

# Prediction of breast cancer recurrence using lymph node metabolic and volumetric parameters from $^{18}\text{F}$ -FDG PET/CT in operable triple-negative breast cancer

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## Abstract

**Purpose** Triple-negative breast cancer has a poor prognosis. We evaluated several metabolic and volumetric parameters from preoperative  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) in the prognosis of triple-negative breast cancer and compared them with current clinicopathologic parameters.

**Methods** A total of 228 patients with triple-negative breast cancer (mean age  $47.0 \pm 10.8$  years, all women) who had undergone preoperative PET/CT were included. The PET/CT metabolic parameters evaluated included maximum, peak, and mean standardized uptake values (SUVmax, SUVpeak, and SUVmean, respectively). The volumetric parameters evaluated included metabolic tumor volume (MTV) and total lesion glycolysis (TLG). Metabolic and volumetric parameters were evaluated separately for tumor (T) and lymph nodes (N). The prognostic value of these parameters was compared with that of clinicopathologic parameters.

**Results** All lymph node metabolic and volumetric parameters showed significant differences between patients with and without recurrence. However, tumor metabolic and volumetric parameters showed no significant differences. In a univariate survival analysis, all lymph node metabolic and volumetric parameters (SUVmax-N, SUVpeak-N, SUVmean-N, MTV-N, and TLG-N; all  $P < 0.001$ ), T stage ( $P = 0.010$ ), N stage ( $P < 0.001$ ), and TNM stage ( $P < 0.001$ ) were significant parameters. In a multivariate survival analysis, SUVmax-N ( $P = 0.005$ ), MTV ( $P = 0.008$ ), and TLG ( $P = 0.006$ ) with TNM stage (all  $P < 0.001$ ) were significant parameters.

**Conclusions** Lymph node metabolic and volumetric parameters were significant predictors of recurrence in patients with triple-negative breast cancer after surgery. Lymph node metabolic and volumetric parameters were useful parameters for evaluating prognosis in patients with triple-negative breast cancer by  $^{18}\text{F}$ -FDG PET/CT, rather than tumor parameters.

**Keywords** Breast cancer · Prognosis · Standardized uptake value · Metabolic tumor volume · Total lesion glycolysis

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## Introduction

Breast cancer is the most common female malignancy and second leading cause of cancer-related death in women [1]. Breast cancer is recognized as a heterogeneous disease with a high degree of diversity in response to therapy and in patterns of metastasis, which are important for patient outcome and prognosis [2]. Among several types of breast cancer, triple-negative breast cancer is a heterogeneous group of tumors characterized by a poor prognosis [3]. Stratification of patients with triple-negative cancer in relation to prognosis would be highly desired, because patients with a better prognosis could benefit from appropriately targeted treatment(s) [4].

Currently,  $^{18}\text{F}$ -Fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) is widely used in clinical evaluation of cancers. In particular,  $^{18}\text{F}$ -FDG PET/CT has been used for breast cancer characterization, staging, predicting treatment response, and detecting recurrence [5–7]. It has also been reported to be effective in predicting tumor recurrence in breast cancer using visual and metabolic parameters, including standardized uptake values (SUV) [8, 9]. Previous studies have shown that tumor uptake of  $^{18}\text{F}$ -FDG in triple-negative breast cancer is significantly higher than in other phenotypes [10–12].

$^{18}\text{F}$ -FDG PET/CT volumetric parameters are also being increasingly studied because they can reflect tumor burden as well as metabolic activity. Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) from  $^{18}\text{F}$ -FDG PET/CT are useful parameters, particularly for prognosis prediction and treatment response monitoring [13, 14]. These volumetric parameters have also been shown to be valuable in the prognosis of breast cancer, but previous studies were performed in patients with phenotypically heterogeneous various cancers [15, 16]. As far as we are aware, there has been no  $^{18}\text{F}$ -FDG PET/CT study to determine the prognostic value of volumetric parameters in patients with triple-negative breast cancer. Most previous  $^{18}\text{F}$ -FDG PET/CT studies in breast cancer were limited to tumor characteristics. However, lymph node uptake of  $^{18}\text{F}$ -FDG can also have prognostic value [17]. Therefore, we hypothesized that volumetric parameters relating to the tumor and the lymph nodes could also have prognostic value.

