D., Writing: B.D., A.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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