The Early and Late Predictive Value of ^{18}F-FAPI-42 PET/MRI for Neoadjuvant Therapy Response in Breast Cancer: A Prospective Study

Sihua Liu, MD[1]; Yuying Zhang, MD[2]; Yuanyuan Yang, MM[2]; Duanyang Zhai, MD[1]; Xiaying Kuang, MD[1]; Yawei Shi, MD[1]; Liang Yu, MD[1]; Yunjian Zhang, MD[1]; Nan Shao, MD[1]; Xiangsong Zhang, MD[2]; Ying Lin, MD, PhD[1]

[1]Breast Disease Center, [2]Department of Nuclear Medicine, The First Affiliated Hospital, Sun Yat-sen University, No.58, Zhong Shan Er Lu, Guangzhou 510080, China.

Introduction

Early response prediction during neoadjuvant therapy (NAT) for breast cancer (BC) enables response-guided precision treatment.

Imaging-based post-NAT evaluation may reduce dependence on pathological complete response (pCR) confirmation and facilitate surgical de-escalation.

Fibroblast activation protein inhibitor (FAPI) PET/MRI represents a promising molecular imaging modality targeting the tumor microenvironment.

This study aimed to evaluate the efficacy of ^{18}F-FAPI-42 PET/MRI for early and late prediction of pCR to NAT in BC.

Methods and Materials

Forty-five consecutive patients with newly diagnosed BC who met the criteria for NAT were prospectively enrolled and underwent ^{18}F-FAPI-42 PET/MRI before treatment initiation (PET1), after two cycles of NAT (PET2), and before post-NAT surgery (PET3).

SUVmax was measured in the primary tumor and metastatic lymph nodes (MLNs). The tumor-to-background ratio (TBR) was calculated as the lesion SUVmax divided by the SUVmean of contralateral normal breast tissue. The percentage changes in SUVmax and TBR from baseline were calculated after 2 NAT cycles (ΔSUVmax1 and ΔTBR1) and before surgery (ΔSUVmax2 and ΔTBR2).

Predictive performance of ^{18}F-FAPI uptake was analyzed by receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC). The Youden index determined optimal cutoffs.

Results

18 patients (40%) achieved pCR, while 27 patients (60%) exhibited residual disease. Among 40 patients with MLNs, 24 (60%) attained axillary pCR.

By molecular subtypes, pCR rates were 21.1% (4/19) in HR+/HER2-, 52.4% (11/21) in HER2-enriched, and 60.0% (3/5) in TNBC cases, respectively.

The ΔSUVmax of primary tumors (r = 0.636; $P < 0.001$) and MLNs (r = 0.560; $P < 0.001$) were significantly correlated between PET2 and PET3. Patients achieving pCR demonstrated significantly lower absolute SUVmax and TBR values at both PET2 and PET3 compared to non-pCR cases ($P < 0.05$, Figure 1). Furthermore, greater reductions in both SUVmax and TBR at any time point were strongly associated with pCR ($P < 0.05$).

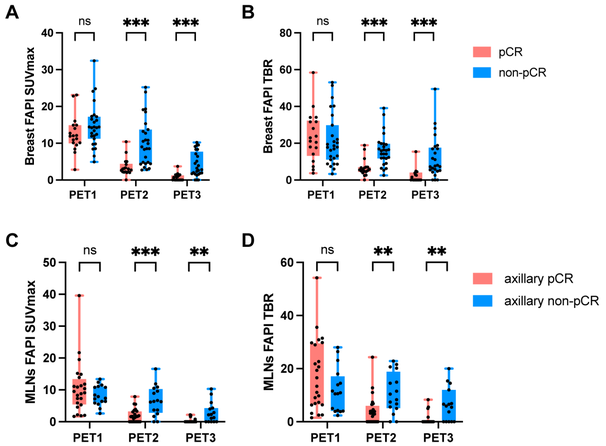


Figure 1. Comparison in (**A**) SUVmax and (**B**) TBR of the primary tumor, and (**C**) SUVmax and (**D**) TBR of metastatic lymph nodes according to pathologic response (pCR vs. non-pCR) at PET1, PET2, and PET3. $^{**}P < 0.01$. $^{***}P < 0.001$.