In this study, we investigated the value of  $^{18}\text{F}$ -FDG PET/CT volumetric parameters in predicting recurrence of surgically resected triple-negative breast cancer. Tumor and lymph node volumetric parameters were compared with metabolic parameters, and their prognostic value was compared with that of clinicopathologic prognostic factors.

## Materials and methods

### Patients

From January 2008 to December 2013, 5,231 breast cancer patients underwent  $^{18}\text{F}$ -FDG PET/CT in our institution. Among these patients, those who underwent surgery for their breast cancer were retrospectively enrolled in the current study with the following inclusion criteria:

1. Pathologically confirmed triple-negative infiltrating ductal carcinoma [estrogen receptor (ER) negative/progesterone receptor (PR) negative/human epidermal growth factor receptor-2 (HER2) negative]
2. Preoperative  $^{18}\text{F}$ -FDG PET/CT performed within 6 months without any previous treatment

3. Measurable tumor (longest diameter >1 cm on CT) with FDG avidity (maximum SUV >2.5)
4. No evidence of distant metastasis before breast cancer surgery
5. Follow-up after breast cancer surgery of more than 36 months in case of no recurrence

Patients were routinely checked using imaging studies including mammography, ultrasonography, contrast-enhanced CT, and/or bone scintigraphy every 4–6 months for 5 years after surgery, and every year thereafter. Imaging studies were also performed when tumor markers (routine check-up at intervals of 4–6 months) increased or other suspicious symptoms or signs presented. Recurrence of a lesion was confirmed based on the follow-up imaging studies. The study design was approved by the Institutional Review Board (IRB) of our institution and informed consent was waived.

A total of 228 patients with triple-negative breast cancer were included in the study (all women, mean age  $47.0 \pm 10.8$  years). Tumor pathology was infiltrating ductal carcinoma in all patients, and patients were followed up at our institution after surgery (mean follow-up  $55.9 \pm 15.9$  months). Tumor recurrence was found in 72 patients (31.6%) 14.8  $\pm$  9.4 months after surgery. Patient TNM stages were I–III (I 12.7%, II 55.3%, III 32.0%). Patients underwent breast cancer surgery in accordance with their surgeon's decision (breast-conserving surgery in 72.8%, modified radical mastectomy in 6.6%, total mastectomy in 20.6%). Chemotherapy was performed in 96.9% of patients, and radiation therapy in 78.9% of patients in accordance with their oncologist's decision (Table 1).

### $^{18}\text{F}$ -FDG PET/CT protocol

After fasting for at least 6 h,  $^{18}\text{F}$ -FDG (5.18 MBq/kg) was injected intravenously, and imaging was performed 1 h later using a hybrid PET/CT scanner (Biograph 40 Truepoint; Siemens Healthcare, Knoxville, TN, USA). CT images were acquired from the skull base to the upper thigh area for the attenuation map and lesion localization (50 mA, 120 kVp, 5-mm section width, 4 mm collimation). PET images of the same area were acquired after the CT scans in three-dimensional mode for six or seven bed positions (1 min per bed position, 21.6 cm increments). Images were reconstructed on  $128 \times 128$  matrices using an iterative algorithm. The images were analyzed using a dedicated workstation and analysis software (Syngo.via, Siemens Healthcare, Knoxville, TN, USA).

### $^{18}\text{F}$ -FDG PET/CT image analysis

All of the following metabolic and volumetric PET/CT parameters were used to define a volume of interest (VOI) on the workstation. The VOI for metabolic and volumetric parameters was defined by nuclear medicine physicians to be large enough to

**Table 1** Baseline characteristics of the patients

Characteristic	Value
Number of patients	228
Gender, <i>n</i> (%)	
Female	228 (100.0)
Age (years), mean ± SD (range)	47.0 ± 10.8 (24.0–75.0)
Tumor pathology, <i>n</i> (%)	
Infiltrating ductal carcinoma	228 (100.0)
Tumor location, <i>n</i>	
Right	106
Left	122
Hormone receptor status, <i>n</i> (%)	
Triple-negative <sup>a</sup>	228 (100.0)
Follow-up after surgery (months), mean ± SD (range)	55.9 ± 15.9 (36.0–97.5)
Patients with recurrence, <i>n</i> (%)	72 (31.6)
Time from surgery to recurrence (months), mean ± SD (range)	14.8 ± 9.4 (2.2–47.4)
T stage, <i>n</i> (%)	
1	41 (18.0)
2	146 (64.0)
3	34 (14.9)
4	7 (3.1)
N stage, <i>n</i> (%)	
0	88 (38.6)
1	78 (34.2)
2	35 (15.4)
3	27 (11.8)
TNM stage, <i>n</i> (%)	
I	29 (12.7)
II	126 (55.3)
III	73 (32.0)
Operation, <i>n</i> (%)	
Breast-conserving surgery	166 (72.8)
Modified radical mastectomy	15 (6.6)
Total mastectomy	47 (20.6)
Chemotherapy, <i>n</i> (%)	
No	7 (3.1)
Yes	221 (96.9)
Radiation therapy, <i>n</i> (%)	
No	48 (21.1)
Yes	180 (78.9)

<sup>a</sup> ER–/PR–/HER2–

cover the lesions. Metabolic and volumetric parameters were evaluated separately for tumor (T) and lymph nodes (N). The VOI was defined on the breast area for the tumor, and on the axillary/supraclavicular area for the lymph nodes. An additional VOI was defined when internal mammary lymph node uptake was found. In this case, higher values for the metabolic parameters were selected by comparing the axillary/supraclavicular VOIs

with the internal mammary VOIs. For volumetric parameters, two axillary/supraclavicular and internal mammary VOIs were added (Fig. 1).

SUVs were calculated using the following equation:  $SUV = (\text{tissue radioactivity [Bq]/tissue weight [g]})/(\text{injected activity [Bq]/body weight [g]})$ . The metabolic parameters maximum SUV (SUV<sub>max</sub>), measured as the SUV of the pixel with the highest uptake, and peak SUV (SUV<sub>peak</sub>) and mean SUV (SUV<sub>mean</sub>), measured as the SUVs of the pixels with the peak uptake and mean uptake, respectively) were recorded. Volumetric parameters included MTV, estimated from VOI SUV isoactivity contours automatically drawn by setting a margin SUV threshold of 2.5, and TLG, calculated as  $SUV_{\text{mean}} \times MTV$ .

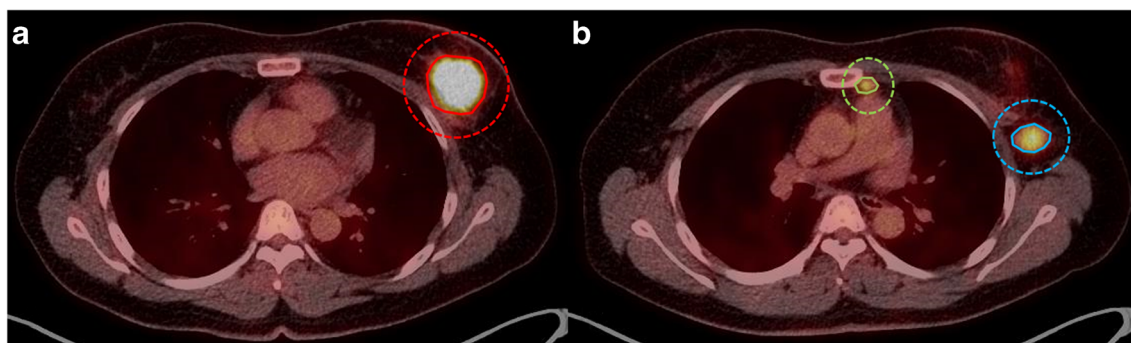
### Clinicopathologic parameters and pathologic evaluation

Clinicopathologic information was obtained from patient medical records. Age, tumor location, pathologic T stage, pathologic N stage, pathologic TNM stage, operation method, chemotherapy, and radiation therapy were included.

Histologic type and tumor grade based on the Elston-Ellis system were evaluated during routine histopathologic examination of surgical specimens [18]. The immunohistochemistry (IHC) parameters evaluated were the expression levels of ER, PR, and HER2. ER and PR expression levels were evaluated semiquantitatively as the percentages of cells with positive nuclear staining (range 0–100%). A 1% cut-off value was used for the expression of ER and PR [19]. Expression levels of HER2 were evaluated by combined IHC and/or fluorescent in situ hybridization (FISH). To assess HER2 expression by IHC, the following semiquantitative scoring system was used: 0 no membrane staining, 1+ weak and inhomogeneous membrane staining in some tumor cells, 2+ weak to moderate membrane staining in a large number of tumor cells, 3+ strong and homogeneous membrane staining in most tumor cells. A score of 2+ was considered equivocal and additional FISH analysis was conducted to confirm HER2 gene amplification. Either a score of 3+ indicating strong positive expression or HER2 gene amplification by FISH was classified as positive [20].