Results

In predicting pCR, the ΔSUVmax1 (AUC = 0.792; sensitivity = 55.6%; specificity = 92.6%) and ΔTBR1 (AUC = 0.774; sensitivity = 61.1%; specificity = 100%) of the primary tumor had the highest specificity; the TBR3 (AUC = 0.855; sensitivity = 94.1%; specificity = 76.0%) and ΔTBR2 (AUC = 0.815; sensitivity = 94.1%; specificity = 72.0%) of the primary tumor showed the highest sensitivity (Table 1). The percentage change in SUVmax of the primary tumor showed better predictive efficacy than the change in tumor diameter (Figure 2).

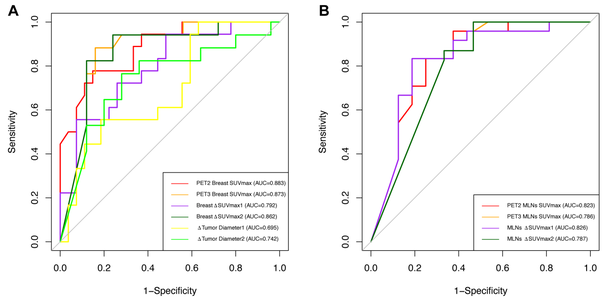


Figure 2. ROC curves for prediction of pathological response based on the SUVmax of (**A**) the primary tumor and (**B**) metastatic lymph nodes.

Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
SUVmax2	77.8	85.2	77.8	85.2	0.883
SUVmax3	88.2	84.0	78.9	91.3	0.873
ΔSUVmax1	55.6	92.6	83.3	75.8	0.792
ΔSUVmax2	82.4	88.0	82.4	88.0	0.862
TBR2	83.3	85.2	78.9	88.5	0.856
TBR3	94.1	76.0	72.7	95.0	0.855
ΔTBR1	61.1	100	100	79.4	0.774
ΔTBR2	94.1	72.0	69.6	94.7	0.851

Table 1. Diagnostic accuracies for predicting pCR based on ^{18}F-FAPI uptake cutoff values of the primary tumor in the entire cohort.

Results

In the HR+/HER2- subgroup, parameters derived from PET2 (SUVmax2 and TBR2; AUC = 0.950; sensitivity = 100%; specificity = 86.7%) and all parameters derived from PET3 (SUVmax3, ΔSUVmax2, TBR3, and ΔTBR2; AUC = 1.000; sensitivity = 100%; specificity = 100%) of the primary tumor showed optimal AUC in predicting pCR; both the ΔSUVmax1 and ΔSUVmax2 of MLNs achieved 100% sensitivity for axillary pCR prediction.

Variable	Primary tumor			Metastatic lymph nodes		
	Sensitivity (%)	Specificity (%)	AUC	Sensitivity (%)	Specificity (%)	AUC
SUVmax2	100	86.7	0.950	85.7	81.8	0.844
SUVmax3	100	100	1.000	100	70	0.825
ΔSUVmax1	50	100	0.750	100	72.7	0.935
ΔSUVmax2	100	100	1.000	100	70	0.825
TBR2	100	86.7	0.950	57.1	90.9	0.688
TBR3	100	100	1.000	100	70	0.825
ΔTBR1	50	100	0.633	71.4	100	0.818
ΔTBR2	100	100	1.000	100	70	0.825

Table 2. Diagnostic accuracies for predicting pCR based on ^{18}F-FAPI uptake cutoff values of the primary tumor and metastatic lymph nodes in the subgroup of HR+/HER2-.

Conclusions

Early-phase ^{18}F-FAPI-42 PET/MRI demonstrates high specificity in predicting pCR, which may facilitate the selection of alternative NAT regimens for non-pCR cases.

Preoperative ^{18}F-FAPI-42 PET/MRI shows high sensitivity for pCR prediction, which can identify potential candidates for surgery de-escalation.

^{18}F-FAPI-42 PET/MRI exhibits excellent potential for both early and late-phase prediction of pathological response to NAT in HR+/HER2- BC.

Contact

Sihua Liu
Breast Disease Center, The First Affiliated Hospital, Sun Yat-sen University
Email: liush368@mail.sysu.edu.cn

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