### Statistical analysis

Clinicopathologic and <sup>18</sup>F-FDG PET/CT parameters were compared between patients with and without recurrence using the chi-squared test for categorical data (Fisher's exact test for chemotherapy), and the independent samples Student's *t* test for continuous data. In survival analyses, optimal cut-off values for quantitative factors that maximized the significance in the survival analysis were determined using an algorithm [21]. Kaplan-Meier analysis and a log-rank test were performed to evaluate disease-free survival (DFS) according to the cut-off values applied. Finally, univariate and multivariate



**Fig. 1** Measurement of  $^{18}\text{F}$ -FDG PET/CT metabolic and volumetric parameters. **a** For tumor measurement, a volume-of-interest (VOI) was drawn (red dashed circle) to include the whole breast cancer and an isoactivity contour was automatically drawn (red solid line) by setting a margin SUV threshold of 2.5. **b** For lymph node (LN) measurements,

VOIs were drawn to include all metastatic axillary and supraclavicular LNs (blue dashed circle), and internal mammary LN metastases (green dashed circle). Similar to tumor measurements, an isoactivity contour was automatically drawn by setting a margin SUV threshold of 2.5 (blue and green solid lines, respectively)

Cox regression analyses were performed to assess the effect of clinicopathologic and PET/CT parameters, where  $P < 0.05$  was considered significant. All statistical analyses were performed using SPSS software, version 18.0 (SPSS Inc., Chicago, IL, USA) and MedCalc, version 12.2 (MedCalc Inc., Mariakerke, Belgium).

## Results

### Clinicopathologic parameters and recurrence

Among clinicopathologic parameters, T stage ( $P = 0.009$ ), N stage ( $P < 0.001$ ), and TNM stage ( $P < 0.001$ ) showed significant differences between patients with and without recurrence. However, patient age, tumor location, operative

method, chemotherapy, and radiation therapy showed no significant differences (Table 2).

### $^{18}\text{F}$ -FDG PET/CT parameters and recurrence

All the lymph node PET/CT metabolic and volumetric parameters showed significant differences between patients with and without recurrence (SUVmax-N, SUVpeak-N, SUVmean-N and MTV-N,  $P < 0.001$ ; TLG-N,  $P = 0.013$ ), whereas tumor metabolic and volumetric parameters showed no significant differences (Table 3).

### Univariate and multivariable analysis

In the univariate analysis, T stage ( $P = 0.010$ ), N stage ( $P < 0.001$ ), TNM stage ( $P < 0.001$ ), SUVmax-N

**Table 2** Comparison of clinicopathologic parameters according to recurrence after surgery in patients with triple-negative breast cancer

Parameter	Recurrence ( $n = 72$ )	No recurrence ( $n = 156$ )	$P$ value
Age (years), mean $\pm$ SD	46.5 $\pm$ 12.2	47.2 $\pm$ 10.1	0.659
Tumor location (right/left)	37/35	69/87	0.314
T stage			
1/2	52	135	0.009*
3/4	20	21	
N stage			
0/1	32	134	<0.001*
2/3	40	22	
TNM stage			
I/II	27	128	<0.001*
III	45	28	
Operation			
Breast-conserving surgery	47	119	0.083
Modified radical or total mastectomy	25	37	
Chemotherapy			
No	3	4	0.681
Yes	69	152	
Radiation therapy			
No	14	34	0.686
Yes	58	122	

\* $P < 0.05$

**Table 3** Comparison of  $^{18}\text{F}$ -FDG PET/CT parameters according to recurrence after surgery in patients with triple-negative breast cancer

Parameter	Recurrence ( <i>n</i> = 72)	No recurrence ( <i>n</i> = 156)	<i>P</i> value
SUVmax-T	12.2 ± 6.2	12.3 ± 7.3	0.859
SUVpeak-T	9.5 ± 5.2	9.4 ± 6.2	0.929
SUVmean-T	5.2 ± 1.8	5.2 ± 1.9	0.902
MTV-T (cm <sup>3</sup> )	33.8 ± 88.7	18.1 ± 35.1	0.151
TLG-T	203.1 ± 572.1	117.9 ± 227.8	0.109
SUVmax-N	7.1 ± 6.2	3.3 ± 5.0	<0.001*
SUVpeak-N	5.2 ± 4.7	2.5 ± 3.8	<0.001*
SUVmean-N	3.4 ± 1.9	2.1 ± 1.8	<0.001*
MTV-N (cm <sup>3</sup> )	12.5 ± 30.9	2.1 ± 8.8	<0.001*
TLG-N	68.5 ± 183.4	12.4 ± 58.9	0.013*

SUV standardized uptake value, MTV metabolic tumor volume, TLG total lesion glycolysis

\**P* < 0.05

(*P* < 0.001), SUVpeak-N (*P* < 0.001), SUVmean-N (*P* < 0.001), MTV-N (*P* < 0.001), and TLG-N (*P* < 0.001) were significant parameters. Among the clinicopathologic and PET/CT parameters, the volumetric parameters showed the highest hazard ratios (HR) (HR of MTV-N = 4.89, HR of TLG-N = 4.75). Among the metabolic parameters, SUVmax-N showed the highest HR (HR of SUVmax-N = 4.23) (Table 4 and Fig. 2).

For the multivariate analysis, TNM stage was selected from among clinicopathologic parameters as it showed a higher hazard ratio than both T stage and N stage, and interaction was found between them. In the multivariate analysis of SUVmax-N and TNM stage, SUVmax-N (HR 2.16, *P* = 0.005) and TNM stage (HR 1.97, *P* < 0.001) were the significant parameters. In the multivariate analysis of the volumetric parameters and TNM stage, MTV-N (HR 2.17, *P* = 0.008) and TLG-N (HR 2.20, *P* = 0.006) were significantly associated with TNM stage (HR 1.98 and 1.96, respectively; all *P* < 0.001; Table 5, Figs. 3 and 4).

**Table 4** Univariate analysis of significant clinicopathologic and  $^{18}\text{F}$ -FDG PET/CT parameters

Parameter	Hazard ratio (95% CI)	<i>P</i> value
T stage (3/4 vs. 1/2)	1.39 (1.08–1.80)	0.010*
N stage (2/3 vs. 0/1)	2.21 (1.75–2.79)	<0.001*
TNM stage (III vs. I/II)	2.24 (1.76–2.85)	<0.001*
SUVmax-N (>9.83 vs. ≤9.83)	4.23 (2.58–6.94)	<0.001*
SUVpeak-N (>3.73 vs. ≤3.73)	3.91 (2.45–6.22)	<0.001*
SUVmean-N (>2.42 vs. ≤2.42)	3.96 (2.41–6.50)	<0.001*
MTV-N (>11.04 cm <sup>3</sup> vs. ≤11.04 cm <sup>3</sup> )	4.89 (2.90–8.23)	<0.001*
TLG-N (>45.93 vs. ≤45.93)	4.75 (2.86–7.88)	<0.001*

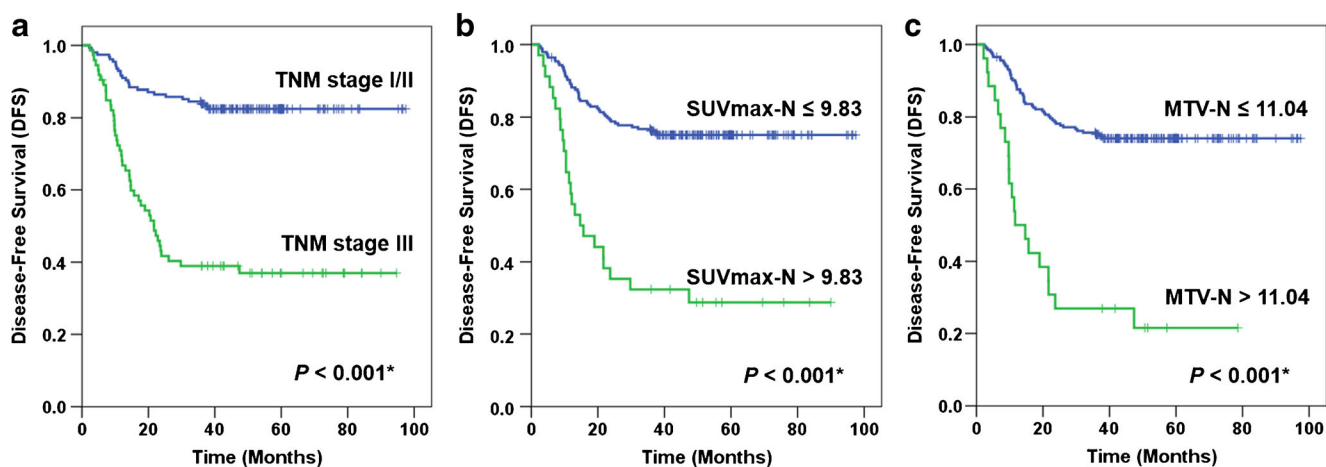
\**P* < 0.05

## Discussion

The results of the current study suggest that  $^{18}\text{F}$ -FDG PET/CT can provide effective prediction of recurrence in patients with surgically resected triple-negative breast cancer. Several  $^{18}\text{F}$ -FDG PET/CT and clinicopathologic parameters were compared, and lymph node metabolic and volumetric parameters along with TNM stage showed significant prognostic value. Thus,  $^{18}\text{F}$ -FDG PET/CT lymph node volumetric parameters (MTV-N and TLG-N) could be prognostic factors.

The main advantage of the current study is that the studied group was homogeneous. All patients had triple-negative infiltrating ductal carcinoma and had undergone breast cancer surgery. Furthermore, the usefulness of  $^{18}\text{F}$ -FDG PET/CT lymph node volumetric parameters has not been previously reported. Song et al. [17] investigated the prognostic value of  $^{18}\text{F}$ -FDG PET/CT lymph node metabolic parameters in patients with operable breast cancer, and found that they provided better prognostic value than tumor metabolic parameters. However, the study was limited to metabolic parameters and phenotypically heterogeneous tumors. Kim et al. [16] evaluated  $^{18}\text{F}$ -FDG PET/CT lymph node metabolic and volumetric parameters in patients with operable phenotypically heterogeneous breast cancer. Lymph node metabolic volumetric parameters showed significant correlations with the histologic grade of tumor, but showed no significant prognostic value. Our study showed that lymph node volumetric parameters have significant prognostic value and higher HRs than lymph node metabolic parameters in patients with operable triple-negative infiltrating ductal carcinoma.

$^{18}\text{F}$ -FDG PET/CT has been used for initial staging and stratification of various phenotypes of breast cancer. In particular,  $^{18}\text{F}$ -FDG PET/CT has been used to identify occult distant metastases and involvement of extra-axillary lymph nodes, which serve as critical indices in initial staging of breast cancer [22]. Previous studies investigating FDG uptake in breast



**Fig. 2** Kaplan-Meier analysis of clinical and <sup>18</sup>F-FDG PET/CT parameters. **a** Patients with TNM stage I/II showed significantly longer disease-free survival (DFS) than those with TNM stage III (5-year DFS 82.5% vs. 37.0%; *P* < 0.001). **b** Patients with low LN SUVmax (SUVmax-N ≤9.83) showed significantly longer DFS than those with

high SUVmax-N (>9.83; 5-year DFS 75.6% vs. 28.8%; *P* < 0.001). **c** Patients with low LN metabolic tumor volume (MTV-N ≤11.04) showed significantly longer DFS than those with high MTV-N (>11.04; 5-year DFS 75.1% vs. 21.5%; *P* < 0.001)

cancers have indicated that triple-negative breast cancer typically has higher metabolic activity than other phenotypes, and that FDG uptake could potentially be used to predict the outcome of neoadjuvant chemotherapy [23–25]. Recently, the correlation between <sup>18</sup>F-FDG uptake and prognostic markers in triple-negative breast cancer has been investigated [26]. The prognostic value of <sup>18</sup>F-FDG uptake was further studied in one histologic type of breast cancer to provide more specific information. Previous studies have also shown that tumor SUVmax predicts survival outcome in patients with luminal type [27] and triple-negative [28] breast cancer.

The current study demonstrated that volumetric parameters (MTV and TLG) have higher HRs than metabolic parameters (SUVmax, SUVpeak, and SUVmean). Among PET/CT parameters, metabolic parameters are the most commonly used for quantitative analysis in clinical situations [29]. However, there has been some debate as to the use of SUV. Heterogeneity of the tumor, partial volume effects, and the timing of SUV evaluation may limit the ability of SUV to represent the exact metabolism of the lesion and to reflect accurately the tumor characteristics [30]. In addition to metabolic parameters, volumetric parameters have

recently become widely used for analyzing FDG PET/CT in various cancers [31–33]. MTV is the volume of tissue that exhibits higher metabolism over a certain threshold, and TLG = MTV × SUVmean. Thus, while SUV reflects only metabolic activity of the tumor cell component, volumetric parameters reflect both metabolic activity and tumor burden from the whole tumor lesion. In previous studies, MTV has been shown to be a better prognostic factor in triple-negative metastatic breast cancer [13] and phenotypically heterogeneous metastatic breast cancer [16] than metabolic parameters. These results support those of our study showing that volumetric parameters have better prognostic value than metabolic parameters.

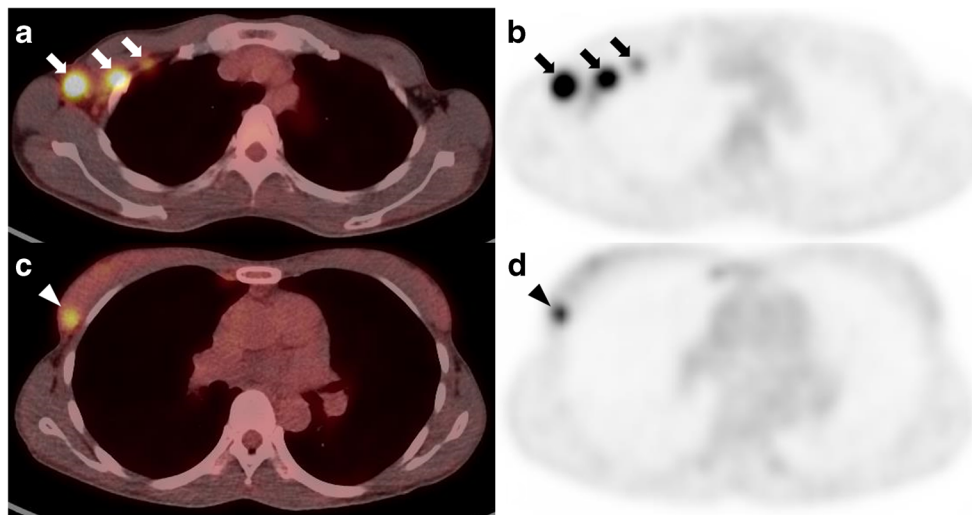
Lymph node metabolic and volumetric parameters showed significant prognostic value, whereas tumor parameters did not. Lymph node involvement in breast cancer is well known to be the most important prognostic factor [34]. Since triple-negative breast cancer is the most aggressive form [35], lymph node metastasis could be a more important factor for recurrence. We defined large VOIs for the evaluation of supraclavicular lymph nodes, and separate VOIs for more accurate evaluation of internal mammary lymph nodes. Including all possible metastatic lesions

**Table 5** Multivariate analysis of clinicopathologic and PET/CT parameters

Parameter	Model with SUVmax-N		Model with MTV-N		Model with TLG-N	
	Hazard ratio (95% CI)	<i>P</i> value	Hazard ratio (95% CI)	<i>P</i> value	Hazard ratio (95% CI)	<i>P</i> value
TNM stage (III vs. I/II)	1.97 (1.52–2.56)	<0.001*	1.98 (1.51–2.58)	<0.001*	1.96 (1.50–2.56)	<0.001*
SUVmax-N (>9.83 vs. ≤9.83)	2.16 (1.26–3.71)	0.005*		N/A		N/A
MTV-N (>11.04 cm <sup>3</sup> vs. ≤11.04 cm <sup>3</sup> )		N/A	2.17 (1.22–3.86)	0.008*		N/A
TLG-N (>45.93 vs. ≤45.93)		N/A		N/A	2.20 (1.26–3.86)	0.006*

N/A not assessed

\**P* < 0.05



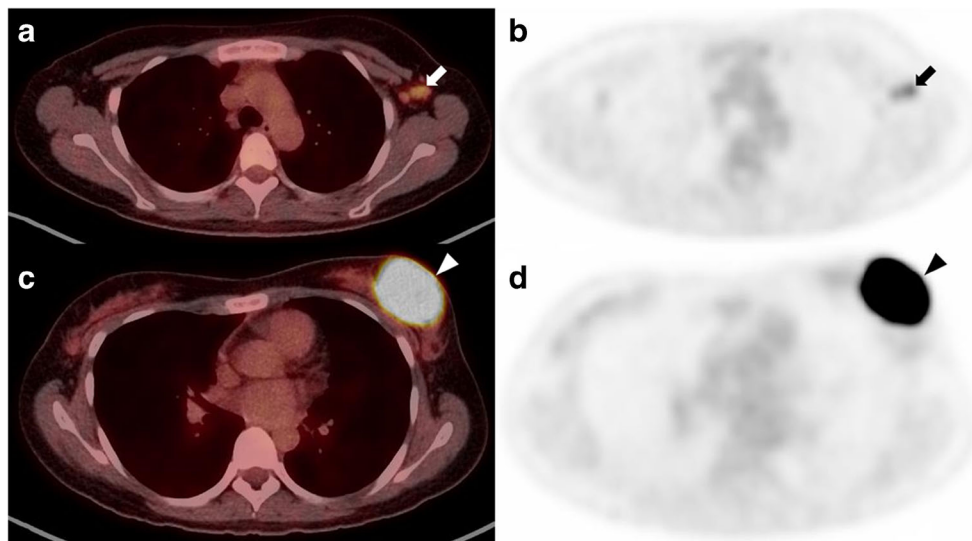
**Fig. 3** Preoperative PET/CT imaging in a 35-year-old woman with stage III triple-negative breast cancer as an example of recurrence prediction using  $^{18}\text{F}$ -FDG PET/CT lymph node (LN) metabolic and volumetric parameters. **a, b** Transaxial PET/CT and PET images of the LNs show significantly increased uptake (SUVmax-N 14.29, MTV-N 30.60  $\text{cm}^3$ ,

TLG-N 153.92). **c, d** However, transaxial PET/CT and PET images of the tumor show only moderately increased uptake (SUVmax-T 5.81, MTV-T 1.19  $\text{cm}^3$ , TLG-T 4.14). The patient had tumor recurrence in the brain pons 9 months after breast cancer surgery

provides more exact evaluation of the lymph nodes. Recent studies have strongly indicated that high  $^{18}\text{F}$ -FDG uptake by lymph nodes predicts a worse outcome in breast cancer [17], and head and neck cancer [36]. The current study outcomes are consistent with lymph node parameters showing a poor prognosis in triple-negative breast cancer.

The current study had several limitations. First, this was a retrospective study and the study protocol was not strictly controlled. There was some variation in the intervals between  $^{18}\text{F}$ -

FDG PET/CT acquisition and breast cancer surgery, which may have led to bias may not have been a critical factor. The status of other mutations, such as epidermal growth factor receptor, which could have influence FDG uptake was not studied. Second, combined chemotherapy and radiation therapy could have interfered with evaluation of the results. Finally, follow-up was relatively short. Patient follow-up was more than 36 months with a mean 55.9 months. A larger scale study with a longer follow-up is required to confirm our results.



**Fig. 4** Preoperative PET/CT imaging in a 24-year-old woman with stage III triple-negative breast cancer as an example of prediction of no recurrence using  $^{18}\text{F}$ -FDG PET/CT lymph node (LN) metabolic and volumetric parameters. **a, b** Transaxial PET/CT and PET images of the LNs show mildly increased uptake (SUVmax-N 2.54, MTV-N 0.82  $\text{cm}^3$ ,

TLG-N 2.41). **c, d** However, transaxial PET/CT and PET images of the tumor show significantly increased uptake (SUVmax-T 39.29, MTV-T 53.87  $\text{cm}^3$ , TLG-T 846.30). The patient had no tumor recurrence 42 months after breast cancer surgery

## Conclusion

$^{18}\text{F}$ -FDG PET/CT volumetric lymph node parameters are effective predictors of recurrence in patients with surgically resected triple-negative breast cancer. We expect that prediction of recurrence in triple-negative breast cancer can be optimized using lymph node metabolic/volumetric parameters and TNM stage, which will assist in the choice of therapeutic strategies.

## Compliance with ethical standards

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**Conflicts of interest** None.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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